Diagnostic Strategies In Pelvic Floor Disorders

A thesis by

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SUPERVISORS

My supervisors during this research period were as follows:

- **Mr Emile Tan**, consultant colorectal and pelvic floor surgeon
- **Mr Christos Kontovounisios**, consultant colorectal surgeon
- **Professor Paris Tekkis,** consultant colorectal surgeon

DECLARATION OF ORIGINALITY

The work in this thesis represents my own, and all other materials used for the purposes of discussion have been fully referenced.

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LIST OF CONTRIBUTIONS

The various statistical analyses performed throughout this thesis were undertaken by myself with supervision and support from both Emile Tan and Constantinos Simillis.

The interpretation of magnetic resonance defecography was undertaken by Nasir Khan, consultant radiologist, Emile Tan and myself. I was trained in the interpretation of MR defecography by Nasir Khan and underwent a supervised training period which included interpretation of approximately 50 scans before performing interpretation unsupervised.

Anorectal manometry and endoanal ultrasound was undertaken as part of a one-stop pelvic floor clinic either by or under the close supervision of Emile Tan. I was trained in

performing and interpreting anorectal manometry by Emile Tan, and had a six month period of supervision prior being able to undertake this test unsupervised.

Data collation and interpretation was carried out predominantly by myself, however Paul McLean aided with data collection for chapter 8 regarding the handsewn versus stapled anastomoses patients, and Clarence Yen was invaluable in collating and interpreting data relating to obstetric anal sphincter injuries, the results of which are detailed in chapter 7.

LIST OF PUBLICATIONS ASSOCIATED WITH THIS THESIS

Anorectal Manometry versus patient reported outcome measures as a predictor of maximal treatment for faecal incontinence Ramage L, Qiu S, Yeap Z, Simillis C, Kontnvounisios C, Tekkis P, Tan E. *Annals of Coloproctology 2019. [In Press]*

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Can we correlate pelvic floor dysfunction severity on MR defecography with patient-reported symptom severity? Ramage L, Georgiou P, Qiu S, McLean P, Khan N, Kontnvounisios C, Tekkis P, Tan E Updates Surg. 2017 Dec 19. doi: 10.1007/s13304-017-0506-0. [Epub ahead of print]

Does a missed obstetric anal sphincter injury at time of delivery affect short-term functional outcome? Ramage L, Yen C, Qiu S, Simillis C, Kontovounisios C, Tan E, Tekkis P. Ann R Coll Surg Engl. 2017 Sep 15:1-7. doi: 10.1308/rcsann.2017.0140.

Functional and quality of life outcomes following obstetric anal sphincter injury (OASI): does the grade of injury affect outcomes? Ramage L, Yen C, Qiu S, Simillis C, Kontovounisios C, Tekkis P, Tan E. Int Urogynecol J. 2017 May 18. doi: 10.1007/s00192-017-3334-3.

Functional outcomes with handsewn versus stapled anastomoses in the treatment of ultralow rectal cancer. Ramage L, Mclean P, Simillis C, Qiu S, Kontovounisios C, Tan E, Tekkis P. Updates Surg. 2018 Jan 8. doi: 10.1007/s13304-017-0507-z.

ABSTRACT

Introduction:

Management of pelvic floor disorders is undertaken within tertiary-level referral centres. However, the majority of patients do not require surgery. This thesis sets out to identify who is most likely to require surgery versus who could be initially managed in a primary care setting.

Methods:

Patient reported outcome measure (PROM) tools and investigatory data collated prospectively was explored alongside maximal treatment interventions. Additionally, MR-defecography (MRD) results were analysed in a cohort of patients with symptoms of obstructed defecation (ODS). Specific patient populations forming a large proportion of those requiring surgery were explored separately: patients with obstetric anal sphincter injury (OASI), and patients who had undergone surgery for ultralow rectal cancer with either a handsewn or stapled anastomosis.

Results:

276 patients with faecal incontinence (FI) and 129 patients with ODS were explored. 17.39% of those with FI and 20.93% with ODS ultimately required surgery. The majority of patients required only Biofeedback. The FI domain of the BBUSQ and several domains of the SF-36 were fair predictors of the need for surgery in FI sufferers. On anorectal manometry, only the squeeze endurance increment was predictive of the need for surgery in patients with FI. There was no demonstrable relationship between the PROMS or MRD and the requirement for surgery in ODS sufferers. Patients with a missed OASI had worse function at initial follow-up. At early follow-up no differences were found between different OASI grades. Patients with a handsewn coloanal anastomosis had worse function than those with a stapled anastomosis.

Conclusion:

There needs to be a move towards more community-based care in patients presenting with pelvic floor dysfunction to ease the burden on tertiary-level services with

development of an integrated care pathway which streamlines referrals based on the likelihood for the need for more invasive treatment strategies.

LIST OF ABBREVIATIONS

AI	Anal incontinence
ACPGBI	Association of Coloproctologists of Great Britain & Ireland
APER	Abdominoperineal excision of the rectum
ARA	Anorectal angle
ARM	Anorectal manometry
ASCRS	American Society of Colorectal Surgeons
AUC	Area under the curve
BBUSQ	Birmingham Bowel, Bladder & Urinary Symptom Questionnaire
BF	Biofeedback
BMI	Body mass index
BP	Body pain
CAA	Coloanal anastomosis
CCD	Colpo-cysto-defecography
CD	Conventional defecography
CI	Confidence interval
CM	Centimeters
CNS	Central nervous system
CRC	Colorectal cancer
CS	Costantinos Simillis
CVA	Cerebrovascular accident
CY	Clarence Yen
DFS	Disease free survival
DRE	Digital rectal examination
EAS	External anal sphincter
ECCD	Entero-colpo-cysto-defecography
ELAPE	Extralevator abdominal perineal excision
EMG	Electromyography
ET	Emile Tan
EUS	Endoanal ultrasound
FDD	Functional defecatory disorder
FGID	Functional gastrointestinal disorder
FN	False negatives

FP	False Positives
FSFI	Female Sexual Function Index
FI	Faecal incontinence
FIQL	Faecal Incontinence Quality of Life
GH	General Health
HDARM	High definition anorectal manometry
HMO	H-line, M-line, Organ descent
HPZ	High pressure zone
HRARM	High resolution anorectal manometry
IAS	Internal anal sphincter
IBD	Inflammatory bowel disease
IBS	Irritable bowel syndrome
ICP	Integrated care pathway
IPAA	Ileal pouch-anal anastomosis
IPG	Implantable pulse generator
ISR	Intersphincteric resection
k	Kappa
LARS	Low anterior resection syndrome
LOREC	Low rectal cancer development programme
LR	Lisa Ramage
MCD	Middle compartment descent
MDT	Multidisciplinary team
MH	Mental health
MPL	Mid pubic line
MR	Magnetic resonance
MRD	Magnetic resonance defecography
MRI	Magnetic resonance imaging
MSHQ	Male Sexual Health Questionnaire
MSPI	Mean squeeze pressure increment
mSV	Milliseverts
MTV	Maximum tolerated volume
NK	Nasir Khan
NHS	National Health Service

NICE	National Institute of Clinical Excellence
NRES	National Research Ethics Committee
OASI	Obstetric anal sphincter injury
ODS	Obstructed defecation syndrome
OR	Odds ratio
PCL	Pubococcygeal line
PD	Perineal descent
PF	Physical function
PDFI	Pelvic floor Distress Inventory
PFIQ	Pelvic Floor Impact Questionnaire
PISQ	Pelvic organ prolapse/urinary Incontinence Sexual Questionnaire
PME	Partial mesorectal excision
POP	Pelvic organ prolapse
POPQ	Pelvic Organ Prolapse Quantification
PROM	Patient reported outcome measure
PRISMA	Preferred Reporting Information for Systematic reviews and Meta-Analyses
PRS	Puborectalis syndrome
QoL	Quality of life
RAIR	Rectoanal inhibitory reflex
RCOG	Royal College of Obstetricians & Gynaecologists
RCT	Randomised controlled trial
RE	Role: emotional
RI	Rectal intussusception
ROC	Receiver operator characteristic
RP	Resting pressure
RP	Role: physical
SE	Squeeze endurance
SF	Social function
SF36	Short form 36
SI	Squeeze increment
SNS	Sacral nerve stimulation
SP	Squeeze pressure
STARR	Stapled transanal rectal resection

TAI	Transanal irrigation
TME	Total mesorectal excision
TN	True negatives
TP	True positives
TSE	Turbo spin echo
TV	Threshold volume
TVL	Total vaginal length
UC	Ulcerative colitis
UH	Urethral hypermobility
UK	United Kingdom
UV	Urge volume
VMR	Ventral mesh rectopexy
VT	Vitality
WIS	Wexner Incontinence score

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Part 1: Introduction and background

CHAPTER 1: INTRODUCTION

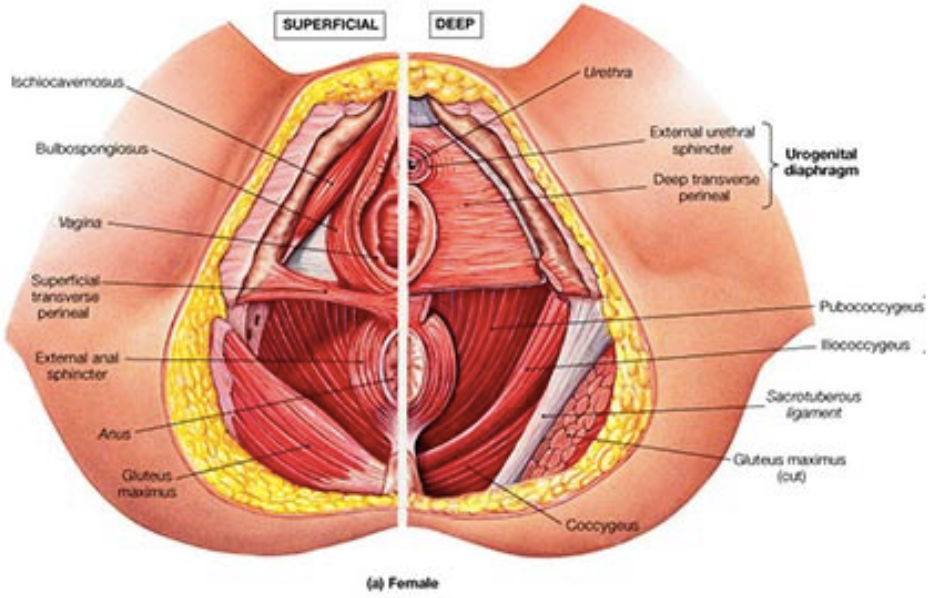
1.1 Overview of the pelvic floor anatomy

Anatomy of the pelvic floor

The pelvic floor is simply described as an inverted bowl shaped structure containing a hiatus for the urethra, vagina in females, and the rectum (Figure 1). It comprises a number of layers including the endopelvic fascia, muscular levator plate, urogenital diaphragm and superficial muscles such as the superficial transverse perineii. The endopelvic fascia acts as a supportive structure for the contents of the pelvic floor. The predominant muscle within this bowl-shaped levator plate is the levator ani. The levator ani muscle complex is further subdivided into a number of named components: pubococcygeus, ileococcygeus and puborectalis. The levator ani arises from the sidewalls of the pubis and ischial spine and overlying fascia[1]. It comprises predominantly of a broad thin muscle layer, which provides support to the pelvic cavity. Its fibres pass posteriorly to attach at its lateral edges to either side of the coccyx, and more medially they unite to form the anococcygeal raphe in the midline, which lies between the posterior border to the anus and the coccyx. Some fibres also blend with the anal sphincter complex, and in males a portion of its anterior fibres also blend with the prostate gland. The puborectalis portion of the levator ani forms a sling that hooks around the rectum, and is an important mechanism in the maintenance of bowel continence.

Also contributing to the pelvic floor diaphragm is the coccygeus muscle. The subdivisions of the levator ani described above refer to the origins and insertions of each portion, however this has little to no bearing in clinical practice[1]. Puboccocygeus is further subdivided onto separate parts that are named in relation to the pelvic viscera of which it is related to: pubovaginalis, puboanalis, puborectalis, puboprostaticus and puboperinealis. Nerve supply to the pelvic floor diaphragm is via the pudendal nerve, perineal nerve and the inferior rectal nerve[2].

Figure 1.1: Anatomy of female pelvic floor showing superficial and deep layers[3]



When considering pelvic anatomy externally, the perineum comprises of two areas: the anterior urogenital triangle, and the posterior anal triangle. The urogenital triangle contains within it the urethral meatus and vaginal orifice in females in addition to the external female genitalia. It also contains the ischiocavernosus and bulbospongiosus muscles in both males and females. The posterior anal triangle contains the external anal sphincter, the anus itself, and also the ischioanal fossae which lie on either side of the anus and permit distension of the anal canal during defecation[2].

It is important that the perineal body is discussed within this brief overview of pelvic floor anatomy, as this structure is vital in maintaining support and integrity of the pelvic floor, especially in females, where it can be damaged during childbirth, leading to later problems with genitourinary organ prolapse. The perineal body is a pyramidal-shaped fibrous condensation contributed to by a number of structures. It is situated at the junction of the urogenital triangle and anal triangle, between the bulb of the penis and anus in males, and between the vagina and anus in females. A number of structures contribute to it, including levator ani, the external anal sphincter, bulbospongiosus

muscle, fibres from the external urinary sphincter and the deep transverse perineal muscles[1].

Blood supply and nerve supply

The major nerve and blood supply to the perineum is the pudendal nerve (formed from 2-4th sacral nerve roots) and the internal pudendal artery, which is the terminal branch of the internal iliac artery. The pudendal nerve runs into the pelvis and along the lateral wall of the ischiorectal fossa in Alcocks canal[4]. It provides motor supply to the majority of muscles forming the pelvic floor, in addition to the external anal sphincter. It also carries sensory fibres from the external genitalia. The pudendal nerve is clinically important as it can be prone to neuropathy secondary to childbirth or chronic constipation and straining, and act as a contributor to the aetiology of faecal incontinence[2].

When considering pelvic floor anatomy clinically and for the purposes of this thesis, it is divided into distinct compartments: with females having three distinct compartments: anterior, middle and posterior, and males having only two (anterior and posterior). The gross structure of each compartment is covered below, with specific emphasis centred on the posterior compartment[5].

Anatomy of the anterior and middle compartment

The urinary bladder lies within the anterior compartment of the pelvic floor, just posterior to the pubic symphysis. It is relatively free within the extraperitoneal tissues, with the exception at its neck, where it is supported by the puboprostatic ligaments in males and the pubovesical ligaments in females. At the neck of the bladder, the urethra runs caudally to pass through the prostate in males and then through the external urethral sphincter and to the external urethral orifice at the tip of the vesicles. Also within the anterior compartment in males lie the seminal vesicles[1].

In females, the urethra is much shorter, at approximately 4cm long. It passes from the bladder posteriorly and inferiorly to the pubic symphysis[2].

Within the middle compartment of the pelvic floor in females lies the uterus, cervix and vagina. The vagina passes through the urogenital diaphragm and communicates with the cervix at its upper end. The angulation of the cervix at the top of the vagina creates the

anterior and posterior vaginal fornices. The posterior fornix is the deepest part, and is closely related to the rectouterine pouch, or Pouch of Douglas, which is created by a peritoneal fold between the uterus and rectum in females. The non-pregnant uterus, which is usually an anteverted structure, tends to have its main body mass overlying the superior aspect of the bladder[5].

Anatomy of the rectum

The rectum is a continuation of the sigmoid colon, commencing at the level of the third sacral verterbra. In clinical practice, it is defined as the proximal 15cm above the anal canal[5]. The large bowel has an inner circular muscular layer, with the outer longitudinal muscle layer condensed into three longitudinal strips, known as taeniae coli. Just proximal to the rectosigmoid junction, these coalesce, initially to form two larger bands, which then becomes a continuous longitudinal muscle layer. The rectum is not anatomically straight; it follows the curvature of the sacrum and additionally has distinct bends within it. These form Houston's valves, which aid in the maintenance of continence. These appear as horizontal folds, two of which lie on the left and one on the right[4]. The rectum meets with the anal canal at the anorectal junction, which is angulated at around 94-114 degrees at rest. This degree of angularity is formed due to the presence of the puborectal sling, and is an important mechanism in the maintenance of bowel continence[6].

The peritoneum is initially in contact with the upper rectum in its anteromedial portion. In its middle third, only an anterior peritoneal covering remains, before the peritoneum is reflected onto the urinary bladder in males, forming a rectovesical pouch, and onto the uterus in females, which forms the pouch of Douglas[4].

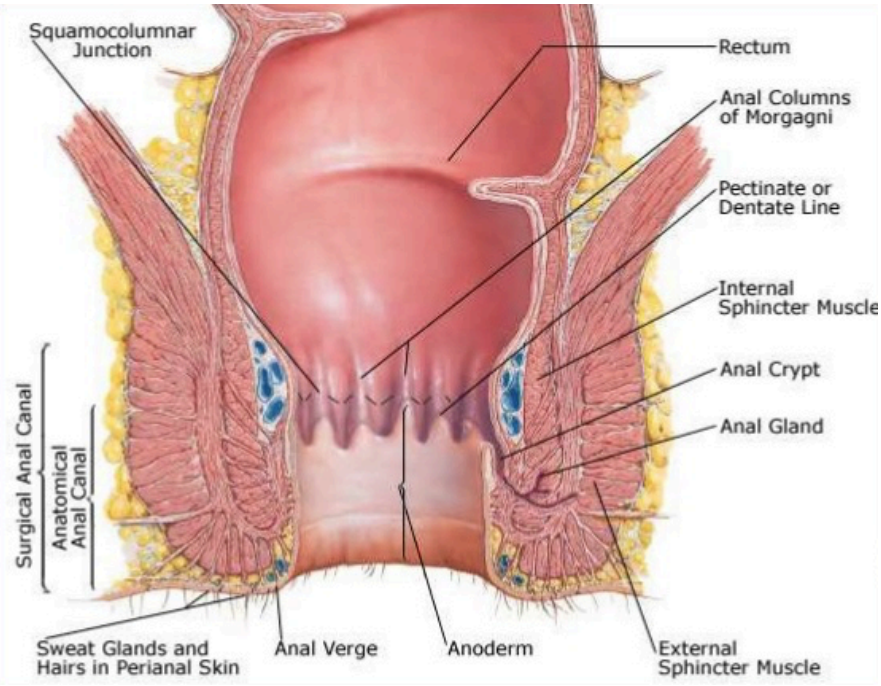
The lower third of the rectum and its anterior relation to the prostate/vagina is interjected by Denonvillier's fascia. Posteriorly, Waldeyer's fascia separates rectum from the lower sacral vertebrae and coccyx[7].

Blood supply is derived from the superior, middle and inferior rectal arteries. The superior rectal artery arises as a direct continuation of the inferior mesenteric artery. The middle rectal artery arises from the internal iliac artery, and the inferior rectal artery from the internal pudendal artery. Venous drainage is via superior haemorrhoidal arteries, which pass upwards before uniting to become superior rectal veins. Ultimately, drainage is to the inferior mesenteric vein, a part of the portal venous circulation[5].

Anatomy of the anal canal

The anal canal is a continuation of the rectum, which commences as the rectum passes through the urogenital diaphragm and ends at the anal verge. It can be thought of as a cylindrical canal, with multiple layers. It is approximately 5cm long, with its anterior wall slightly shorter than its posterior wall[1] (Figure 2).

Figure 2: Anatomy of the anal canal[8]



Anteriorly, there is an attachment to the perineal body in its middle third via dense connective tissue. The anal canal is composed of the following layers: anal mucosa, internal anal sphincter, the intersphincteric space, a longitudinal muscle layer and the outermost external anal sphincter[4]. Usually the internal and external anal sphincters are considered when discussing anal continence mechanisms; these two entities can be considered as separate structures working synergistically to help maintain anal continence through voluntary and autonomic control. Between these lie the intersphincteric space, which contains fat and a longitudinal muscle layer which is a continuation of the smooth muscle longitudinal layer of the rectum[5]. The puborectalis sling, discussed earlier, hooks around the anal canal, and maintains a degree of angulation between rectum and anal canal, and hence aids in continence. This muscle is distinct from the external anal sphincter. The external anal sphincter (EAS) is composed of skeletal muscle fibres which are arranged circumferentially around the anal canal[4]. The EAS is traditionally divided into three parts: deep, superficial and subcutaneous.

Surgically, these are indistinguishable from one another[4]. The EAS can be considered as an extension of the pelvic floor, with some fibres attaching to the coccyx posteriorly, and to the pelvic floor musculature anteriorly. The external anal sphincter is under voluntary control, and receives its nerve supply from the pudendal nerve[4].

Internally, the anal canal is composed of anal mucosa; the uppermost part of which is colonic mucosa; this is arranged in 6-10 folds known as anal columns. At the lower end of each column, just above the dentate line, are the anal valves; these contain anal glands which aid in lubrication of the anal canal[7].

The dentate line marks the watershed area between somatic and autonomic innervation, and is also the junction between hindgut and proctodeum.

1.2 Physiology of defecation and anal continence

Physiology of defecation

Colonic transit of waste products with simultaneous absorption of water and electrolytes occurs through propagating contractions of the muscular walls of the colon. Upon reaching the lower portion of the rectum, there is a reflex relaxation which occurs; this allows for sampling of rectal contents to occur. This stool sampling reflex allows for the conscious interpretation of whether rectal contents are gaseous/liquid or solid stool. This reflex is known as the rectoanal inhibitory reflex (RAIR).

The urge to defecate occurs after a critical distension volume is reached; this differs depending on patient factors such as rectal compliance and the presence of rectal wall inflammation, which will reduce rectal capacity and the ability to defer defecation. When socially appropriate, the person assumes usually a sitting or squatting position; the latter is actually the most beneficial position for defecation as it allows the anorectal angle to be straightened and is therefore allows for easier passage of stools through the anal canal[9].

Strong and coordinated contractions of the muscular wall of the rectum and sigmoid propel contents forward, at the same time, the puborectalis and external and internal anal sphincters relax. During this time, the person also aids in expelling of contents through valsava manoeuvres. Upon completion of defecation, the sphincters contract again, closing the anal canal.

Physiology of anal continence

The physiological anal canal can be defined as an area of high pressure on anorectal manometry. It is approximately 2.5cm in females, and 3cm in males. Anal continence relies on the interplay of a number of features, including the previously discussed puborectal sling, which forms the acute anorectal angle. Numerous previous EMG studies have demonstrated evidence of continuous tonicity of the puborectalis muscle and the EAS, as well as the IAS [10]. The EAS, also under voluntary control, can be squeezed at will, allowing the healthy individual to double the pressure within the high pressure zone [11]. The rectum acts as a reservoir, and can accommodate up to 400ml, therefore allowing deferral of defecation up until a socially appropriate time is attained[11].

1.3 Overview and prevalence of pelvic floor dysfunction

Although this thesis focuses primarily on disorders of the posterior compartment of the pelvic floor, it is prudent to give a brief overview of anterior and middle compartment dysfunction as part of this introductory chapter which will therefore allow for ease of discussion of later terminology and pathology, particularly within the MRD studies.

Anterior and middle compartments

Anterior and middle compartment dysfunction typically manifests secondary to prolapse of the organs. In simple terms, pelvic organ prolapse (POP) can be defined as a herniation of the anterior or posterior vaginal wall, vaginal apex or uterus down into the vaginal canal [12]. For the most part, pelvic organ prolapse of the urogenital apparatus affects women, with parity (in particular vaginal delivery) and the dwindling levels of oestrogen in later life representing a major cause of anatomical and functional decline. It should be noted that POP is a separate entity from posterior compartmental prolapse, which affects both males and females. POP is incredibly common, with studies quoting a detection rate at clinical examination of 40-60%[13]. There are numerous risk factors for the development of POP, including pregnancy, increased birth weight, spontaneous and instrumental vaginal delivery, young age at first delivery, advancing age, raised BMI, chronic constipation, previous hysterectomy, and chronic cough[14]. With an aging population, and growing concerns about obesity in today's society, significant POP rates

are likely to increase. These factors, in addition to the reduction in circulating oestrogen in postmenopausal women weaken the strength of the pelvic floor discussed in detail previously, leading to a symptomatic failure of the urogenital diaphragm with protrusion of intrapelvic contents below the pelvic floor, and in more severe cases externally.

Symptoms experienced depend on the exact nature and degree of prolapse. A significant number of patients are asymptomatic; this is especially the case in younger females with lesser severities of prolapse. A cystocoele, which occurs as a result of descent of the bladder itself may manifest as a dragging sensation within the pelvis, which typically worsens during the day, or symptoms of urge or stress urinary incontinence. Patients may also describe a sensation of a bulge within the vagina, or difficulty in fully emptying the bladder. Irritation symptoms are also common, with women experiencing urinary frequency and urgency[15]. The presence of POP and symptoms such as urinary incontinence may significantly impact on sexual function and QoL [16]. One study found that 72/105 (69%) of sexually active patients presenting with POP experienced dyspareunia during intercourse[15]. Middle compartment descent can manifest as either mild uterine descent or full uterovaginal prolapse. In those who have had a hysterectomy, then vaginal vault prolapse is common. Rectoceles are detected as a bulge in the posterior vaginal wall; higher prolapses may be secondary to enteroceles or sigmoidoceles.

The degree of POP can be evaluated clinically through the use of the internationally validated Pelvic Organ Prolapse Quantification System (POPQ)[17] (Table 1.1). This scoring system is relatively well established within the literature, however as with all functional disorders, there are different scoring systems used, which have slightly varied definitions in their staging of prolapse.

Table 1.1: Pelvic Organ Prolapse Quantification System

	Description
Stage 0	No prolapse evident, distal most part of all organs at least 3cm above level of hymen.
Stage1	Criteria for stage 0 not met, and the most distal prolapse is situated more than 1cm above the level of the hymen
Stage 2	The most distal prolapse is situated between 1cm above and 1cm below the level of the hymen
Stage 3	The most distal prolapse is more than 1cm below the level of the hymen but is no further than 2cm less than the total vaginal length (TVL-2cm)
Stage 4	Complete procidentia or vault eversion. The most distal prolapse protrudes to beyond TVL-2cm

Posterior compartment

As according to the guidelines published by the American College of Gastroenterology in 2014 [18], the major classifications of benign anorectal disorders are as follows:

1.1.1 defecatory disorders

1.1.2 faecal incontinence

1.1.3 proctalgia

1.1.4 anal fissure

1.1.5 haemorrhoids

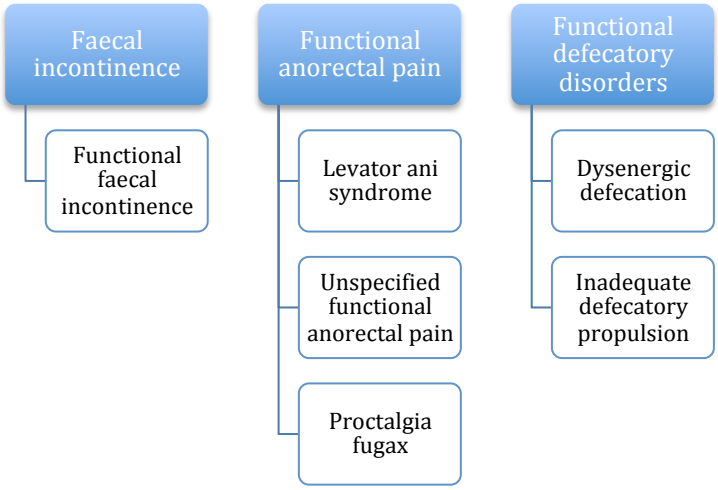
When considering posterior compartment pelvic floor dysfunction and for the most part of this thesis, our interest lies predominantly within the first two categories. Within these categories are a number of different diagnoses, which can be further classified as functional or structural.

A functional gastrointestinal disorder can simply be defined as one which has no underlying structural aetiology. Often there is a mixed picture, with evidence of combined structural and functional components. The diagnosis of a functional anorectal disorder requires the presence of specific features in addition to supplementary confirmatory radiological or manometric evidence.

The ROME III diagnostic criteria are based on symptom clusters which remain relatively constant across both clinical and population groups. They are periodically updated so that they remain up to date. The ROME III definitions of functional anorectal disorders which are described as part of the functional gastrointestinal disorders (FGID) will be discussed in further detail below.

Functional anorectal disorders can be classified as follows as according to the ROME III criteria [19] (figure 1.1):

Figure 1.3: Functional anorectal disorder classifications



These disorders will now be explored in more detail in the next section of this chapter alongside structural manifestations of posterior compartment dysfunction.

1.4 Structural and functional manifestations of posterior compartment pelvic floor dysfunction

Faecal incontinence

In general, faecal incontinence (FI) can be defined as the involuntary loss of liquid and/or solid stool through the anus [20]. Anal incontinence (AI) can therefore be considered as the involuntary passage of either faecal matter or flatus.

Faecal incontinence is a common phenomenon, and it is likely highly underreported due to the highly embarrassing nature of the problem. Estimated prevalence is thought to be in the region of 7.7% (range 2.0-20.7%)[21]. This wide variation is likely to be the result of differing definitions of FI and AI; in addition, many studies report wholly on an older or institutionalised population, which are known risk factors and therefore the prevalence is likely to be significantly higher[22].

The presence of FI has a major negative impact on physical and psychological health and lifestyle; in many cases it causes severe social restriction. It has also been found to have a marked impact on mood, with depression amongst its sufferers being a common occurrence[23].

Faecal incontinence can be thought of as passive (occurring without the knowledge of the sufferer), or urgency-related (occurring as a result of the inability to defer

defecation). Patients can present with both of these elements in the history, giving a mixed passive/urge picture. A subset of patients with passive FI describe the unconscious leakage of stool shortly after defecation; this is known as post-defecatory soiling. The sufferer usually gives a history of staining of the underwear with small amounts of liquid or solid stool. Passive faecal soiling tends to be the result of impairment of either internal anal sphincter function or rectal sensation. The mechanism of post-defecatory soiling is thought to be different. Pucciani et al [24], in their series of 72 patients found that those with post-defecatory faecal incontinence had significantly higher obstructed defecation scores, positive straining tests and conscious rectal sensitivity thresholds than those with passive FI without post defecatory incontinence, suggesting that post-defecatory leakage was a secondary phenonemon to a failed defecatory mechanism.

The underlying aetiology of faecal incontinence may be broadly categorised into being related to functional or structural pathologies, or a combination of these two. As discussed earlier, an underlying functional cause denotes a largely structurally intact sphincter with intact neurological function.

The definitions for a diagnosis of functional faecal incontinence as according to the ROME III criteria are outlined in the box below (figure 1.2)[25].

Functional FI may be associated with other conditions such as fibromyalgia[26]. Additionally, it has been shown that children exposed to significant and stressful life events including bullying and sexual abuse have an increased risk of functional GI disorders, including faecal incontinence [27].

Figure 1.4: Rome III criteria for diagnosing functional faecal incontinence

Functional Faecal Incontinence

Recurrent uncontrolled passage of faecal material in an individual with a developmental age of at least 3 years and *one or more* of the following:

1. Abnormal functioning of normally innervated and structurally intact muscles
2. Minor abnormalities of sphincter structure and/or innervation
3. Normal or disordered bowel habits, (i.e., faecal retention or diarrhoea)
4. Psychological causes

AND
Exclusion of *all* the following:

1. Abnormal innervation caused by lesion(s) within the brain (e.g., dementia), spinal cord, or sacral nerve roots, or mixed lesions (e.g., multiple sclerosis), or as part of a generalized peripheral or autonomic neuropathy (e.g., due to diabetes)
2. Anal sphincter abnormalities associated with a multisystem disease (e.g., scleroderma)
3. Structural or neurogenic abnormalities believed to be the major or primary cause of faecal incontinence

Structural causes of FI

There are many organic causes of faecal incontinence, which can be broadly categorised into anal sphincter weakness, pelvic floor disorders, conditions affecting rectal capacity and/or sensation, CNS disorders and disturbances to global bowel function [19]. Anal sphincter weakness may be as a result of trauma or atraumatic in nature. A commonly encountered traumatic cause of sphincter weakness is obstetric anal sphincter injury sustained during childbirth. Iatrogenic causes involving surgery to the anal sphincter complex are also seen, such as following recurrent fistula-in-ano surgery or as a complication of haemorrhoidectomy. A common iatrogenic cause of FI is secondary to lateral sphincterotomy, a procedure for the management of chronic anal fissure; where rates of around 14% of disturbance of anal continence have been reported [28]. Atraumatic insult to the anal sphincter complex can also occur in conditions such as scleroderma, and as a consequence of advancing age, which results in a global weakening of muscle strength [29].

A relatively rare, however important patient cohort worth consideration are those who have sustained anal sphincter injury secondary to either blunt or penetrating trauma. This includes numerous mechanisms such as stabbings, blast injuries, shootings and

pelvic disruption secondary to significant blunt trauma. Papadopoulos et al in their series of ten patients with colonic, rectal and anal injuries recommended primary repair in patients with intraperitoneal rectal injuries, however if an extraperitoneal rectal injury or anal sphincter injury is sustained then diversion was necessitated[30]. The need for faecal diversion for extraperitoneal injuries has been debated, with Levine et al publishing a series of 30 patients, in whom five had transanal repair of five extraperitoneal injuries without consequence[31]. Zuccon et al published a small study of 10 patients who had been subjected to penetrating trauma. Four cases involved significant perineal and anorectal injury; these were treated with primary reconstruction[32]. There exists very little guidance as to the best way to manage anal trauma in current literature[33]. The largest study published by Glasgow et al in 2014 relates to battlefield trauma and included 46 combatants with blast injuries. 78% underwent faecal diversion, however many of these also had significant additional intra-abdominal injuries. Sphincteroplasty was undertaken in the acute phase in 11 patients, but was not found to influence colostomy reversal rates. The permanent colostomy rate was 30%[34]. Ulger et al still recommend temporary diversion if there is associated sphincter injury, but there were still certain circumstances where it was acceptable to perform primary repair of an extraperitoneal rectal injury[35].

Neuropathic causes of anal sphincter weakness can be as a consequence of a systemic disease, such as diabetes mellitus. Localised neuropathy of the pudendal nerve, which again can be associated with childbirth and pregnancy can also occur.

The subject of obstetric anal sphincter injury is dealt with in detail in a chapter later in this thesis.

CNS-related bowel incontinence can be as a result of conditions such as multiple sclerosis, Parkinson's disease and spinal cord injury and following a stroke. These patients predominantly experience constipation, with FI being less commonly experienced, although still experienced at least once a year by 75%, and is a daily occurrence for 5% [36].

Another cohort of patients in whom faecal incontinence is often prevalent are those who have disorders affecting the rectal capacity or rectal sensory mechanisms. This includes inflammatory conditions such as UC, Crohn's disease and radiation proctitis. Additionally, those who have had surgery centred on the anorectal complex – this

encompasses those who have had ileal pouch formation as part of treatment for ulcerative colitis and ultra low anterior resection for low rectal malignancy may also experience anal continence problems.

Rectoanal intussusception, or occult rectal prolapse, although more commonly the culprit of obstructed defecation, can also be a cause of FI. Several studies have shown a correlation between the degree of anatomical deformation and the severity of symptoms [37, 38].

Finally, there are a number of bowel conditions which can cause diarrhoea which then predispose an individual to incontinence episodes, such as hyperthyroidism, IBS, post-cholecystectomy diarrhoea, and constipation with overflow. Any patient presenting with symptoms of anal incontinence +/- diarrhoea require full diagnostic work-up to ascertain the underlying cause.

Functional anorectal pain

Chronic proctalgia can be characterised by pain or an aching be felt in the rectum, sacrum or coccygeal area, and in some patients may extend into the gluteal/thigh region[39]. Based on findings at DRE, it can be further classified into levator ani syndrome or unspecified anorectal pain. The predominant difference between levator ani syndrome and unspecified functional anorectal pain is that the patient meets the criteria for chronic proctalgia in both, but the absence of tenderness during posterior traction on the puborectalis sling rules out levator ani syndrome. The definitions of levator ani syndrome, unspecified functional anorectal pain and proctalgia fugax as according to the Rome III criteria are outlined in Figure 1.3[25]. These may coexist with one another.

The prevalence of an anorectal pain syndrome, levator ani syndrome and proctalgia fugax were found in one study to be 11.6%, 6.6% and 8% respectively [40].

Levator ani syndrome

Levator ani syndrome has a number of alternative names, including levator spasm, puborectalis syndrome, piriformis syndrome and pelvic tension myalgia. The pain tends to be worse with sitting or lying down. Symptoms can last from hours to days [41]. Thought to be the result of increased tonicity of the pelvic floor muscles, its exact aetiology is unknown. There are thought to be psychological associations such as stress and anxiety, and it is a recognised somatization disorder[42]. Levator ani syndrome tends

to affect females more than males, usually aged 30-60 years. On clinical examination, the presence of tenderness and discomfort on direct palpation of the posterior puborectalis sling is found[43].

Proctalgia fugax

In contrast, proctalgia fugax is a condition where the subject experiences intense pain in the rectum which lasts from seconds to a few minutes. Pain is felt in the rectum, and can be cramping, aching or stabbing in nature. It affects all ages, and both sexes equally. Bouts of pain tend to occur rather infrequently. It is associated with normal anorectal physiology between episodes, and increased anal tone during an episode of pain[44].

Figure 1.5: Rome III diagnostic criteria: functional anorectal pain

F2. FUNCTIONAL ANORECTAL PAIN

F2a. Chronic Proctalgia

*Must include **all** of the following*:*
a. Chronic or recurrent rectal pain or aching
b. Episodes last 20 minutes or longer
c. Exclusion of other causes of rectal pain such as ischemia, inflammatory bowel disease, cryptitis, intramuscular abscess, anal fissure, haemorrhoids, prostatitis, and coccygodynia
* Criteria fulfilled for the last 6 months with symptom onset at least 3 months prior to diagnosis. (*Chronic proctalgia may be further characterized into levator ani syndrome or unspecified anorectal pain based on digital rectal examination).*

F2a.1. Levator Ani Syndrome

Diagnostic criterion

Symptom criteria for chronic proctalgia plus tenderness during posterior traction on the puborectalis

F2a.2. Unspecified Functional Anorectal Pain

Diagnostic criterion

Symptom criteria for chronic proctalgia but no tenderness during posterior traction on the puborectalis

F2b. Proctalgia Fugax

*Diagnostic criteria Must include **all** of the following:*

a. Recurrent episodes of pain localized to the anus or lower rectum

b. Episodes last from seconds to minutes

c. There is no anorectal pain between episodes

Defecatory disorders

Functional defecatory disorders

Functional defecatory disorders, or FDD, involve inadequate relaxation and/or paradoxical contraction of the pelvic floor muscles on attempted defecation with or without inadequate propulsion of rectal contents to enable defecation [19]. The presence of FDD in patients who complain of chronic constipation is significant, but estimated prevalence varies from 20-36% [45, 46]. The diagnostic criteria set out in Rome III are shown in figure 1.4 [25].

Figure 1.4: Rome III diagnostic criteria: functional defecation disorders

F3. Functional Defecation Disorders

*Diagnostic criteria**

The patient must satisfy diagnostic criteria for functional constipation**
During repeated attempts to defecate must have *at least two* of the following:

1. Evidence of impaired evacuation, based on balloon expulsion test or imaging
2. Inappropriate contraction of the pelvic floor muscles (i.e., anal sphincter or puborectalis) or less than 20% relaxation of basal resting sphincter pressure by manometry, imaging, or EMG
3. Inadequate propulsive forces assessed by manometry or imaging

* Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

**** Diagnostic criteria for functional constipation:**

Must include *two or more* of the following: (a) Straining during at least 25% of defecations, (b) Lumpy or hard stools in at least 25% of defecations, (c) Sensation of incomplete evacuation for at least 25% of defecations, (d) Sensation of anorectal obstruction/blockage for at least 25% of defecations, (e) Manual manoeuvres to facilitate at least 25% of defecations (e.g., digital

F3a. Dyssynergic Defecation

Diagnostic criterion

Inappropriate contraction of the pelvic floor or less than 20% relaxation of basal resting sphincter pressure with adequate propulsive forces during attempted defecation

F3b. Inadequate Defecatory Propulsion

Diagnostic criterion

Inadequate propulsive forces with or without inappropriate contraction or less than 20% relaxation of the anal sphincter during attempted defecation

Structural defecatory disorders

Structural defecatory disorders affecting the posterior compartment are common. They may present with symptoms of obstructed defecation: a sensation of incomplete emptying of the rectum, chronic constipation, stool trapping, faecal incontinence (which may be passive in nature) or the presence of a bulge felt in the posterior vaginal wall.

Rectocele

A rectocele can be defined as a protrusion of the rectum through the posterior vaginal wall through the rectovaginal fascia[47]. The presence of small rectoceles in females is incredibly common, with quoted incidences in the literature of as high as 93% in asymptomatic females[48]. As such, many experts believe a small rectocele to be considered as a normal variant, and therefore the presence of symptomology and rectoceles >2cm in size are more important factors when considering treatment options. Additionally, the size of rectocele does not necessarily correlate with the severity of symptoms experienced[49]. Symptoms can include features of ODS such as incomplete evacuation, the need for interdigitation of the rectum or vagina in order to facilitate emptying, in addition to constipation, abdominal pain and tenesmus. Rectoceles may occur in association with other pathologies such as enteroceles and intussusception[50].

Enteroceles, Peritoneoceles and Sigmoidoceles

Peritoneoceles include both enteroceles and sigmoidoceles; however a true peritoneocele involves protrusion of peritoneum only into the rectovaginal space. As their name suggests, enteroceles contain peritoneum and small intestine, and sigmoidoceles contain a loop of sigmoid colon[51]. In patients with symptoms of ODS, enteroceles have been reported in as many as 35%[52]. Suggested causative factors for the development of an enterocele include a deep pouch of Douglas, or failure to close this space following hysterectomy[53]. Opinions as to the impact of the presence of a peritoneocele are varied, with some authors suggesting that they can cause rectal compression and obstructive defecatory symptoms[54], whilst others suggest that rectal obstruction does not occur [55].

Rectal prolapse/intussusception

Recto-anal intussusception refers to the invagination of the rectum inside the anus. It is essentially a concealed rectal prolapse, with more severe forms protruding through the

anus to become a full thickness rectal prolapse. It is the result of chronic excessive straining leading to connective tissue injury, which can also include a degree of neuropathy, and failure of the counter-forces preventing organ prolapse within the pelvic floor basin[56]. It may occur concurrently with functional conditions that predispose to chronic straining, such as PRS. Experienced symptoms may include a mass protruding through the anus, a sensation of incomplete evacuation of the rectum, faecal incontinence, mucoid discharge or other ODS symptoms.

Neurogenic bowel dysfunction

Neurogenic bowel disturbance can occur secondary to lesions such as spinal cord injury, multiple sclerosis and following a Cerebrovascular Accident (CVA). The type of symptoms experienced depends on the location of the lesion. The location can be categorised into two broad categories: supraconal (above the conus medullaris) and within the conus or in the cauda equina. Supraconal lesions tend to cause slowed whole gut transit and hypertonia and hyperreflexia of the hindgut. Anal tone tends to be preserved. This causes reduced rectal compliance and predisposes to reflex defecation and incontinence. In contrast, lower lesions cause hypotonia and hyporeflexia, with reduced anal tone[36].

1.5 Management of posterior compartment dysfunction

Various treatment options exist in the management of pelvic floor dysfunction, which are usually arranged in a step-wise fashion, with increasing levels of invasiveness depending on severity of symptoms and lack of responsiveness to lower-scale interventions. A brief synopsis of treatment options in both FI and defecatory disorders is given below.

Treatment of faecal incontinence disorders

Treatment for FI ranges from conservative treatment such as lifestyle adaptations, stool bulking agents, biofeedback and transanal irrigation to more invasive procedures such as sacral nerve stimulation (SNS) and sphincter repair[57]. Biofeedback physiotherapy is discussed in more detail below. Rectal irrigation may be performed using a device such as the Peristeen system, which has proven efficacy in controlling symptoms and improving QoL in both faecally-incontinent patients[58] and those with defecatory

disorders[59]. Sacral nerve stimulation involves the implantation of a quadripolar electrode along the sacral nerve foramina, usually at the S3 or S4 level on one side in close proximity to the sacral nerve root. This is then attached to an implantable pulse generator (IPG) that is placed in the subcutaneous tissues of the buttock. The exact mechanism of action is not fully known, but is thought to act at a pelvic afferent or central level[60]. The results are relatively good, with one systematic review finding success rates for SNS on an intention-to-treat basis at 63% (33-66) in the short term, and 54% (50-58) with longer-term follow-up[61].

There are numerous surgical options that can be employed in the treatment of FI. These include anterior levatorplasty and postanal pelvic floor repair, which aim to correct abnormalities of the pelvic floor itself. An anterior levatorplasty acts to lengthen the anal canal as well as repairing an occult anterior anal sphincter injury if present. A postanal pelvic floor repair helps to form an acute anorectal angle, and therefore aids in continence by creating a control valve out of the puborectal sling[62]. Physical defects in the anal sphincter complex itself can be repaired through either an overlapping or end-to-end sphincteroplasty. Overlapping repair has been shown to have good long-term results with improvements in QoL and maintained patient satisfaction[63], and is recommended as a primary procedure for OASIs sustained during childbirth[64]. At shorter follow-up, it has been shown to have lower risk of faecal urgency and anal incontinence compared to an end-to-end repair[65], however there are some reports of increased dyspareunia and wound infections in comparison[66].

Another surgical option in the management of severe FI is construction of a neosphincter, through the use of a pedicled muscle flap harvested from gracillis, obturator internus or gluteus maximus. The gracillis is the muscle of choice, and may additionally be electrically stimulated. This has been shown to produce higher resting pressures than a non-electrically stimulated neosphincter, and therefore improved continence, with improvements in symptoms of FI as high as 90%[67]. Alternatively, an artificial neosphincter may be inserted – such as the Fenix magnetic device, or a hydraulic silastic balloon cuff. Several studies regarding the use of artificial sphincters report satisfactory results[68, 69], whereas others have raised concerns about associated morbidity[70]. Another key option is the SECCA procedure, which involves the use of temperature-controlled radiofrequency energy applied to the anal canal. This has been shown to improve results with mild to moderate FI[71].

If all of the above fail, then the final option is permanent faecal diversion with colostomy formation. In general, this is utilised if other measures fail or if the patient is not deemed suitable for the other options as described above[72]. A cross-sectional study undertaken by Colquhoun et al demonstrated higher quality of life scores compared with patients living with FI[73]. Another study noted that 80% of patients who had undergone stoma formation for FI would choose to have a stoma again[74]. Rates of permanent diversion following sphincter-preserving surgery for ultra low rectal cancer are in the range of 11% at 1 year to 22% at 10 years[75].

Treatment of defecatory disorders

Again, treatment of defecatory disorders is instigated in a step-wise fashion. Biofeedback physiotherapy is used in the first instance in the majority of cases in patients with defecatory dysfunction (see below). For structural defecatory dysfunction non-responsive to conservative treatment, there exist a number of surgical options. A number of approaches exist for rectocele repair: transabdominal, transperineal, transvaginal and transrectal. Transvaginal repair, also known as a posterior vaginal repair, is sometimes performed with concomitant mesh placement. This can be associated with dyspareunia and full resolution of ODS symptoms does not always occur[76]. However compared to a transanal approach, the recurrence rates of rectocele have been shown to be lower[77]. Transanal repairs, which involve anal mucosal resection and plication of the anterior rectal wall, have been linked to higher recurrence rates and a risk of postoperative anal sphincter dysfunction[47]. Transperineal repairs may confer some advantages over transanal and transvaginal repairs as they avoid anal sphincter damage and vaginal vault insult; the technique involves transperineal dissection down to the level of the levator ani, and either suture or mesh augmentation of the perineal supporting tissues[47].

Rectopexy, often performed laparoscopically, and sometimes robotically[78], is a procedure for patients with external rectal prolapse or internal intussusception and associated symptoms of obstructed defecation of faecal incontinence[79]. There are a number of surgical options available; the most commonly employed are resection rectopexy and ventral rectopexy. Both techniques are effective in the management of rectal prolapse, however complication rates have been found to be higher with resection rectopexy[80]. Ventral rectopexy is performed through initial mobilisation of the rectum down to the level of the pelvic floor, and then lifting and securing it against the sacral

promontory using either sutures or a synthetic or biological mesh[81]. The procedure has gained widespread acceptance globally, with many considering it to be the treatment of choice for external rectal prolapse[82]. However, there have been concerns raised regarding the use of mesh, with reports of mesh erosion and fistula formation into the vagina, rectum or other intra-pelvic organs[83, 84]. These concerns have been largely regarding mesh inserted during vaginal procedures, and current guidance with respect to ventral rectopexy is that it is safe for use provided it is being placed by appropriately experienced surgeons in specialist centres[85]. Additionally there have been concerns raised about patient selection. The consensus statement from the Association of Coloproctologists of Great Britain and Ireland identifies external rectal prolapse (with suitability for general anaesthesia) as being the only absolute indication for ventral rectopexy[86]. Relative indications were Oxford grade 3 or 4 internal rectal prolapse or solitary rectal ulcer syndrome that had failed to respond to treatment [86].

An alternative and widely accepted method of resection of rectal prolapse or rectocele is the 'stapled transanal resection of the rectum', or STARR procedure. A recent meta-analysis found that the performance of the STARR procedure did result in a reduction of ODS scores, but that the effect was probably overestimated[87]. Additionally, complication rates and recurrence rates have been reported as high by some authors[88], whereas others dispute this and advocate it as a safe an effective procedure in the management of ODS[89]. The 2017 practice recommendations from the Association of Coloproctologists of Great Britain and Ireland have concluded that the STARR procedure is safe, with low rates of major morbidity. In their review of 47 studies (8340 patients), a good or satisfactory outcome was reported in 73-80%[86].

Should a patient not wish to undergo surgery, or is considered not suitable for a surgical procedure, then a number of home irrigation catheters exist, such as the Peristeen or Qufor systems. These involve the insertion of a catheter into the rectum, with a predetermined volume of water then instilled into the rectum. These systems have proven effective in both the management of faecal incontinence and chronic constipation/ODS sufferers[90, 91].

Biofeedback physiotherapy

Biofeedback physiotherapy comprises of a prescribed and individualised course of puphysiotherapy that also includes feedback methods through visual and verbal

techniques. The predominant principle underlying this treatment method is that a behaviour that is reinforced repeatedly can be learned[92].

Biofeedback physiotherapy can be deployed as a treatment method in cases of dysenergic defecation and faecal incontinence.

With regards to patients with symptoms suggestive of dysenergic defecation, the aims of treatment are to optimise coordination of the pelvic floor and abdominal musculature used in defecation and to help increase sensory thresholds for rectal contents in patients with rectal hyposensitivity. Electromyography or anal manometry training is used in order to give direct feedback to the patient in order to help facilitate retraining of coordination of muscle contraction and relaxation. Simulated defecation and rectal balloon training help further with coordination of defecation and increasing awareness of rectal filling. Numerous studies have shown biofeedback to be a beneficial treatment in dyssenergic defecation. One study reported a 59% satisfactory response (defined as a reduction in the constipation score of >50%) for patients presenting with obstructed defecation associated with PRS[93]. Lee et al found that 72.3% of their cohort of 347 patients with dyssenergic defecation had a good response to BF, and that the probability of maintaining a good result was 60% at 2 years and 58% over 5 years[94]. Rao et al conducted a RCT which demonstrated that patients who had BF compared to those who had undergone either standard treatment (e.g. dietary modifications, laxatives) or sham BF were significantly more likely to correct their dyssenergia, reduce balloon expulsion time, and increase the number of complete spontaneous bowel movements[95].

Biofeedback physiotherapy also has a role in the treatment of patients presenting with faecal incontinence. In this situation, primary goals of treatment are to improve strength and coordination of pelvic floor musculature, and improve the ability of the patient to recognise smaller rectal volumes to allow for defecation prior to an incontinence episode. Additionally, biofeedback physiotherapy can be used to increase the maximum tolerated volume within the rectum and reduce feelings of uncontrollable faecal urgency[92].

1.6 Aims and objectives of thesis

The work presented within this thesis is largely related to the need for a change in the way that healthcare services are designed in order to accommodate the growing patient demand seen across the National Health Service coupled with national funding

shortfalls. With regards to pelvic floor services, this is likely to represent a significant problem due to the highly specialist nature of the disease, the need for multidisciplinary input, and also the rising tide of elderly patients who are more likely to present with pelvic floor dysfunction. A shift towards community-based services and development of integrated care pathways acting as a bridge between the community and tertiary services could help facilitate delivery of pelvic floor services moving forward.

Therefore, the predominant aim of this thesis is to identify whether there are specific patient populations who benefit most from early involvement of the pelvic floor tertiary centre and its MDT versus those who could be safely managed in a community-based setting. This includes the systematic exploration of some commonly used tests (patient reported outcome measures, anorectal manometry, MR-defecogaphy) and to ascertain their role in the work-up in the patient presenting with symptoms of pelvic floor dysfunction. It also encompasses a thorough analysis of specific patient populations who contribute significantly to the work undertaken within this particular pelvic floor unit, namely those with obstetric anal sphincter injuries and patients who have had surgery for ultra-low rectal cancer.

Hypotheses:

1. **Specific patient-reported outcome measures (PROMS) and existing diagnostic test parameters can predict those most likely to require surgical intervention and tertiary centre referral**
2. **Specific disease states necessitate the need for more intensive pelvic floor MDT input within a tertiary centre**

Aims

1. To identify whether specific PROMS, anal manometry and MR-defecography parameters can predict the need for surgical intervention
2. To identify which patient groups could safely be managed in the community initially versus those who need more intensive MDT input within a tertiary pelvic floor unit

Objectives

1. To evaluate the correlation with specific PROMs and the need for surgery in patients presenting with faecal incontinence or obstructed defecation

2. To evaluate the sensitivity and specificity of ARM performed in the context of faecal incontinence in the prediction of the need for surgical intervention.
3. To identify the role of MR defecography versus clinical examination and fluoroscopy in the detection of pelvic floor structural abnormalities
4. To evaluate the degree of correlation between MR defecography and patient-reported symptom severity
5. To evaluate the sensitivity and specificity of various MR factors seen on MR defecography in the prediction of need for surgical intervention in patients presenting with obstructed defecation
6. To identify whether there are any observed functional differences in patients who have had a missed OASI versus those who have undergone primary repair
7. To identify the impact of differing grade of obstetric sphincter injury on patient-reported outcome measures (PROMS) and anorectal physiology
8. To identify the impact of ultralow rectal cancer resection on the long-term PROMs and anorectal physiology results

These objectives will be explored in the subsequent chapters of this thesis. The body of work is split into two parts, with one concerning the various diagnostic modalities described above (MRD, PROMs, ARM) and their value in determining who is more likely to require surgery, and the other looking at specific patient populations: OASIs and those with ultra-low anastomoses following rectal cancer resection. These patient populations form the largest proportions of those ultimately requiring surgical intervention (47.92% and 20.8% respectively of all patients with FI requiring surgery); therefore a clearer understanding of which patients within these groups require more intensive tertiary centre input will allow a greater understanding of how future services could be aligned to best suit the needs of the patients whilst also adapting to meet the future needs of the NHS.

CHAPTER TWO: LITERATURE REVIEW

2.1 Chapter outline

The following chapter comprises a literature review of the predominant imaging modalities used for the assessment of pelvic floor disease within the local tertiary pelvic floor service, and of particular focus in this thesis. Following on from this, a brief overview of the literature on OASI and patients who have undergone rectal resection is given. This review was conducted systematically using a number of search terms. Pubmed, Google scholar and the Cochrane Database were searched for relevant articles.
Section 2.1 discusses anorectal physiology. On conducting the literature search the following phrases and words in various combinations were used: anorectal, manometry, physiology, technique, solid-state, pull-through, air-perfused, water-perfused, high-resolution-anorectal-manometry (HR-ARM), high-definition-anorectal-manometry (HD-ARM).
Section 2.2 focuses on MR defecography. For this section, the search was conducted using combinations of the following phrases: Magnetic-resonance-defecography, MRD, magnetic-resonance-proctogram, magnetic-resonance-proctography, interpretation.
Section 2.3 focuses on the functional consequences of rectal resection, in particular relation to treatment for low rectal cancer. The literature search incorporated a number of search terms: low-rectal-cancer, treatment, functional-outcomes, coloanal-anastomosis, inter-sphincteric-resection, extralevator-abdominoperineal-excision, abdomino-perineal-excision, low-anterior-resection-syndrome.
Section 2.4 relates to obstetric anal sphincter injury. Search terms include obstetric-anal-sphincter-injury, functional-outcomes, quality-of-life, risk-factors, management.

2.1 Anorectal physiology

Anorectal physiology measurements include a variety of different tests, such as manometric assessment of sphincter muscle tone, pudendal terminal motor latency and testing of rectal compliance. These tests are commonly used in various combinations in the assessment of patients presenting with faecal incontinence, defecatory disorders, and anorectal pain disorders. Additionally, it is used to monitor response to treatments such as Biofeedback, and in the preoperative assessment of patients prior to rectal resectional surgery where a chance of postoperative deterioration in function is anticipated.

ARM assessment allows for the assessment of motor function of the anal sphincter complex and rectal sensation. It was first described in 1877 by Gowers [96], and has since become an integral part of colorectal pelvic floor assessment.

Two main techniques are described for performance of ARM: the pull-through technique and the stationary technique. In existence are expert advisory papers as to the minimum standards required for the acceptable performance of ARM[97, 98]. However, there is no general consensus as to the optimal method of performance of these techniques, or in what constitutes normal and abnormal values[98]. The pull-through technique involves taking multiple measurements at 0.5-1cm intervals as the inserted catheter is withdrawn through the anal canal. The stationary technique involves measurement of pressures at each longitudinally placed sensor site over a period of around 60 seconds. Different opinions exist as to the best method of obtaining results, with some advocating a stationary[99, 100] and others a pull-through technique[101]. Azpiroz et al (2002)[99] stated that the stationary technique was superior as the act of pulling the catheter through the anal canal evoked a reflex motor response and therefore would give falsely high resting pressure results.

Required equipment comprises four main components: a thin catheter with intraluminal pressure-sensing abilities, pressure transducers, a balloon which can be inflated inside the rectum, and a recording/display system[98]. There are a variety of catheter types and techniques used to perform ARM reported in literature. At least six pressure sensors are recommended for use on the chosen catheter device[97]. The most commonly used are water (or air) perfused or solid-state catheters. The water-perfused catheters are considerably cheaper, but have been argued to obtain comparable results compared to solid-state systems [101]. These findings were corroborated by a number of authors[102, 103]. However, others dispute this, with Johnson et al finding similar resting pressures but higher squeeze pressures with a solid-state probe [104].

Given the heterogeneity of the various techniques used, it comes as no surprise that it is difficult to quantify “normal” parameters for ARM measurements. Additionally, there is a documented difference between males and females, with females shown to have lower resting pressures and squeeze pressures compared to males. However, young nulliparous females have been shown to have similar pressures to males[105]. It has been recommended that institutions employing the use of ARM either develop their own set of normal parameters with the equipment and methodology used locally, or that if

parameters are taken from already published literature, then methodology used should be similar to that described in that literature[106].

More recently the development of high resolution anorectal manometry (HR-ARM) and high definition anorectal manometry (HD-ARM) have taken precedence over older methods. HR-ARM allows for the production of spatiotemporal colour-contoured tophographical maps: these give a vibrant representation of dynamic motor pressures within the anal canal[107]. This means of manometry is far from novel, having previously been used for some time in oesophageal studies. It allows for a more highly detailed and visual representation of motor pressures and data which is easier to interpret[108]. Although it has been suggested by a number of papers[107, 109, 110] that there are benefits to HD-ARM in terms of gaining a more comprehensive physiological assessment of sphincter motor function, there is no real body of evidence to suggest a huge clinical benefit with these more expensive systems[107].

A few studies exist in the current literature which look at how well ARM correlates with symptom severity. A recent meta-analysis which explored the diagnostic accuracy of ARM in the prediction of FI included seven studies, totalling 1768 patients (1041 with FI, the rest healthy volunteers)[111]. The results demonstrated a summary sensitivity and specificity of ARM as an overall test for predicting FI of 0.80 (95% CI 0.69-0.88) and 0.80 (0.65-0.90). The authors demonstrated that ARM results indicative of anal sphincter dysfunction increased the pre-test probability of a FI diagnosis from 25-58% and lowered it to 9% when normal. Pehl et al[112] similarly looked at the ability of ARM to predict FI with 144 controls and 558 FI patients. They found a 91.4% sensitivity and a specificity of 62.5%. They also found that sensitivity increased with worsening FI severity. Grossi et al[113], through the use of a prospective age-matched single-blinded study, investigated whether differing HR-ARM patterns of dyssenergic defecation could differentiate between patients with functional constipation and healthy volunteers. They found that a type IV dyssenergia HR-ARM pattern – failure of anal pressure to decrease with inadequate propulsory rectal pressures – was moderately useful in discriminating patients with functional constipation from healthy volunteers, with a positive predictive value of 70% and a positive likelihood ratio of 2.3. Otherwise, its role was rather limited, as 90% of healthy volunteers had HR-ARM profiles that were considered to be abnormal.

Rao et al[114] studied a series of 143 consecutive patients, with the aim of evaluating whether anorectal physiology results influenced patient management in those with

diagnosed defecatory disorders. They reported that anorectal physiology testing discovered new information in 88% of patients, and that this led to a change in management strategies in 76%. They also found that virtually all patients who had been referred with FI had evidence of sphincter weakness on manometry. Seven of 10 (70%) patients referred for preoperative evaluation had abnormalities that contraindicated surgery. Additionally, 70% of those referred for a preoperative evaluation had results that precluded surgical intervention. They concluded that anorectal physiology testing remained important for diagnosis and could have an influence on treatment decisions.

2.3 MR-defecography

Magnetic-resonance defecography (MRD), also known widely as MR proctography, was first introduced as method of assessment of pelvic floor abnormalities in 1993[115]. MRD allows for the dynamic visualisation of the anterior, middle and posterior compartments of the pelvic floor. Images are T2 weighted, and this allows for optimal distinction of the soft tissues in the pelvic region[116]. Additionally, the use of MRI means that the use of ionising radiation is not required; therefore this test has its benefits over conventional defecography (CD). With regards to the posterior compartment, MRD can be used to detect underlying aetiology of problems such as obstructive defecation and faecal incontinence. Hetzer et al[117] published a small series of 50 patients with faecal incontinence who underwent sitting MRD. They found the presence of severe rectal descent (>6cm below the pubococcygeal line, PCL) in 94% of patients. A number of other abnormalities (e.g. rectal prolapse, anterior rectoceles, enteroceles) were detected. Importantly, the intended surgical procedure prior to investigation was changed in 67% of cases according to the radiological findings.

MRD has also facilitated the development of three-dimensional interactive pelvic floor models[118, 119] which can be utilised to better understand the dynamic structural relationships of the pelvic floor. Several studies undertaken by colorectal surgeons interested in predominantly posterior compartment dysfunction have found that added benefits of MRD over CD include the ability to identify enteroceles and the presence of levator ani hernias[120, 121]. However, some studies have shown MRD to be less accurate than traditional fluoroscopic techniques, with underestimation of the presence and degree of organ descent[120, 122, 123]. A newly published study which examined the accuracy of MRD, fluoroscopy and transperineal and transvaginal ultrasound in

detecting clinically-significant ODS found that all were similar in results, and that not one was optimal above the others[124]. The merits of MRD versus CD is discussed in full as part of a later chapter of this thesis, as are its correlation with clinical symptoms.

For the majority of studies documented in current literature, the reference line used in image interpretation was the pubococcygeal line (PCL), which runs from the inferior border of the symphysis pubis to the lowest coccygeal bones. It is from the PCL that measurements of vertical descent such as the anorectal junction descent (M line), cystocele size and degree of middle compartment descent are measured from. There exist alternative lines of reference considered to have similar validity in the assessment of vertical descent; this includes the mid-pubic line (MPL)[125]. Drawn through the long axis of the pubic bone, it has been shown to have a higher agreement with clinical staging of POP than the PCL, although neither had good agreement, particularly with the posterior compartment (kappa 0.08 with PCL versus 0.25 with MPL)[126]. As discussed in the general methods section, the PCL was used throughout this thesis as the line of reference.

2.4 Functional disturbances associated with rectal resection

Indications for resection of the rectum include malignancy, severe diverticular disease and inflammatory bowel conditions, such as ulcerative colitis (UC). In cases of UC, patients may undergo panproctocolectomy with ileal pouch-anal (IPAA) anastomosis in order to restore bowel continuity.

Rectal cancer surgery

Surgical options for resection of low rectal tumours include anterior resection, intersphincteric resection (ISR) and abdominoperineal excision of the rectum (APER) with formation of end colostomy. When the formed bowel anastomosis in rectal resection lies beneath the peritoneal reflection, then this procedure is known as anterior resection[127]. Revolutionising rectal cancer survival has been introduction of total mesorectal excision, or TME. This is performed for tumours involving the mid and distal rectum, and a partial mesorectal excision (PME) is performed for upper rectal tumours. TME has been shown to have significantly improved both cancer survival and locoregional recurrence rates[128, 129], and can also be performed safely laparoscopically[130].

Distal resection margins have been a hot topic for some time; initial recommendations were for a minimum of 5cm of distal bowel to be resected along with the tumour in order to minimise the risk of microscopic tumour being left behind[131]. Therefore, for distal tumours within the distal third of the rectum, or those within 6cm of the anal verge (ultralow rectal tumour), patients often underwent APER and colostomy. However, more recent evidence has disproven this guidance, and the recommended distal resection margin decreased first to 2cm, and is now 1cm[132]. This change in opinion has facilitated the developments of techniques where ultralow anastomoses with or without intersphincteric resection (ISR) can be employed. This allows for restoration of normal bowel continuity with tumours in close proximity to or involving the uppermost internal anal sphincter.

Therefore, the performance of APER has markedly decreased, and is now in the region of 10%. It is considered a marker of surgical quality[133], with a study by Hodgston et al which demonstrated that hospitals undertaking higher volumes of colorectal resection had a reduction in the risk of APER with permanent end colostomy, 30 day mortality and survival rates at 2 years compared to units with lower numbers of procedures[134]. It has been the general opinion that living with a permanent stoma was inferior to having normal bowel continuity in terms of quality of life; however there has been evidence to suggest functional and QoL outcomes were comparable[135]. However, when looking at oncological outcomes compared to anterior resection, APER has been shown to have higher local recurrence rates and lower survival rates than anterior resection, in addition to an increased risk of circumferential margin involvement[136]. As a consequence of the significant variation in the practice of APER[133], the English National Low Rectal Cancer Development Programme (LOREC) was formed. One of their aims was to optimise performance of extralevator abdominoperineal excison (ELAPE), in order to improve oncological and quality of life outcomes [137]. ELAPE has been shown to have significantly improved results in terms of marginal involvement compared to APER [138]. The increased risk of perineal wound complications with ELAPE was offset, at least in part by the use of biological mesh[139]. However, some surgeons express concern with this technique[140].

ISR with coloanal anastomosis is an alternative to APER, or ELAPE. Current recommendations from the MERCURY II study group state that in the presence of tumour extension on MRI beyond the muscularis propria or IAS and into the

intersphincteric plane, then ELAPE should be performed[141]. Otherwise, ISR is considered to be a safe alternative.

The technique of ISR was first described in 1977 by Lytle and Parks, initially in the context of inflammatory bowel disease[142]. It was first used in 1992 in the context of resection of malignancy. A 62% 5 year survival versus 58% with APER was found[143]. Additionally, 85% of patients reported good postoperative functional results. These findings were backed up by Rullier et al, who published a series of 73 patients with T3 and 6 patients with T4 disease where there was evidence of IAS involvement[132]. They managed to achieve R0 resection in 89%, with a local recurrence rate of 2% and distal recurrence of 19%. 5 year overall survival was 81%.

In a later manuscript, Rulier goes on to describe a classification system which allowed localisation of tumours which were within 6cm of the anal verge[144]. This location-based system classified tumours into four types. Type 1, or supra-anal tumours were located >1cm from the point at which the anal canal begins. Type II, or juxta-anal tumours were close to the IAS, and required partial ISR. Type III, or intra-anal tumours, had invasion of the IAS and therefore required total ISR. Type IV tumours involved both EAS and IAS and therefore in these instances, APER was performed. Those with intersphincteric resection were found to have comparable oncological outcomes when compared to those with a straight coloanal anastomosis. A more recent series undertaken within our unit[145], the functional results of which are discussed in a later chapter of this thesis, looked at oncological outcomes of 71 patients with had undergone coloanal anastomosis (CAA) with or without ISR. A R0 resection was reported in 97.1% of the series. The level of the anastomosis had no effect on disease-free survival or overall survival rates.

Functional consequences of rectal cancer treatment

As cancer survivorship has increased, so has the interest in obtaining the best functional outcomes possible in order to minimise the impact on QoL. In 2000, estimated survival rates for rectal cancer were 52% in females and 50% in males. This is now higher, likely in the region of 60%, as it is estimated that every 5 years, there is a 5-6% increase in 5 year survivals in both sexes[146]. It is estimated that around 50-80% of patients undergo some form of sphincter-preserving surgery[147]. Symptoms of bowel dysfunction following rectal cancer treatment are common. Treatment for low rectal cancer often results in disturbance of bowel function which may be severe in up to 50% of patients[148]. Frequently observed symptoms include loose stools, increased frequency,

fragmentation of stool (where multiple visits to the toilet in quick succession are required in order to achieve one complete bowel motion), urgency, and feelings of incomplete emptying. These symptoms have more recently been encompassed under an umbrella term, low anterior resection syndrome, or LARS. LARS is thought to be multifactorial in aetiology, secondary to loss of the rectal reservoir, a reduction of sphincter tone, and through the effects of additional chemotherapy and radiotherapy used in treatment[147]. Contin et al[149] found the use of neoadjuvant radiotherapy and performance of a low anterior resection were significantly associated with the subsequent development of FI, with a hazard ratio for the development of FI of 3.3 (95%CI 1.3-6.8) in those who had undergone additional radiotherapy. Several studies have found an increase in the incidence of FI in irradiated versus non-irradiated patients[150, 151].

It is also believed that the act of surgical resection itself can result in direct IAS damage through stretching when creating the anastomosis; this is thought to be a contributory factor in 1/5 of cases[152]. Additionally, there is the potential for intramural nerve plexus injury, during mobilisation of the bowel, and denervation of the left colon during mobilisation is thought to result in a significant increase in motility[153]. Juul et al believed that full TME was an additional contributory risk factor[127].

Christensen et al have created an internationally validated scoring system for LARS, which takes into consideration these multiple symptoms, giving patients' a diagnosis of no, minor or major LARS[154]. A more detailed description of the LARS score is given in the patient and methods section of this thesis. Brenegdhal and colleagues[155] performed an epidemiological study to determine the incidence of LARS in rectal cancer survivors. In their series, the overall incidence of LARS was 64.56%, with 41% of patients reporting major LARS (i.e. a LARS score of >30). Longer-term follow-up has also found similar findings, with symptoms of bowel dysfunction still present in a significant number of patients[156].

2.5 Obstetric anal sphincter injury

Patients who have sustained an anal sphincter injury during childbirth form a huge part of the population of a tertiary colorectal pelvic floor service. This patient population also form a large part of the penultimate part of this thesis.

Introduction and definition

Obstetric anal sphincter injury (OASI) is where perineal trauma sustained during childbirth results in an injury to the anal sphincter complex. It has been subdivided into varying grades of severity, based on the degree of sphincter disruption[157], and forms part of the general classification of perineal tears. A grade 1 (G1) perineal injury (or first degree tear) describes injury to the vaginal mucosa or perineal skin only. A grade 2 (G2) injury (second degree tear) extends to involve the muscles of the perineum, but not into the anal sphincter complex. A grade 3A (G3A) injury (3rd degree tear) also involves up to the first 50% of the EAS. Following on from this, a grade 3B (G3B) injury involves all up to 100% of the EAS, without IAS involvement. A grade 3C (G3C) injury involves the IAS, without anal mucosal involvement. The most severe injury, a grade 4 (G4) obstetric tear (4th degree tear), involves injury completely through the IAS and into the rectal mucosa or anal epithelium. As a whole entity, OASI complicates 5.9% of vaginal deliveries in England[158]. Within the UK, the majority occur in primiparous women at a rate of 6.7%. The rate in multiparous women is less, at around 1.7%[159].

Risk factors for OASI

Risk factors for sustaining an OASI have been well researched. These include macrosomia (infant birth size 4kg), the need for instrumental delivery, nulliparity, shoulder dystocia, prolonged 2nd stage of labour and Asian ethnicity[158, 160, 161]. One large study performed by Boggs et al[162] which concerned 9,857 women with OASI (with a OASI rate of 5.3%) found that risk factors for a subsequent tear after repeat vaginal delivery (91.9% of women with OASI had a subsequent vaginal delivery) was an infant considered large for gestational age (OR 2.2, 95% CI 1.3-3.6) and an instrumental delivery (OR 2.4, 95% CI 1.2-4.6). Interestingly, the rate of recurrent tear was the same at 5.3%.

Identification of OASI

Following vaginal childbirth, part of routine immediate postnatal care involves careful inspection of the perineum in order to assess for the degree of perineal injury. As a rule of thumb, in cases where a G3 or G4 OASI is identified, then this is repaired in theatres under a spinal anaesthetic by an obstetrician. G2 tears are repaired by the attending midwife or obstetrician, usually within the place of delivery. Missed OASI at the time of delivery is common. Several studies have tried to quantify the frequency of missed

OASI. Groom et al[163] in their study of 121 women found that 40% of 3rd degree OASIs were missed on initial perineal assessment. They suggested that improvements in training and increased vigilance were necessary to improve detection rates of significant sphincter injury. Andrews et al[164] in their study of 241 patients found that the incidence of OASI increased from 11% to 24.5% when ladies were re-examined at a later stage. All OASI, including those missed clinically, were apparent on endoanal ultrasound scan. Faltin et al[165] contacted a series of 150 women 3 months following vaginal birth who had undergone primary repair of a clinically-diagnosed G2 tear. At clinical re-assessment, they found clinically undetected OASI immediately following delivery in 42/150 women (28%).

The reasons behind this relatively large proportion of under-classified perineal injury may be at least in part explained by a lack of understanding of the classification system of OASIs and an inability to recognise anal sphincter involvement. Fernando et al identified that 33% of consultants wrongly classified OASIs as 2nd degree tears[157]. In addition, it is important to recognise that in the immediate post-delivery phase, there is a high likelihood of tissue distortion secondary to oedema and bleeding, with shearing forces creating indistinct tissue borders which may be difficult to recognise for less experienced eyes.

Management of OASI

There exist clinical guidelines published by the Royal College of Obstetricians & Gynaecologists (RCOG) regarding the management of 3rd and 4th perineal tears[166].

One of the recommendations made by the RCOG is that all patients who sustain an OASI should be followed up, where feasible in a specialist clinic which has availability of endoanal ultrasound and anorectal physiology performance and interpretation in order to allow full assessment of the anal sphincter complex post delivery, and to make recommendations with regards to future mode of delivery.

Functional consequences of OASI

OASI usually results in at least some form of dysfunction in the short term at least, with the majority of patients suffering flatal incontinence. It is estimated that of patients suffering with flatal incontinence in the immediate post-delivery phase, approximately

2/3 will recover within 1 year[167]. An early follow-up study at 3 months post delivery undertaken by Visscher et al[168] demonstrated a 63% rate of flatal incontinence, 50% rate of incontinence to liquid stool and 20% to solid stool. They also demonstrated manometry results that were worse with EAS and IAS tear in combination compared to an isolated EAS disruption. Nazir et al[169], examined 132 patients who had sustained their first OASI and found that at 5 months post delivery, the overall rate of flatal incontinence was 60% across all grades of tear, with a 7% rate of liquid FI. The rate of faecal urgency was 30% in this cohort. A further study undertaken by Richter et al[170] of 343 patients quoted similar figures: they found a 7% prevalence of FI at 6 months post delivery and a 24% prevalence of AI. 21% of patients described symptoms of faecal urgency. Flatal incontinence was significantly more common in patients who had sustained a G4 OASI (35% versus 16%). Recovery has been shown to improve over the first 12 months, however longer-term studies have shown a general decline in function over time. A few studies examine patients with a longer period of follow-up. For example, Sangali et al[171], in their series of 177 patients who responded to a postal survey found that at 13-years follow-up of 129 G3 and 48 G4 OASIs, anal incontinence affected 25% of G4 versus 11.5% of G3 injuries. Fornell et al[172] in contacted 82 patients at 10 years following delivery found that an intact IAS and good perineal body were important factors in maintaining continence in the long term.

CHAPTER 3: GENERAL METHODS

3.1 Patient groups

Since 2008, all patients presenting to a single tertiary pelvic floor unit were invited on attendance to complete a series of questionnaires measuring degrees of various experienced symptoms and overall quality of life whilst awaiting review. This included the Wexner Incontinence score, the Birmingham Bowel, Bladder & Urinary Symptom Questionnaire (BBUSQ), the modified Obstructed Defecation Score (ODS) and the Short form 36 (SF36), which measures health-related QoL. These will be discussed in more detail later in this chapter. Completed questionnaires were collected by the doctor at the start of the clinic appointment, where relevant information including previous treatment interventions, diagnoses and treatment plans were also recorded. This data was then amalgamated onto an anonymised research database; each patient was given a unique identifier which linked to a separate password-protected file so that patients could be identified by those maintaining the database, without compromising patient anonymity. Patients had been referred either locally or as tertiary referrals. All referred patients were suffering with symptoms of functional or structural bowel or pelvic floor disturbance. Patient reported outcome measure (PROM) data was captured at each clinic through voluntary completion of a set of questionnaires whilst waiting to see the clinician at initial appointment and any subsequent follow-up. It should also be noted, that any decisions made regarding surgery were made after having gone through the pelvic floor MDT which comprised the colorectal pelvic floor surgical team, pelvic floor and biofeedback physiotherapists, pelvic floor radiologists and the urogynaecology team. All individualised patient treatment pathways commenced with an initial period of conservative management with employment of strategies such as biofeedback physiotherapy; a step-wise increase in intrusiveness was taken as required in order to gain symptom control.

3.2 Database maintenance and ethical approval

Each patient who had agreed to complete PROMS and for clinical data inclusion was assigned a unique patient identifier which was completely unrelated to any on going clinical care. True patient identification was kept in a single encrypted file with strict

limitations on access to the principal investigator and database collaborator. Each database entry for a patient was coded according to the stage in the treatment process.

The pelvic floor research database was granted ethical approval in 2014 for a period of five years by the Research Ethics Committee (NRES Committee South West – Central Bristol 14/SW/0051). A comprehensive structured protocol was in put in place for database management and maintenance. Data collected prior to this period was collected as a part of patient management and assessment of treatment response and stored as clinical audit data.

Each dataset entry was coded into patient episode and primary and secondary diagnosis. Diagnoses were coded according to a predefined coding system, based on the three main categories of pelvic floor dysfunction as according to the American Society of Colorectal Surgeons (ASCRS) discussed earlier in this thesis[18]: faecal incontinence, anorectal pain syndromes and constipation. These headings were then further subdivided as according to the diagrams below, with the consideration of functional and structural causes of each of the main categories listed above, which allowed for each primary diagnosis to have a separate code which allowed for easy identification of relevant patients for each study. The categorisation system used in database maintenance is shown below (figure 3.1-3.3).

Between 2008-2016, there were a total of 1228 entries of patient data onto the database. There were 817 patients overall included in the database. The table below gives the breakdown of patient data held within the database for each subcategory as listed in the previous flow diagrams (table 3.1). It should be noted that all patients were coded according to primary diagnosis, i.e. the original cause for referral and predominant problem. In some cases, there was a secondary diagnosis evident in co-existence.

Figure 3.1: Faecal incontinence disorders.



Figure 3.2: Defecatory disorders

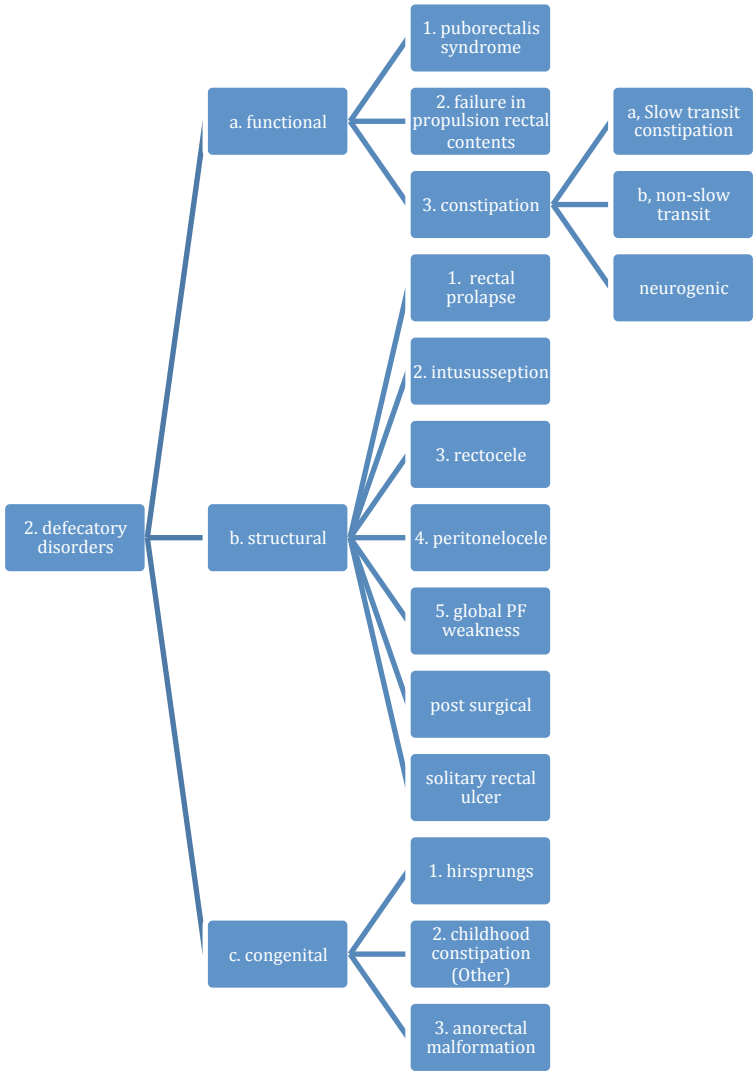


Figure 3.3: Anorectal pain syndromes

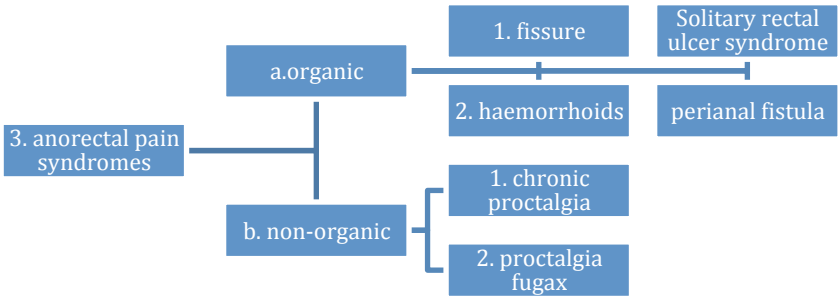


Table 3.1: Breakdown of case mix held in pelvic floor database

Defecatory disorder	n	Faecal incontinence	n	Anorectal pain syndromes	n
Functional	72	Sphincter weakness	279	Organic	12
Structural	185	Neuropathic	13	Non-organic	4
Congenital	9	Inflammatory	12		
Unknown/idiopathic	7	Pelvic floor disturbance	32	No identified abnormality	16
		Diarrhoea	21	Other pathology	75
		Rectal resection	46	Unknown/idiopathic	8
		Unknown/idiopathic	26		
TOTALS	**273**		**429**		**115**
					817

A significant proportion of the overall database population (34.1%) were classified as having a sphincter weakness. This population was largely represented by women referred directly from the local perineal clinic following obstetric anal sphincter injury. The next most common population were those with structural pelvic floor abnormalities such as rectal prolapse and rectocele (22.6%). A small number of patients presented with faecal incontinence symptoms which were actually related to the presence of structural pelvic floor disturbance (3.9%); these patients were included in relevant analyses for structural defecatory disorders. The records held within the database were fairly representative of the true case mix of a tertiary pelvic floor colorectal service.

3.3 Patient reported outcome measures (PROMs)

Various PROMS were used within this thesis. Those which form an integral part of the work presented are discussed in detail below. Other study-specific PROMs will be visited within the methods section of the relevant chapters. The selection of these specific questionnaires was at the discretion of the research supervisor and lead of the pelvic floor clinic, as it was felt these were most representative of the symptoms described by the patient population encountered. The utilised questionnaires were chosen at the commencement of the database in 2009. It is recognised that there are newer and more widely accepted questionnaires which may have been valuable in the works presented within this thesis, however in order to maximise the data utilised within the various studies discussed, the previously chosen questionnaires were continued throughout.

Birmingham Bowel, Bladder & Urinary Symptom Questionnaire (BBUSQ)

The BBUSQ is a validated 22-point questionnaire which focuses on the presence and frequency of symptoms of constipation, faecal incontinence, urinary function disturbance and rectal evacuation[173]. It was first developed in 2002, and scores from 0-100% in these four different domains, with a higher score indicating worse function in that particular area. Hiller et al also gave a predefined cut-off for each score which could be used to categorise patients into having either a 'normal or 'abnormal' result: constipation >64%, rectal evacuation >17%, faecal incontinence >17%, urinary symptoms >20%.

Although there are 22 questions, only 21 contribute to the final score, with the question "Have you consulted a doctor in the last six months about constipation?" being omitted from the scoring system. The constipation domain comprises two questions, and the evacuation domain eight questions. There are seven urinary questions and four faecal incontinence questions. For the score to remain valid, missing responses are allowed, but there must be one more than half the total number of questions completed for that domain present. In the case of a missing question, the average score of the remaining questions is taken to give the overall result. The original questionnaire was validated for use in females. This is pertinent when considering one question, which discussed the presence of a bulge in the vagina. In order to make this questionnaire applicable to both sexes, in males it was therefore omitted and the score adjusted as described above in order to allow its usage in the male population. The applicability of the BBUSQ to male patients has not been validated elsewhere, however it was felt that the adjustment for this single question was sufficient to allow for distribution to both sexes in order to maintain consistency throughout.

The Wexner Incontinence Score

The Wexner Incontinence Score[174] is arguably the most commonly used and reported scoring system for faecal incontinence in the literature. First created in 1993, it comprises of five elements, each scoring a maximum of 4 points, giving a maximum score of 20, which indicates maximal incontinence. It can be self-administered by the patient, or by the clinician, and grades symptoms of incontinence in terms of their

frequency to Question 1: gas, Question 2: liquid stool, Question 3: solid stool. Question 4 refers to the frequency of need to use pads or anal plugs, and Question 5 assesses the frequency of the need to alter one's lifestyle as a result of their faecal incontinence. Scores are awarded as follows: 0 = never; 1 = rarely; 2 = sometimes; 3 = usually; 4 = always. The major criticism of this assessment tool is that it does not incorporate the symptom of faecal urgency. This is addressed by the St Mark's Incontinence (or Vaizey) score[175] where urgency is included within the scoring system; however this score has only recently been included in pelvic floor database collection and therefore for the most part of this thesis, faecal incontinence assessment has been performed through the use of the Wexner Score.

The obstructed defecation symptom score (ODS)

The score used within this thesis for the purpose of detection of symptoms of obstructed defecation was first published in 1996 by Renzi and collegaues[176]. It comprises of five questions, each of which score a maximum of 4 points, giving a total maximum score of 20, indicating the presence of maximally severe ODS symptoms. Questions relate to the frequency (never/rarely/sometimes/always) of the presence of: 1. constipation; 2. straining; 3. Incomplete evacuation of stool; 4.the need to interdigitate the rectum or vagina or use perineal support to initiate defecation; 5. Laxative or enema use.

The Short Form SF36 health survey

The SF-36 [177] is a self-reported outcome measure tool which assesses quality of life across eight domains: physical functioning; role: physical; role: emotional; vitality; bodily pain; mental health; social functioning; general health.

Each domain is scored from 0-100% with the highest score indicating perfect and unaffected QoL. The questionnaire itself is concerned with the effects of health problems on the preceding four weeks. Patients answered each question based on a relevant Likert score, and these were combined for each domain to give a percentage score. Again, missing responses were allowed, provided that at least 50% of that domain's questions had been answered. In cases where more than one answer had been selected, the mean value was calculated and used in the final calculation for the score for that domain.

3.4 The pelvic floor MDT

The local pelvic floor service has evolved significantly since its commencement. The complexity of decisions in the management of pelvic floor disorders has necessitated the need for the development of a pelvic floor multidisciplinary team (MDT). The MDT incorporates a number of different key personnel including colorectal surgeons, urogynaecologists, pelvic floor and biofeedback physiotherapists, bowel continence nursing staff and radiologist. MDT management of pelvic floor disorders promotes high quality care through collaboration between specialists. Within this unit, the pelvic floor MDT meeting is held fortnightly and complex cases are discussed, with future operative planning and scheduling of joint cases between colorectal and gynaecological surgeons where needed. The MDT-based management of patients is in accordance with recommendations set out by the Pelvic Floor Society[178].Suggested patients for discussion include those considering surgery, all patients with FI considering SNS, patients with multi-compartmental pelvic floor dysfunction, and those who have failed conservative management.

3.5 Performance and interpretation of MR defecography

Magnetic resonance imaging (MRI) deploys the use of radiowaves and magnetic fields, with the utilisation of hydrogen (H^2) ions, which are present in abundance in the human body, to provide good differentiation of differing tissue types. The hydrogen ions, with their positive charge (protons) and a spinning motion, and are able to align with an external magnetic field.

During MRI examination, the patient is positioned within the magnet itself. The magnet then causes the hydrogen ions to align across the magnetic field in a parallel or anti-parallel fashion. Radiowaves are emitted to pass through the body, which cause excitation of the hydrogen ions The transmitter is then turned off, and the patient re-emits these radiowaves, which are then translated into an image[179].

Performance of MR defecography

The Siemans Avanto 1.5 Tesla MRI scanner was used to complete all examinations undertaken within the department. Patients were not given any bowel preparation or enema prior to the examination, however were instructed to have a full bladder. Patients were advised to attend the department 15 minutes prior to the start of the procedure in order to prepare and change into hospital gowns. Patients were

positioned supine within the MRI scanner. 30-50ml of ultrasonic gel was inserted into the vagina in females, and 50-100ml was inserted into the rectum of all patients. An initial sequence of T2-weighted turbo spin echo (TSE) images were acquired in 3mm slices through the pelvis in sagittal, coronal and axial directions.

Imaging was briefly paused to allow the radiologist to identify the midpoint of the anal canal on the sagittal image, before a single image was then taken which was centred on the anal sphincter complex. Following this, Trufisp (TE: 1.69s; TR: 4.26s) 5mm thickness images were rapidly acquired in runs of 25-image sequences: A single run was acquired whilst the patient was instructed to contract their pelvic floor, in a way as if they were trying to prevent the passage of flatus or urine. After this, the patient was given a number of attempts to evacuate the rectum whilst lying on the scanner. Patients were instructed to bear down as hard as possible as if trying to defecate, and patients were given 3-5 attempts to empty their rectum as required in order to maximise the diagnostic accuracy of the procedure.

MR defecography interpretation

A supervised period of training was undertaken with a radiologist (NK) in addition to supplementary reading material and additional training from the project supervisor (ET) prior to image analysis being undertaken alone. Further support was given by NK & ET when needed. For the purposes of the studies and also to ensure that data interpretation was accurately performed, all MRD images were interpreted on two separate occasions by two reviewers (LR & NK). At the time of MRD interpretation, both reviewers were blinded to the clinical findings and treatment decisions which had been made. In cases of disagreement, a third opinion was sought from ET, the overall research supervisor who had extensive knowledge in pelvic floor pathology and was additionally experienced in the interpretation of MR proctograms. Each individual MRD was analysed in accordance with standardised reporting measures for the interpretation of MRD[180]. A predefined data collection tool was designed based upon these standardised reporting measures that was used for data collection throughout the study period by both reviewers.

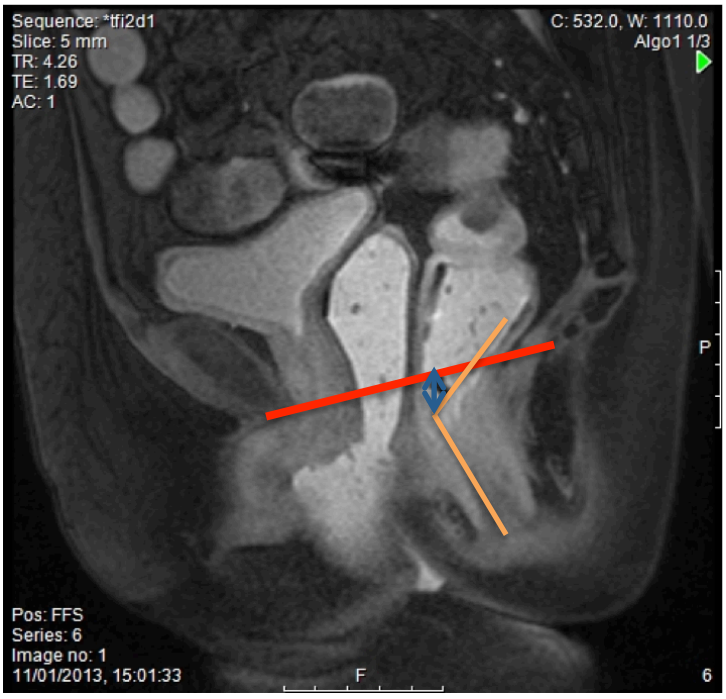
MRD images were first assessed for adequacy. If a patient had completely failed the examination, i.e. had been unable to follow the instructions for the evacuation phase, and there was no visible demonstration of pelvic floor movement on successive

strain/evacuatory views with 0% emptying of the rectal (or vaginal in females) contents, then these were excluded from any further data analysis. Additionally, if the obtained images were of insufficient quality to allow for accurate study interpretation then these were also excluded from analysis, however a formal assessment of quality was not undertaken.

For the purposes of the studies described in chapter 5, we have used the pubococcygeal line (PCL) as the predominant reference line. This was measured from the inferior border of the pubic symphysis to the tip of the coccyx. We chose the PCL as the primary reference line as it was a fixed reference point for all measurements.

Measurements at rest were made on the initial single image centred on the anal sphincter complex (figure 3.4). The M line and anorectal angle (ARA) were measured, as well as recording any evidence of prior hysterectomy. The M line, which can be defined as the distance between the PCL and the posterior wall of the anorectal junction, was measured perpendicularly from its intersection with the PCL. Changes in height of the M line relative to the PCL was therefore synonymous with anorectal junction descent during strain views. The ARA was measured along the posterior wall of the rectum and through the midpoint of the anal sphincter complex.

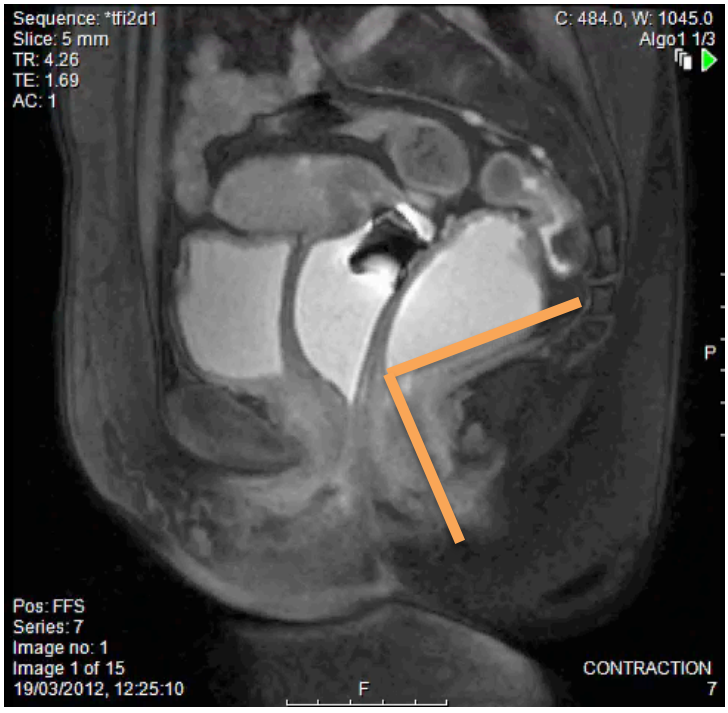
Figure 3.4: Static Pelvic floor image



PCL (red) ARA at rest (orange) and anorectal junction below the PCL (blue arrow) (M line)

Next, the sequence of images demonstrating pelvic floor contraction were assessed (figure 3.5). The anorectal angle was re-measured using the image with maximal contraction. Evidence of adequate pelvic floor contraction was defined as a decrease in the anorectal angle by at least 15 degrees. Those who were unable to decrease the ARA by 15 degrees were considered abnormal. Patients with absolutely no movement or evidence of straining rather contraction and pelvic floor elevation were excluded from analysis of this MRD variable as it was assumed that they had been unable to follow the instructions given to them.

Figure 3.5: Pelvic floor contraction (elevation)

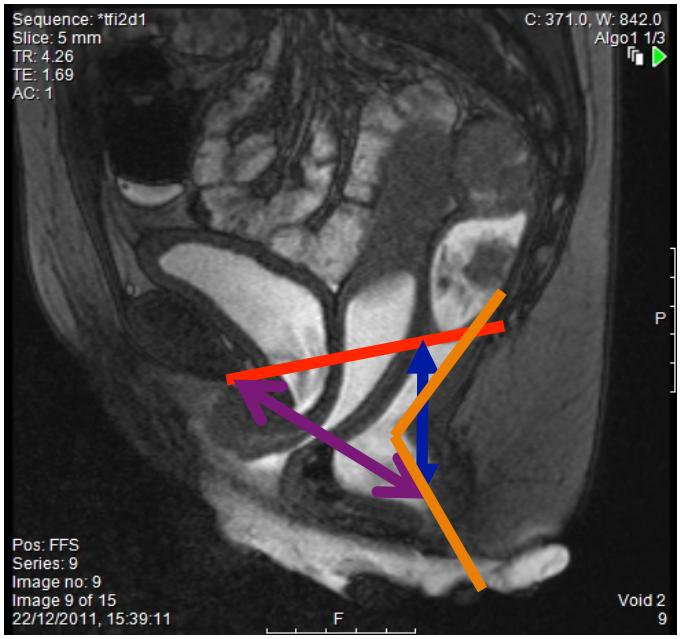


The ARA (orange) should reduce. A reduction of 15 degrees or less was considered abnormal.

Finally, patients were given 3-5 attempts strain in order to attempt to evacuate the rectal contents (figure 3.6). The sequence demonstrating the greatest degree of dynamic change from baseline was used for measurement of the various parameters. On maximal strain, a number of parameters were assessed, again using the PCL as a line of reference: H line, M line, ARA, presence of urethral hypermobility (UH),

presence of cystocele, enterocele, uterine/vaginal vault descent, rectocele, evidence of rectoanal intussusception or prolapse, degree of rectal emptying.

Figure 3.6: Strain views on MRD

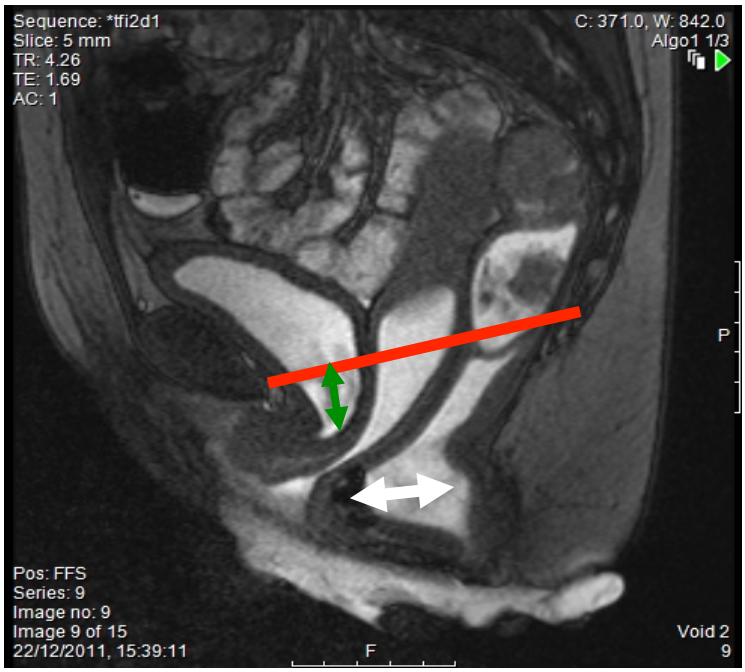


PCL shown in (red). The M line (blue arrow) indicates the degree of descent of the anorectal junction on attempted defecation. The anorectal angle (orange) should increase by 15-20 degrees. An abnormal H line (purple arrow) indicates excessive hiatal widening and pelvic floor laxity.

The M line was assessed again, with both the absolute value and the change in M line from rest on maximal straining noted. The H line was also calculated, which was an indicator of hiatal widening with pelvic floor strain. This was calculated as a line running from the inferior border of the symphysis pubis to the posterior border of the anorectal junction. An H line of <6cm on strain views was within normal limits.
Additionally, a failure to increase the ARA by 15 degrees compared to the measured rest ARA on attempted defecation was considered abnormal. Urethral hypermobility was defined as horizontalisation of the urethra by 30 degrees or more on straining. An enterocele was considered present if there was small bowel loops present below the level of the PCL. The presence of a cystocele was defined as the neck of the bladder descending below the PCL. In a similar fashion, the presence of uterine prolapse was defined as the posterior vaginal fornix lying below the PCL, or the top of the vaginal vault in those who had undergone prior hysterectomy. The degree of descent below

the PCL was measured in cm to allow classification of both cystoceles and vaginal vault/uterine descent. Rectoceles were measured as a protrusion of the anterior rectal wall, and were measured from the midpoint of the anal canal to the rectocele wall. A bulge of 2cm or less was considered to be mild and clinically insignificant with rectoceles of 2cm or greater indicating the presence of significant pathology. This is shown in figure 3.7.

Figure 3.7: Presence of a cystocele and rectocele on strain views



The presence of a cystocele (green arrow) or rectocele (white arrow) may be demonstrated. The cervical tonsils should remain above the PCL.

The MRD variables described above were graded as normal, mild, moderate or severe as according to criteria derived from the HMO classification[181] (table 3.2)

Finally, the strain images were viewed in their entirety in order to make a clinical assessment with regards to the:

1. presence of paradoxical puborectalis syndrome
2. presence of rectal mucosal prolapse, intussusception or external rectal prolapse
3. degree of rectal emptying, estimated in %.

Features considered indicative of paradoxical puborectalis syndrome included a thickened IAS, an inability to empty rectal contents and the failure of the ARA to increase or the ARA to become more acute during successive evacuation attempts.
All of the above parameters were assessed on two occasions as described earlier. In situations where there was a significant difference of opinion resulting in re-classification of an abnormality (e.g. from mild to moderate or moderate to severe) then the scan was reviewed for a third time with an additional reviewer (ET).

Table 3.2: Grading of severity of MR variables

Variable	Normal	Mild	Moderate	Severe
H line	<6cm	6-8cm	8-10cm	>10cm
M line	<2cm	2-4cm	4-6cm	>6cm
Rectocele		0-2cm	2-4cm	>4cm
Middle compartment descent	Above PCL	0-3cm	3-6cm	>6cm
Cystocele	<1cm below PCL	1-3cm	3-6cm	>6cm
Enterocele	Above PCL	0-3cm	3-6cm	>6cm
	Normal		**Abnormal**	
Anorectal angle	• 94-114° (rest) • varies 15° between rest/squeeze and rest/defecation		• Becomes more acute on defecation • <15° change on rest/squeeze and rest/defecation	
Urethral Hypermobility	Absent		Present	

3.6 Performance and interpretation of anorectal manometry

Performance of anorectal manometry

Anorectal manometry (ARM) was performed as part of diagnostic work-up in patients presenting with symptoms of both faecal incontinence and obstructed defecation. It provided information as to the sensory and motor aspects of sphincter function, and was used both as an initial screening tool, and in some cases, in particular those with OASI, as part of the assessment of response to treatment strategies. The ability to perform ARM relied on a high level of patient understanding in order to maximize results. In cases where there was a language barrier, then a registered face-to-face

interpreter was used. If patients were unable to understand instructions for other reasons such as cognitive impairment then the procedure was abandoned. ARM was carried out within the pelvic floor clinic either by or under the close supervision of a colorectal pelvic floor surgeon who had extensive experience in the performance and interpretation of the results.

Following informed consent and the provision of a chaperone, patients were positioned in the left lateral position in order to carry out testing. Initial visual examination of the perineum was performed before digital rectal examination in all cases, which included asking the patient to squeeze the examiner's finger. ARM testing was carried out using the T-DOC® Air-Charged™ ARM Catheters (LABORIE International, ON, Canada). These have four pressure sensors which measure pressure by dividing the anal sphincter into four quadrants, plus a fifth, distal balloon which was filled with air in order to allow for rectal sensation and RAIR. The catheter was connected to the Delphis IP processor (LABORIE International, ON, Canada), which serves to pump air to prime the catheters as well as digitizing and recording pressure readings from the pressure sensors. Prior to usage, the four pressure sensors were primed with air and the system zeroed in order to improve feedback and accuracy of results.

After DRE, the catheter was gently inserted cranially into the rectum to a depth of 4-5cm. After a period of approximately 1 minute to allow time for the patient to relax into a resting state, the catheter was gently moved within the anal canal to identify the beginning of the physiological anal canal, demarked by a sudden increase in pressure. The high pressure zone (HPZ) was identified where resting pressure was maximal; The maximal resting pressure (RP) was recorded at this level. Next in order to determine the maximal squeeze pressure (SP), the patient was asked to squeeze their anal sphincter as hard as they could. This was performed three times, and a mean reading taken to indicate the mean SP. Additionally, the RP was subtracted from the SP to give the mean squeeze pressure increment (MSPI). The final assessment of sphincter motor function was the ability of the patient to hold a sustained squeeze, known as the squeeze endurance (SE). Patients were asked to squeeze the anus maximally and hold at this pressure for five seconds. After a rest period of 1 minute, this was repeated a further two times, and the mean squeeze endurance calculated the mean pressure over the five seconds, with noting of any significant early fatigue. All motor measurements were taken at the level of the HPZ.

Following from this, rectal sensory parameters were assessed by slowly inflating the balloon on the catheter tip with air whilst it was placed within the rectum and beyond the anal sphincter complex. Patients were asked to identify the point at which they first noted the sensation of something within the rectum; this was taken to be the threshold volume (TV), measured in ml of air. Next, filling continued slowly, and patients were asked to identify the point at which they felt an urge to defecate: volume to defecatory urge (UV). Beyond this, the balloon was filled further, with patients asked to indicate the maximal tolerable volume (MTV), i.e. the point at which they would no longer be able to tolerate distension and had an extreme urge to defecate. The maximal volume instilled was 240ml. The rectal anal inhibitory reflex (RAIR) was assessed by inflating the intrarectal balloon with 50mls of air and pulling sharply down on the catheter whilst in the rectum. During this the screen was monitored for the presence of a sharp rise in rectal pressures denoting an intact reflex.

Finally, patients who had presented with symptoms of ODS were asked to expel the balloon in the left lateral position with the difficulty of expulsion being noted.

Whilst newer ARM modalities have become available during the study period, all patients in this study underwent manometry using the calibrated air filled system to ensure consistency within obtained results.

Interpretation of ARM

Under ideal circumstances, a set of asymptomatic patients should have undergone ARM testing within the unit in order to determine a range of acceptable normal values for each parameter. Instead 'normal' value ranges for each parameter were defined based on existing studies using existing systems in the literature[182]. Normal parameters defined for the purposes of this thesis are outlined in the table below (table 3.3)

Table 3.3: Definitions of normal ARM parameters used within this thesis

Parameter	Normal Range
Anal canal length	2.5-4cm
Resting pressure (RP)	60-93mmHg
Maximum squeeze pressure (SP)	138-279mmHg
Mean endurance 5 second squeeze pressure increment (SE)	30-50mmHg
Sensory threshold volume (TV)	20-50ml
Urge volume (UV)	60-100ml
Maximum tolerated volume (MTV)	115-180ml

Results for pressure measurements were expressed in mmHg. The mean of three readings was calculated and recorded in the database. The TV, UV and MTV were recorded in millilitres.

3.7 Statistical methodology

Statistical calculations were performed using IBM SPSS Statistics version 20. This software was capable of performing all required calculations for this thesis with the exception of the meta-analyses, which were performed using Revman version 5.3.

General statistical methods

Although there are a number of statistical methods employed in the various studies which will be discussed in more detail on a chapter-by-chapter basis, there are a few recurring themes which can be discussed as part of the general statistical methods.

The first is the use of univariate and multivariate logistic regression analysis. The second is the use of receiver-operator characteristic (ROC) curves when assessing the predictive value of the MRD, PROMS and anorectal manometry in prediction of the need for surgery.

Univariate logistic regression analysis involves the individual analysis of each variable in the analysis against the outcome of interest in a binary fashion, i.e. whether the positivity or negativity of a variable leads to a positive or negative outcome. This analysis was performed using SPSS, and the end result gave a 95% confidence interval, odds ratio (OR) and p value. If the p value was <0.2, then that variable was subsequently included in multivariate analysis.

Multivariate logistic regression analysis acknowledges that variables do not occur in isolation, rather there can be a number of variables that are related to the outcome being investigated. Therefore when considering the complexity of pelvic floor dysfunction, it was important to complete a multivariate analysis when possible in order to fully explore important relationships between the predefined variables and the outcome of interest. The technique of logistic regression analysis was used throughout part two of this thesis, where the relationships of PROMS, ARM and MRD against surgery and also MRD and PROMS were explored. The 'rule of 10' was used as a guide as to how many predictive variables could be included within a multivariate analysis to avoid model over-fitting[183].

Receiver-operator characteristic (ROC) curves assess the whether a variable can predict a certain outcome. ROC curve statistics rely on a binary outcome; in the case of this thesis, the outcome of interest has been surgery versus no surgery as a maximal treatment outcome. Generated along with the AUC are a given sensitivity and specificity.

The sensitivity of a test can be defined as the number of true positives which are correctly identified as being positive:

$$Sensitivity = TP/(TP+FN)$$

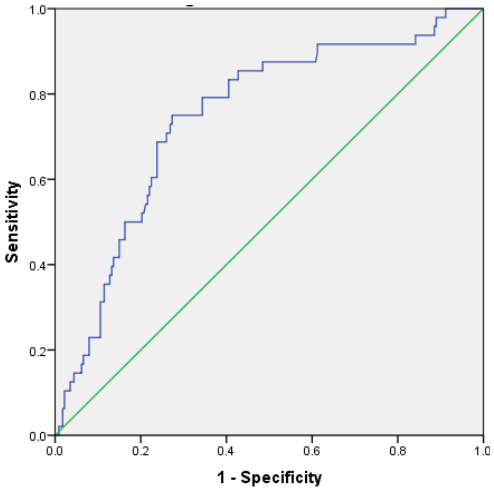
(TP: true positives; FP: false positives; TN: true negatives; FN: false negatives)

The specificity of a test is defined as the number of true negatives correctly identified as being negative:

$$Specificity = TN/(TN+FP)$$

In order to plot a ROC curve, the sensitivity is plotted against (1-specificity). An example of the graph generated is given below (figure 3.8). The closer the graph to the top left hand corner, the better the test:

Figure 3.8: ROC curve example



The area under the curve (AUC) statistic is used to define the overall ability of a test to discriminate between two outcomes[184]. Table 3.4 shows the definitions used for differing AUC values.

Table 3.4: AUC and corresponding definition

AUC	Definition
<0.6	Failed test
0.6-0.69	Poor
0.7-0.79	Fair
0.8-0.89	Good
>0.9	Excellent

Next, in order to identify the optimum cut-off value for each variable, with a corresponding sensitivity and specificity, the Youden index (*J*) is calculated. This is a measure of diagnostic accuracy. It is the maximum vertical distance of the ROC curve from the 'line of random chance', which is shown in figure 3.8 by the diagonal green line. The Youden index is calculated from the formula:

Youden index = sensitivity – [1-specificity]

This gives a value between 0 and 1, with 0 indicating a worthless test and 1 indicating a perfect test. The Youden index can be used to give the cut-off value for the predictive model with a respective sensitivity and specificity[185]. Use of the Youden Index does however have its limitations, namely the risk of negative biases if there are factors present which are unqualifiable for inclusion in data analysis as they are below

the limit of detection, and are therefore missing from the data set[186]. However, this would relate more to concentrations of a particular substance rather than how the test has been utilised within this thesis.

Where feasible, continuous data was used for ROC curve analysis. Clearly, this was not always possible with certain domains that had a binary response, i.e. the presence or absence of a certain feature; therefore a single coordinate with its corresponding AUC was generated[187].

In this thesis, ROC curve analysis was used in an attempt to identify the predictive ability of patient-reported outcome measures (chapter 4), anorectal manometry (chapter 5) and magnetic resonance defecography (chapter 6) in identifying patients who would require surgical intervention.

This was performed for each variable of interest against the binary outcome of surgery versus no surgery as the maximal treatment outcome. Variables with an area under the curve (AUC) value of greater than 0.7 were considered fair discriminators for the need for surgical intervention.

Meta-analytical methods

A meta-analysis is a study which involves the systematic review and statistical analysis of a number of papers relating to the same question, pooling results in order to give a single estimate of treatment effect. There are a number of different methods available, depending on the type of research question asked by the investigator. This thesis incorporates one such like paper, on MRD versus clinical examination and fluoroscopy. It is important to ensure that potential sources of bias are identified prior to amalgamation of results in order to reduce errors. Additionally, there exist specific guidelines as to the performance and reporting of a systematic review or meta-analysis, published by the Cochrane Collaboration: the Preferred Reporting Items of Systematic Reviews and Meta-Analyses (PRISMA)[188]. These guidelines have been adhered throughout the relevant chapter.

Part 2: Diagnostic tools in pelvic floor dysfunction

CHAPTER 4: THE ROLE OF PATIENT REPORTED OUTCOME MEASURES IN THE ASSESSMENT OF PELVIC FLOOR DYSFUNCTION

Publications related to this chapter:

Anorectal Manometry versus patient reported outcome measures as a predictor of maximal treatment for faecal incontinence Ramage L, Qiu S, Yeap Z, Simillis C, Kontnvounisios C, Tekkis P, Tan E. *Annals of Coloproctology 2019. [In Press]*

4.1 Introduction and aims of chapter

This chapter concerns the role of patient-reported outcome measures, or PROMs, in the work-up of patients with pelvic floor dysfunction. PROMs are inexpensive, easy to apply and can be readily implemented in a community setting. The main challenge is choosing the most effective PROM tool and understanding the significance of the results. There are a vast number of assessment tools that are used to measure both symptom burden and quality of life; this becomes immediately apparent when attempting to perform a systematic review or meta-analysis, as heterogeneity of reported data is a significant problem when considering functional disorders.

Chapter outline and objectives

This chapter focuses on two specific cohorts of patients: a group with faecal incontinence symptoms, and another with symptoms suggestive of obstructed defecation disorders. The aim of this chapter's study was to identify whether there was any diagnostic role of the various PROMs used throughout this thesis in terms of identifying the need for surgical intervention, indicative of worse symptomology. This was performed using a combination of logistic regression and receiver-operator curve analysis.

4.2 Study: Can PROMs be used to predict the need for surgical intervention in patients presenting with 1: faecal incontinence and 2: obstructed defecation?

Methods:

Patients were identified from the previously discussed prospectively-maintained research database which contains patient data from 2008-2016 inclusive.

As according to the pre-defined coding system, patients who had a presenting symptom of faecal incontinence and who had final treatment data available, i.e. conservative management versus surgical intervention in the form of sphincter repair or sacral nerve stimulation were identified and included in the analysis.

Likewise, patients who had follow-up data and final treatment data with a diagnosis suggestive of obstructive defecation, which may have included symptoms such as incomplete defecation, constipation, difficulty in evacuation and passive faecal incontinence were analysed separately. Treatment outcome was any surgical intervention, which may have included perineal procedures such as anterior or posterior vaginal repairs or intra-abdominal surgery such as ventral rectopexy.

As discussed in previous chapters, PROMS have been collected for the purposes of maintenance of a research database, and therefore these results were not typically used in clinical decision-making.

Questionnaires used for the purpose of these analysis were as previously described: the Birmingham Bowel and Urinary Symptoms Questionnaire (BBUSQ)[173] and Wexner Incontinence Score (WIS)[174] in addition to the SF-36[177]. For patients presenting with symptoms suggestive of obstructed defecation, the ODS score was also used in analysis.

Other diagnostic modalities used such as anorectal manometry and MR-defecography are discussed in subsequent chapters.

Statistical analysis

Firstly, means of each domain for conservative and surgically managed groups were compared using Mann-Whitney U test. Next, univariate logistic regression analysis was undertaken against each PROM scale (four domains of BBUSQ, eight domains of SF-36, WIS, ODS score) against a binary treatment outcome of surgery versus no surgery Following on from this, receiver-operator characteristic (ROC) curve analysis was performed for each variable and Youden's Index calculated in order to formulate the "optimal cut-off value" for each variable. An area under the curve (AUC) of 0.7-0.8 was considered a fair predictor. An AUC of 0.6-0.7 was considered poor, and 0.8-0.9 was good.

Results: faecal incontinence

A total of 276 patients were identified who had the presenting symptom of faecal incontinence and had maximal treatment outcome data available. Sixty patients (21.74%) required no intervention. The majority of patients (55.07%) underwent Biofeedback physiotherapy as a final treatment. A few patients (5.80%) used transanal irrigation. Forty-eight patients (17.39%) underwent some form

of surgical intervention, with 37/48 undergoing SNS and 11/48 undergoing some other form of surgery (6 sphincter repairs, 1 gracillis flap, 2 colostomies, 2 Delormes) The mean values for each score for conservatively and surgically managed patients are given in the table below (table 4.1). The use of SNS was more frequent than the various methods of sphincter repair; this was due to the preferences of the lead operating surgeon and the local unit's positive results with SNS.

Table 4.1: Treatments received in FI patients

Treatment received		n
Conservative	None	60
	Biofeedback	152
	Transanal Irrigation	16
Surgical	SNS	37
	Other surgery	11
Total		276

Interestingly, all scores are significantly different between the surgically managed and conservatively managed groups. Patients who were managed surgically were older, with a mean age of 54.63 versus 41.25 P = 0.000). BBUSQ constipation scores were significantly lower (p = 0.019) with those who had surgery, and faecal incontinence scores were significantly higher: BBUSQ incontinence score of 29.18 and WIS of 6.24 with conservative group versus 46.06 and 8.96 with surgically managed group (p = 0.000). Patients who were managed surgically also had a significantly higher BBUSQ urinary (27.18 versus 19.68, p = 0.028) and evacuation domain (20.73 versus 13.89, p = 0.000) score. Patients who were managed conservatively had a significantly higher mean SF-36 score across each of the eight domains compared to those requiring surgical intervention (table 4.2).

Logistic regression

The results of the univariate logistic regression analysis are shown below in table 4.3. On univariate logistic regression analysis, all variables were found to be significant in the prediction of the need for surgical intervention, and therefore it was not feasible to perform multivariate analysis.

Table 4.2: Mean scores in conservative versus surgically-managed groups

		Conservative	Surgical	P value*
	Age	41.25 ± 14.3	54.63 ± 15.1	**0.000**†
BBUSQ	**Constipation**	54.07 ± 36.9	44.90 ± 20.3	**0.019**†
	Incontinence	29.18 ± 17.7	46.06 ± 25.0	**0.000**†
	Evacuatory	13.89 ± 11.5	20.73 ± 11.6	**0.000**†
	Urinary	19.68 ± 12.8	27.18 ± 19.0	**0.028**†
Wexner Incontinence Score		6.24 ± 3.4	8.96 ± 4.7	**0.000**†
SF36	**Physical Function**	83.30 ± 22.2	63.77 ± 31.7	**0.000**†
	Role Physical	78.62 ± 24.2	58.33 ± 32.6	**0.000**†
	Role Emotional	86.35 ± 23.16	69.10 ± 32.7	**0.000**†
	Vitality	54.07 ± 17.2	45.40 ± 21.5	**0.001**†
	Mental Health	73.79 ± 15.8	59.26 ± 21.6	**0.000**†
	Social Function	76.40 ± 21.9	51.30 ± 27.4	**0.000**†
	Pain	75.08 ± 22.7	63.28 ± 29.1	**0.018**†
	General Health	68.33 ± 18.1	55.08 ± 20.8	**0.000**†

 # 95% confidence interval of Odds Ratio
BBUSQ: Birmingham Bowel and Urinary Symptoms Questionnaire, SF36: Short Form 36 quality of life questionnaire.
** p-value calculated via Mann-Whitney U test † p-value < 0.05*

Table 4.3: Results of univariate logistic regression analysis

Variables		B	Std. Error	Wald	p-value	Odds Ratio	95% C.I.#	
							Lower	Upper
BBUSQ	**Constipation**	-0.025	0.009	7.023	**0.008**†	0.975	0.958	0.994
	Incontinence	0.039	0.008	24.097	**0.000**†	1.039	1.024	1.056
	Evacuatory	0.043	0.012	12.129	**0.000**†	1.044	1.019	1.070
	Urinary	0.032	0.010	10.071	**0.002**†	1.032	1.012	1.053
Wexner Incontinence Score		0.158	0.039	16.702	**0.000**†	1.171	1.086	1.263
SF36	**Physical Function**	-0.025	0.006	20.704	**0.000**†	0.975	0.965	0.986
	Role Physical	-0.024	0.005	19.874	**0.000**†	0.977	0.966	0.987
	Role Emotional	-0.021	0.005	15.679	**0.000**†	0.979	0.969	0.989
	Vitality	-0.024	0.008	8.544	**0.003**†	0.976	0.961	0.992
	Mental Health	-0.040	0.009	21.321	**0.000**†	0.961	0.945	0.977
	Social Function	-0.037	0.006	33.051	**0.000**†	0.963	0.951	0.976
	Pain	-0.018	0.006	8.920	**0.003**†	0.982	0.970	0.994
	General Health	-0.033	0.008	17.164	**0.000**†	0.968	0.953	0.983

 # 95% confidence interval of Odds Ratio
BBUSQ: Birmingham Bowel and Urinary Symptoms Questionnaire, SF36: Short Form 36 quality of life questionnaire
† p-value < 0.05

ROC curve analysis

The results of the ROC curve analysis are shown below (table 4.4).

Table 4.4: Results of ROC curve analysis

Variables		AUC[#]	Std. Error	p-value	95% C.I.[##]		Cut-off (Youden)	Sensitivity	Specificity
					Lower	Upper			
Age		**0.748**[†]	0.039	0.000	0.672	0.823	37.605	0.854	0.573
BBUSQ	**Constipation**	0.386	0.053	0.022	0.282	0.490	44.167	0.452	0.315
	Incontinence	**0.717**[†]	0.047	0.000	0.625	0.809	39.583	0.651	0.707
	Evacuatory	0.698	0.043	0.000	0.614	0.782	17.708	0.690	0.713
	Urinary	0.615	0.052	0.021	0.512	0.718	32.143	0.429	0.828
Wexner Incontinence Score		0.696	0.050	0.000	0.598	0.795	8.500	0.649	0.693
SF36	**Physical Function**	**0.701**[†]	0.047	0.000	0.608	0.794	67.500	0.575	0.778
	Role Physical	**0.704**[†]	0.047	0.000	0.611	0.797	71.880	0.700	0.707
	Role Emotional	0.673	0.051	0.001	0.574	0.772	79.170	0.684	0.646
	Vitality	0.644	0.053	0.005	0.540	0.747	53.130	0.725	0.575
	Mental Health	**0.730**[†]	0.043	0.000	0.645	0.815	67.500	0.700	0.675
	Social Function	**0.787**[†]	0.038	0.000	0.712	0.862	68.750	0.800	0.697
	Pain	0.627	0.052	0.014	0.525	0.728	53.130	0.500	0.787
	General Health	**0.709**[†]	0.046	0.000	0.618	0.800	57.500	0.632	0.743

BBUSQ: Birmingham Bowel and Urinary Symptoms Questionnaire, WIS: Wexner Incontinence score, SF36: Short Form 36 quality of life questionnaire.# AUC = Area under curve
95% confidence interval of AUC
† AUC > 0.7

In this series, age was a fair predictor for the need for surgical intervention in FI patients with an AUC of 0.748 (p = 0.000). Using Youden's calculation, patient age of 37.6 years or higher predicted the need for surgery with a sensitivity of 85.4% and specificity of 57.3%. (figure 4.1).

The BBUSQ incontinence domain was also found to be a fair predictor the need for surgical intervention, with an AUC of 0.717. A score of 39.58 or higher had a sensitivity of 65.1% and specificity of 70.7% for predicting the need for surgery (figure 4.2) . The WIS had an AUC close to 0.7, at 0.696. A WIS of 8.5 or higher had a sensitivity of 64.9% and specificity of 69.3% in predicting the need for surgery (figure 4.3).

Figure 4.1: Patient age as a predictor of the need for surgery

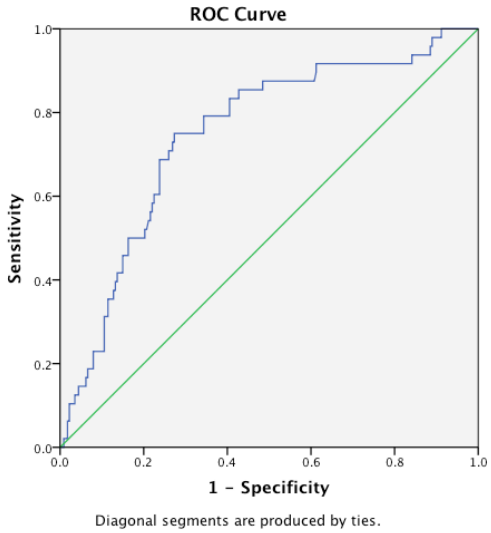
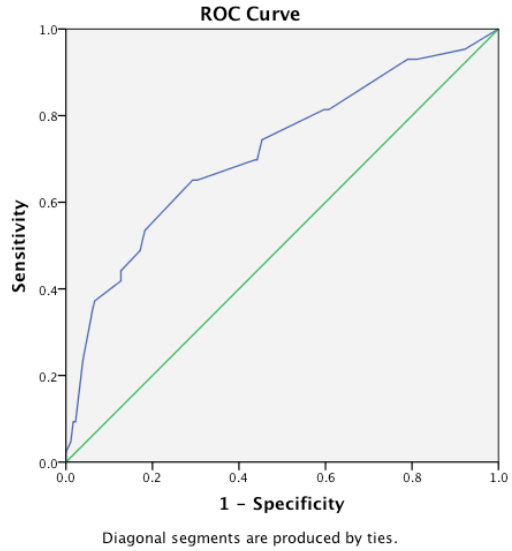


Figure 4.2: Incontinence domain of BBUSQ as a predictor of the need for surgery



Several domains of the SF-36 were found to be fair predictors of the need for surgical intervention: A physical function score of less than 67.5% had a sensitivity of 57.5% and a specificity of 77.8% in predicting the need for surgery, with an AUC of 0.701 (p = 0.000) (figure 4.4). A role-physical score of 71.88 or less had a sensitivity of 70% and specificity of 70.7% in predicting the need for surgery, with an AUC of 0.704 (p – 0.000) (figure 4.5).

Figure 4.3: Wexner incontinence score as a predictor of the need for surgery

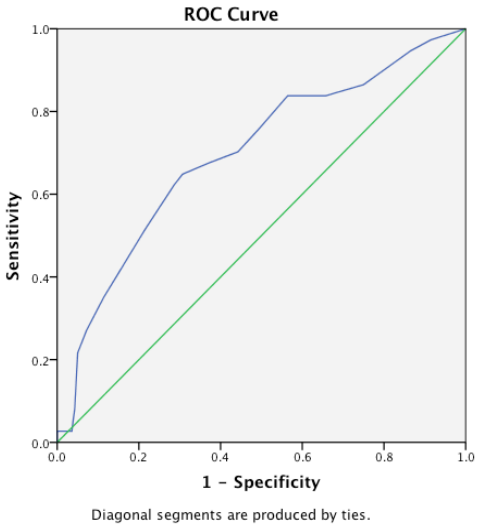
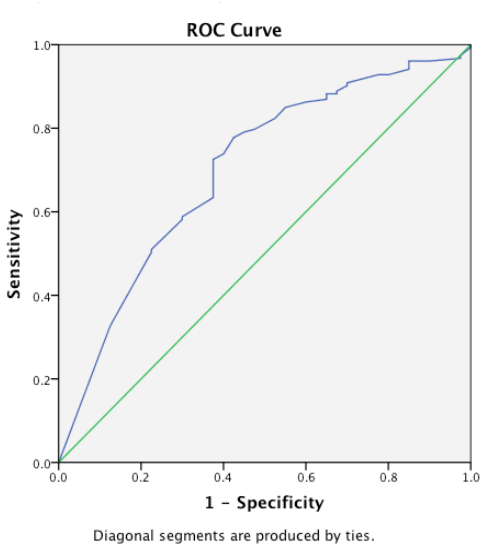


Figure 4.4: SF-36: physical function domain as a predictor of the need for surgery



A mental health score of 67.5 had 70% sensitivity and 67.5% specificity for predicting the need for surgery with an AUC of 0.730 (p = 0.000) (figure 4.6), The highest AUC for the entire series was the social function score, which had an AUC of 0.787. A score of less than 67.5, which gave a sensitivity of 80% and a specificity of 78.7% in the prediction of the need for surgery (figure 4.7).

Figure 4.5: SF-36: role physical as a predictor for the need for surgery

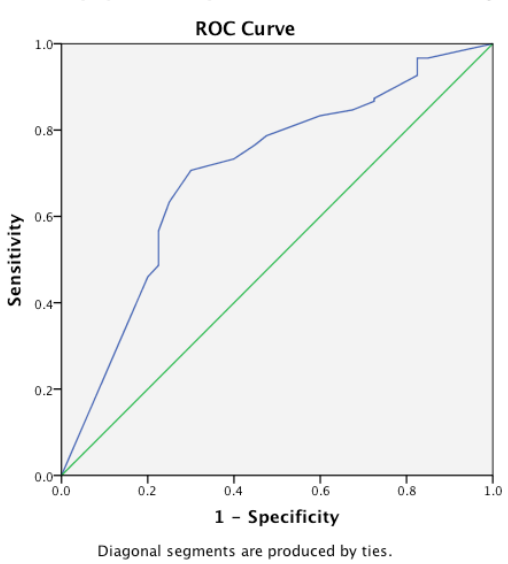
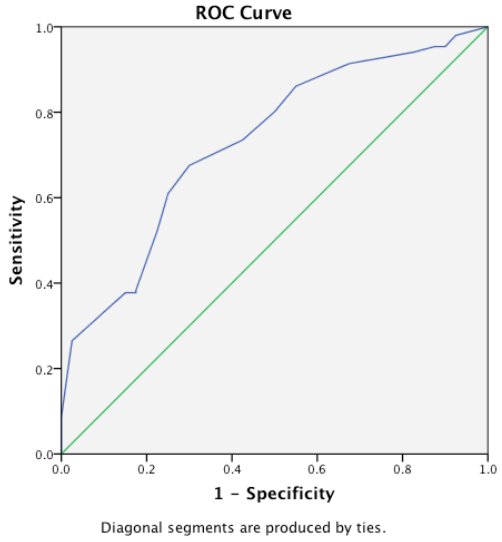


Figure 4.6: SF-36: mental health as a predictor of the need for surgery



Finally, the general health domain of the SF-36 had an AUC of 0.709, and with a cut-off of 57.5, had a sensitivity of 63.2% and specificity of 74.3% in predicting the need for surgery ($p = 0.000$) (figure 4.8).

Figure 4.7: SF-36: Social function domain as a predictor of the need for surgery.

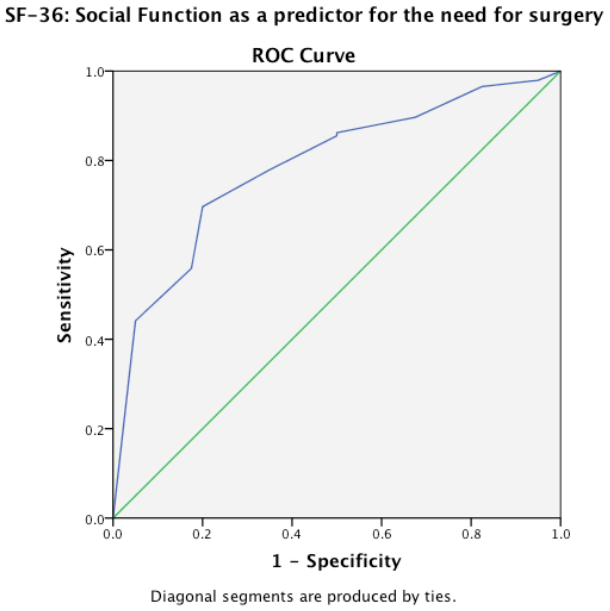
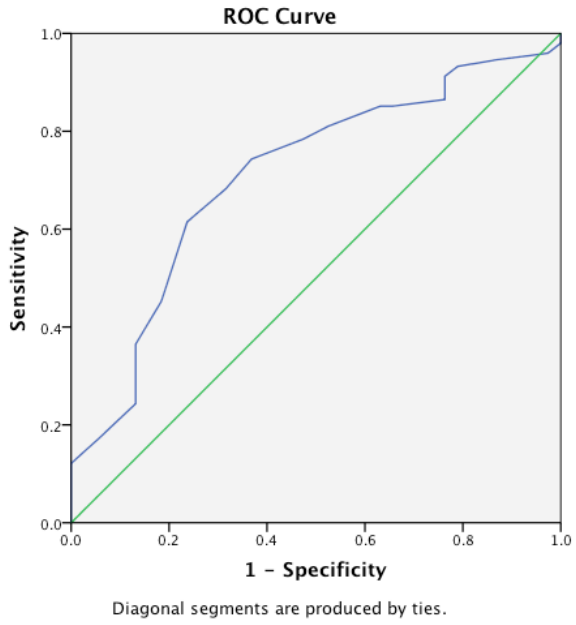


Figure 4.8: SF-36: general health as a predictor of the need for surgery



Results: Obstructed defecation patients

Functional and clinical outcome data was available for 129 patients who had presenting symptoms suggestive of obstructed defecation. Of these, 21.6% were males and 88.4% females. Mean age was 54.5+/- 17.7 in the conservatively managed group versus 48.8+/- 12.06 in the surgery group (p = 0.437). The proportion of patients who had undergone prior hysterectomy (p = 0.514) or prior

pelvic floor surgery (p = 0.088) were not significantly different between groups. Overall, 15.5% of females had undergone prior hysterectomy, and 13.18% of the entire cohort had undergone prior pelvic floor surgery.

As with patients presenting with faecal incontinence, the majority of patients underwent Biofeedback physiotherapy as a maximal treatment outcome. 27/129 patients (24.77%) underwent surgery. This included 15 ventral rectopexies, 8 anterior/posterior vaginal repairs (4 combined with tension-free vaginal tape insertion), 2 stapled transanal resction of the rectum, 2 sacrospinous fixation.

The mean values for each score or score domain are shown in the table 4.5 below.

Table 4.5: Mean results for conservative versus surgically-managed groups.

	Variable	Mean ± SD		P value*
		Conservative	Surgical	
BBUSQ	Constipation	57.69 ± 23.24	51.37 ± 25.04	0.317
	Incontinence	28.57 ± 20.71	28.97± 21.150	0.658
	Evacuatory	38.06 ± 19.66	38.76 ± 19.20	0.310
	Urinary	30.17 ± 17.64	30.51 ± 18.49	0.850
Wexner Incontinence Score		6.49 ± 4.69	5.52± 3.98	0.450
ODS score		10.64± 4.54	10.47± 4.52	0.727
SF36	Physical Function	64.39± 30.01	73..52 ± 28.01	0.332
	Role Physical	56.49 ± 33.70	64.40 ± 29.99	0.309
	Role Emotional	62.78 ± 30,91	66.67 ±30.57	0.596
	Vitality	49.28 ± 13.97	46.58 ± 17.08	0.588
	Mental Health	59.08 ± 15.62	59.50 ± 18.55	0.630
	Social Function	50.79 ± 31.09	58.00 ± 33.63	0.332
	Bodily pain	52.39± 30.97	58.50 ± 29.91	0.404
	General Health	48.47 ± 22.99	47.50 ± 18.62	1.00

**Mann-Whitney U test*

Univariate logistic regression

On univariate analysis of all PROM and QoL outcomes, not one was found to be statistically significant in the prediction of the need for surgical intervention in patients with symptoms suggestive of obstructed defecation (table 4.6). Multivariate logistic regression was not possible, as there was only one variable identified with a p value of <0.2 on univariate analysis.

Table 4.6: Results of univariate logistic regression analysis

PROM variable	Odds ratio	95% Confidence Interval		P value
		Lower	Upper	
BBUSQ constipation	0.988	0.970	1.007	0.230
BBUSQ evacuation	1.009	0.986	1.033	0.435
BBUSQ incontinence	1.004	0.984	1.025	0.687
BBUSQ urinary	1.05	0.981	1.029	0.694
ODS score	0.992	0.888	1.108	0.886
Wexner Incontinence Score	0.952	0.858	1.057	0.360
SF-36				
Physical Functioning	1.010	0.995	1.026	0.197
Role: Physical	1.008	0.993	1.022	0.299
Bodily Pain	1.007	0.992	1.021	0.337
General Health	0.998	0.997	1.019	0.883
Vitality	0.987	0.958	1.018	0.413
Social Functioning	1.007	0.993	1.022	0.311
Role: Emotional	1.004	0.989	1.020	0.587
Mental Health	1.002	0.974	1.029	0.908

Receiver-operator characteristic curve analysis

On ROC curve analysis, again, no variable was found to be predictive of the need for surgery in patients with ODS symptoms (table 4.7). In an attempt to understand the reasons behind the lack of meaningful statistical correlation between PROMs and the need for surgery, each individual ODS score response was compared between those identified as suffering with obstructed defecation with an identified structural cause versus a functional cause, such as puborectalis syndrome. This data was held within the database. Through Mann-Whitney testing of each individual response of the ODS (scored from 0-4) and the final total ODS score (max 20), for those with a structural versus functional defecatory disorder, there were statistically significant differences identified between groups with relation to straining, enema/laxative use, presence of constipation and the overall score, with those patients presenting with a functional defecatory disorder having higher scores in these categories in addition to a higher overall ODS score (table 4.8).

Table 4.7: results of ROC curve analysis

	AUC	SE	P value	95% Confidence Interval		Cut-off (Youden's)	Sensitivity	Specificity
				Lower	Upper			
BBUSQ Constipation	0.435	0.068	0.313	0.301	0.569	45.85	0.563	0.676
BBUSQ Incontinence	0.531	0.071	0.624	0.393	0.670	4.15	0.125	0.926
BBUSQ Evacuation	0.564	0.064	0.329	0.439	0.668	42.73	0.625	0.485
BBUSQ Urinary	0.514	0.075	0.828	0.368	0.661	22.6	0.5	0.632
ODS score	0.470	0.072	0.686	0.329	0.612	14.5	0.938	0.206
Wexner Score	0.454	0.065	0.498	0.328	0.581	11.25	0.938	0.176
Physical Function	0.567	0.062	0.339	0.444	0.690	67.08	0.818	0.47
Role Physical	0.561	0.068	0.382	0.428	0.694	67.71	0.545	0.614
Body pain	0.544	0.070	0.524	0.407	0.682	68.75	0.455	0.651
General Health	0.473	0.062	0.697	0.352	0.594	47.5	0.591	0.506
Vitality	0.484	0.072	0.819	0.342	0.626	40.625	0.773	0.265
Social Function	0.554	0.070	0.436	0.417	0.691	68.75	0.455	0.651
Role Emotional	0.535	0.068	0.614	0.400	0.670	37.51	0.864	0.253
Mental Health	0.525	0.068	0.720	0.393	0.657	55.63	0.682	0.434

Table 4.8: Individual ODS scores for structural versus functional causes of obstructed defecation

	Structural cause (n=112)	Functional cause (n= 34)	P value[#]
Presence of straining	2.47+/-1.15	3.02+/- 1.03	**0.009**
Incomplete evacuation	2.87+/-0.93	2.94+/-1.10	0.720
Laxative/enema use	1.66+/-1.61	2.32+/-1.66	**0.046**
Need to interdigitate	1.63+/-1.52	1.59+/-1.58	0.905
Presence of constipation	2.32+/-1.36	2.79+/-1.32	**0.075**
Overall ODS score	10.86+/-4.56	12.68+/- 4.40	**0.041**

Values expressed as Mean +/- SD. Only those from database with a completed ODS score at initial visit shown. [#]Mann-Whitney test

Discussion

This is the first study of its kind in the literature which explores the relationship between the initial subjective scoring systems applied in a clinic setting and the subsequent treatment journey the patient embarks on. A BBUSQ incontinence domain score of 39.5 or more was a fair predictor of the need for surgery with a sensitivity of 65.1% and specificity of 70.7% for patients presenting with faecal incontinence. The WIS had an AUC of 0.696, which was close to being a fair predictor.

Several domains of the SF-36 were also found to be fair predictors of the need for surgical intervention in FI sufferers: SF (AUC 0.787), PF (AUC 0.701), RP (AUC 0.704), MH (AUC 0.730) and GH (AUC 0.709). This does make sense given that one would expect a patient with FI that is severe enough to warrant surgery would also have significantly impacted global QoL.

None of the variables were good predictors, suggesting that in isolation a scoring system is not enough to make any treatment assumptions. However, if a patient demonstrated scores above the cut-off point defined by Youden's index for each of these domains, then this could certainly indicate this patient may be one worthy of referral to a tertiary referral centre sooner rather than later.

In stark contrast to these findings was the ODS cohort of patients, where no relationship between the used PROMS and maximal treatment outcomes was demonstrable. The same series of PROMS were shown to be more closely associated with the need for surgical intervention in patients with faecal incontinence compared to those with obstructed defecation. This is despite the PROMS used acting as a wide representation of all symptoms encountered in both disease states. The underlying reasons for this are likely to be multifactorial. Patients presenting with faecal incontinence with a recognised and treatable cause such as a sphincter defect post OASI may be more readily offered treatment, and also more willing to accept an invasive treatment strategy over conservative measures due to the social embarrassment of faecal incontinence. It is likely that the sufferer has had a sudden and discernable change in bowel habit after an insult to the anal sphincter complex in the majority of cases, such as post low anterior resection or OASI, and therefore may find the change in bowel function to be insurmountable. In contrast, in patients with obstructed defecation, the mechanism is more likely to be multifactorial, the solution more complex and requiring a more MDT approach. Symptoms have likely developed gradually over time, and therefore this degree of chronicity may impact on immediate treatment decisions. Additionally, in patients who maintain anal continence, social embarrassment may be less so than those with uncontrolled continence issues. Patients may therefore be persuaded to manage their symptoms with more conservative measures such as interdigitation of the vagina, laxatives and biofeedback physiotherapy.

An additional analysis of each question within the ODS score for those with a functional versus structural cause of obstructed defecation was performed. This showed that there were significant differences both in a number of individual score items and the overall ODS score, but with those with a functional cause scoring higher (indicating worse symptoms). Therefore, it is very difficult to ascertain from PROM data alone who requires surgery versus who does not, as some of those who have a functional cause and can be managed with biofeedback training rate their obstructed defecation scores higher than those who have a true structural cause. On examining the literature,

there exist no similar studies attempting to identify a relationship between PROMs and the requirement for surgery in patients presenting with symptoms of defecatory dysfunction. This highlights that in isolation it is likely that PROMs are not sufficient within this patient cohort to identify those requiring surgical intervention.

Limitations

It is feasible that the choice of questionnaires used may have impacted on the lack of positive correlation between PROMs and maximal treatment outcomes. There are numerous PROM questionnaires readily available, and the choice of one over another is down to centre preference. Similar studies could replicate this study using a variety of different PROMs to determine if a different score is more closely correlated with treatment outcomes.

4.3 Chapter Conclusions

This chapter aimed to ascertain the predictive ability of PROMS in two separate cohorts of patients; one presenting with symptoms of anal incontinence and another presenting with symptoms of obstructed defecation in the determination of who is likely to require surgical intervention. The results between the two patient groups assessed are quite remarkably different. In particular with ODS patients, the PROMs used had no early predictive role in identifying who may need surgery. In patients with FI, the BBUSQ faecal incontinence domain was a fair predictor, along with several domains of the SF36. These two PROMs questionnaires could conceivably be applied in a community setting, and if patients score highly in these domains, then consideration given for early referral to a tertiary centre given.

In a similar fashion, the next two chapters include a similar analysis of ARM and MRD and their ability to predict the need for surgery.

CHAPTER 5: THE ROLE OF ANORECTAL MANOMETRY IN THE PREDICTION OF THE NEED FOR SURGICAL INTERVENTION IN FAECALLY INCONTINENT PATIENTS.

Publications related to this chapter:

Anorectal Manometry versus patient reported outcome measures as a predictor of maximal treatment for faecal incontinence Ramage L, Qiu S, Yeap Z, Simillis C, Kontnvounisios C, Tekkis P, Tan E. *Annals of Coloproctology 2019. [In Press]*

5.1 Introduction and aims of chapter

This chapter explores the role of anorectal manometry in the prediction of the need for surgical intervention in patients presenting with faecal incontinence.

Objectives of the chapter

Following on from the previous chapter, where the role of specific PROMS were assessed in their relationship with the need for surgical intervention were explored, this chapter aims to ascertain whether specific and commonly used anorectal manometry parameters can act as predictors of the need for surgery in faecally incontinent patients.

The diagnostic accuracy of ARM is largely unclear, with sensitivities and specificities in its ability to diagnose the presence of FI varying significantly between studies [112, 189]. With significant variations in practice and newer models being developed, including HR-ARM, it is difficult to account for such heterogeneity when comparing results from different centres.

This primary objective of this chapter was to ascertain whether any correlation existed between ARM measurements taken with a consistent system and methodology and the need for surgery in faecally incontinent patients, which can be thought of as a surrogate marker for significant disease severity.

Additionally, a further objective of this chapter was to ascertain the degree of correlation between patient reported outcome measures (PROMs) and ARM measurements specific to external and internal anal sphincter function.

5.2 Study: Is anorectal manometry predictive of the need for surgery in faecal incontinence?

Methods

Data was prospectively collected of all-comers to the pelvic floor unit who were undergoing assessment and treatment of reported symptoms of faecal incontinence and entered onto the approved database as previously discussed in chapter 3. Patients presenting with faecal incontinence underwent clinical assessment in the same manner as discussed in previous chapters, with the use of patient interview, PROMS, physical examination and the use of ARM. ARM values compared were at first consultation and prior to any subsequent treatment intervention. Additionally, patients underwent endoanal sphincter ultrasound assessment to assess for the presence of any sphincter defect. All patients presenting with FI were initially sent for pelvic floor physiotherapy and/or started on bulking agents such as loperamide. Patients who needed surgical intervention were managed as according to the NICE clinical guidelines for the management of faecal incontinence in adults, and underwent either some form of sphincteroplasty or implantation of a sacral nerve stimulator device[57]. Patients who had incomplete datasets were excluded from analysis.

The primary outcome measure was whether patients required surgery as a maximal treatment intervention (SNS or sphincter repair), or were managed in full conservatively.

Patients were included if they had presented with symptoms of anal incontinence, and had undergone anorectal manometry testing as part of initial assessment prior to any treatment intervention taking place, and where final treatment outcomes were readily available.

Statistical methods

Spearman's rank test was used to assess the degree of correlation between ARM and PROM measurements of external anal sphincter (EAS) and internal anal sphincter (IAS) function. Symptoms of faecal urgency and faecal urge incontinence were taken to be most indicative of poor EAS functionality [190, 191]. In the included questionnaires, these symptoms were best denoted by the BBUSQ Q3 (*can you hold onto your motions for more than five minutes*?), Q4 (*do you ever have to rush to the toilet to open your bowels?) and Q5 (do you ever leak stool as a result of having to rush to the*

toilet?) IAS function, evidenced by passive faecal incontinence was largely assessed through the maximum resting pressure on ARM testing [191], and with Q6 of the BBUSQ " *do you leak stool for no obvious reason and without feeling that you want to go to the toilet*?" For all of the above BBUSQ questions, those indicating never or occasionally were considered to have a negative answer, and those indicating symptoms which were most or all of the time had a positive answer.

Binary logistical regression analysis was performed for ARM, to determine significant variables within each in determining the maximal treatment required. The ARM measurements obtained and used in this study have been described in the general methods chapter. Univariate analysis of all factors was performed, with subsequent multivariate logistic regression analysis on factors with a $p<0.2$ on univariate analysis.

Finally, the predictive ability of different ARM parameters domains in terms of determining need for surgical intervention were assessed through the performance of a diagnostic accuracy test, with construction of receiver operating characteristic (ROC) curves. The Youden index was used for each variable to determine the optimal cut-off value with its respective sensitivity and specificity. An AUC greater than 0.7 was deemed to be a fair discriminator for predicting the need for maximal treatment intervention, which can therefore be considered as a marker of worse symptom severity.

Results

Data was available for 276 patients. 228 patients underwent conservative treatment: the majority (n=152) had biofeedback alone. A significant proportion had no treatment for their symptoms. Only a handful (n=16) elected to use a transanal irrigation device such as Peristeen. A total of 48 patients underwent surgical intervention, either in the form of sacral nerve stimulation (n=37) or sphincter reconstructive surgery (n=11) (table 5.1)

Table 5.1: Maximal treatment received

Treatment received		Number of patients
Conservative	None/medical	60
	Biofeedback	152
	Transanal Irrigation	16
Surgical	SNS	37
	Other surgery	11
Total		**276**

The majority of patients were female (89.8%). The mean overall age of the group was 43.59 years. Sphincter weakness was the major aetiology (79.3% of all patients), predominantly secondary to obstetric injury during childbirth. Mean age and the proportion of male gender were found to be significantly different in the conservatively versus surgically managed patients. In term of aetiologies, there was a significant difference in the proportions of obstetric sphincter injury, rectal resection and idiopathic patients between the conservative and surgical groups (table 5.2) Significantly more OASI patients were managed conservatively than surgically. In contrast, more patients with idiopathic FI or those who had undergone prior rectal surgery were managed surgically. Looking at the mean ARM parameters of interest in the conservatively managed versus surgically managed groups (table 5.3), the MSPI was significantly lower in the surgically managed group ($p = 0.001$). However, there were no statistically significant differences found between groups in the other anorectal physiology parameters.

Table 5.2: Patient demographics

		Maximal treatment			p-value
		Conservative (% of conservative)	Surgical (% of surgical)	All/total (% of total)	
Number		228	48	276	-
Gender (female/male)		211/17	37/11	248/28	**0.001***†
Age (mean ± SD)		41.25 ± 14.30	54.63 ± 15.11	43.59 ± 15.28	**0.000****†
Aetiology					
Sphincter weakness	**Postsurgical sphincter injury**	7 (3.07%)	3 (6.25%)	10 (3.62%)	0.386*
	Obstetric sphincter injury	170 (74.56%)	23 (47.92%)	193 (69.93%)	**0.001***†
	Sphincter defect unknown aetiology	1 (0.44%)	1 (2.08%)	2 (0.72%)	0.318*
	No sphincter defect	11 (4.82%)	2 (4.17%)	13 (4.71%)	1.000*
Neuropathic/Central nervous system		8 (3.51%)	1 (2.08%)	9 (3.26%)	1.000*
Proctitis		2 (0.88%)	1 (2.08%)	3 (1.09%)	0.438*
Structural pelvic floor abnormality (eg intususseption		9 (3.95%)	1 (2.08%)	10 (3.62%)	1.000*
Prior rectal resection (eg IPAA, low anterior resection)		5 (2.19%)	10 (20.8%)	15 (5.43%)	**0.000***†
Paradoxical puborectalis contraction		2 (0.88%)	0 (0.00%)	2 (0.72%)	1.000*
Idiopathic		13 (5.70%)	6 (12.5%)	19 (6.88%)	**0.099***†

** p-value calculated via Fisher's exact test; ** p-value calculated via Mann-Whitney U test; † p-value < 0.05*

Table 5.3: Mean ARM parameters

		Conservative	Surgical	P value*
ARM	**Anal Canal Length**	2.94 ± 0.4	3.01 ± 0.2	0.170
	Maximum resting pressure (RP)	61.68 ± 18.6	51.98 ± 17.2	**0.001**†
	Maximum squeeze increment	35.21 ± 29.8	29.87 ± 22.2	0.245
	5-second squeeze increment	27.59 ± 19.1	21.46 ± 6.8	0.054
	Involuntary Cough Pressure	46.17 ± 23.9	44.10 ± 15.5	0.623
	Threshold Volume to distension	31.18 ± 12.6	36.42 ± 23.3	0.217
	Urge Volume to distension	56.49 ± 18.8	63.50 ± 25.1	0.119
	Maximum Tolerated Volume	100.56 ± 28.7	104.48 ± 35.4	0.962

ARM: Anorectal Manometry, BBUSQ: Birmingham Bowel and Urinary Symptoms Questionnaire, WIS: Wexner Incontinence score, SF36: Short Form 36 quality of life questionnaire. p-value calculated via Mann-Whitney U test† p-value < 0.05*

Spearman's correlation between ARM and PROMS in assessing EAS and IAS function

Looking at the correlation between specific questions within the BBUSQ which were taken to be surrogate markers of EAS and IAS function and corresponding ARM measurements, as described in the methods section, the MSPI showed significant correlation with defecation deferral time (Spearman's correlation -0.155, p = 0.023). The presence of the symptom of faecal urgency also showed a correlation with MSPI approaching statistical significance (Spearman's correlation -0.131, p = 0.055) (table 5.4).

Table 5.4. Non-parametric correlation: ARM variables and specific BBUSQ questions

ARM variable	BBUSQ questions	Correlation coefficient	p-value[#]
Maximum squeeze increment	BBUSQ question 3	- 0.155	**0.023**[†]
	BBUSQ question 4	- 0.131	0.055
	BBUSQ question 5	- 0.078	0.254
5-second squeeze increment	BBUSQ question 3	- 0.136	0.208
	BBUSQ question 4	- 0.064	0.556
	BBUSQ question 5	- 0.071	0.509
Maximum resting pressure	BBUSQ question 6	- 0.211	**0.002**[†]

ARM: Anorectal Manometry, BBUSQ: Birmingham Bowel and Urinary Symptoms Questionnaire
 # p-value calculated via Spearman's rank test. † p-value < 0.05

IAS function, evidenced by passive faecal incontinence was assessed for correlation with the maximum resting pressure on ARM testing, and was shown to be statistically significant; Spearman's correlation coefficient was -0.211 (p = 0.002).

Logistic regression analysis

Univariate binomial logistic regression analysis was performed using continuous data for all sensory and motor ARM variables (Table 5.5).

Table 5.5: Binomial logistic regression analysis of ARM variables

Variables		B	Std. Error	Wald	P value	Odds Ratio	95% C.I.#	
							Lower	Upper
ARM	**Anal Canal Length**	0.739	0.536	1.901	0.168	2.094	0.732	5.988
	Maximal Resting Pressure	-0.032	0.010	10.334	**0.001**†	0.969	0.950	0.988
	Maximal Squeeze Increment	-0.008	0.007	1.371	0.242	0.992	0.979	1.005
	5-second Squeeze Increment	-0.042	0.018	5.659	**0.017**†	0.959	0.927	0.993
	Cough Pressure	-0.004	0.008	0.328	0.567	0.996	0.981	1.011
	Threshold Volume to Distension	0.019	0.009	4.091	**0.043**†	1.019	1.001	1.037
	Urge Volume to Distension	0.015	0.007	4.535	**0.033**†	1.015	1.001	1.029
	Maximal Tolerated Volume	0.004	0.005	0.679	0.410	1.004	0.994	1.014

 # 95% confidence interval of Odds Ratio
† p-value < 0.05

Of the ARM results, maximum resting pressure (p = 0.001), 5-second squeeze increment (p = 0.017), threshold volume to distension (p = 0.043) and urge volume to distension (p = 0.033) were found to be statistically significant.

On multivariate analysis of all ARM variables with a p value of <0.2 on univariate analysis (table 5.6), anal canal length, the maximum resting pressure and the 5-second squeeze pressure were all found to be statistically significantly associated with the need for surgery.

Table 5.6: Results of multivariate analysis

Variables		B	Std. Error	Wald	P value	Odds Ratio	95% C.I.#	
							Lower	Upper
ARM	**Anal Canal Length**	1.512	0.751	4.057	**0.044**†	4.537	1.042	19.765
	Maximal Resting Pressure	-0.033	0.010	10.587	**0.001**†	0.967	0.948	0.987
	5-second Squeeze Increment	-0.050	0.022	5.359	**0.021**†	0.951	0.911	9.992
	Threshold Volume to Distension	0.017	0.011	2.231	0.135	1.017	0.995	1.040
	Urge Volume to Distension	0.013	0.006	2.003	0.157	1.013	0.995	1.031

 # 95% confidence interval of Odds Ratio
† p-value < 0.05

Receiver-operator curve analysis

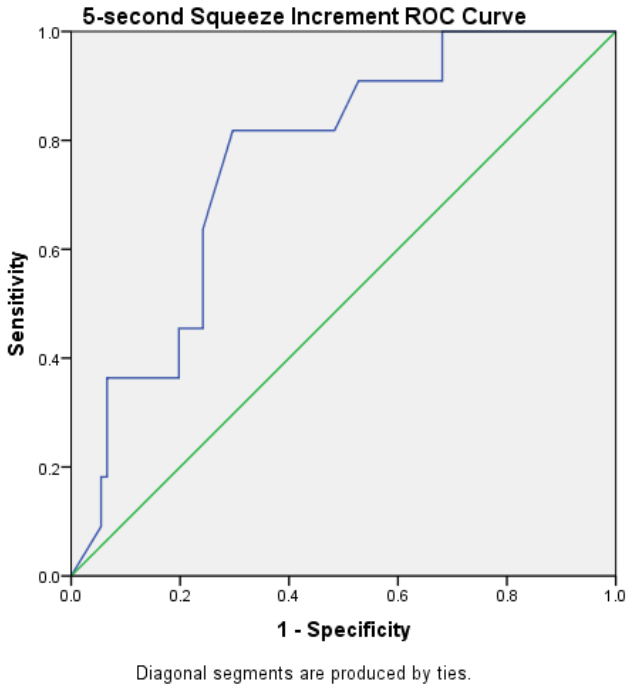
ROC curve analysis was performed on the variables to determine their ability in predicting maximal treatment. This was performed as a separate analysis to the univariate and multivariate analysis performed earlier (table 5.7).

Table 5.7. ROC curve analysis of patient variables.

Variables		AUC[#]	Std. Error	P value	95% C.I.[##]		Cut off (Youden)	Sensitivity	Specificity
					Lower	Upper			
Age		**0.748**[†]	0.039	0.000	0.672	0.823	37.605 yrs	0.854	0.573
ARM	**Anal Canal Length**	0.539	0.042	0.391	0.457	0.622	2.750 cm	0.979	0.127
	Max Resting Pressure	0.648	0.043	0.001	0.563	0.732	56.000 mmHg	0.667	0.583
	Max Squeeze Increment	0.556	0.046	0.225	0.465	0.647	27.500 mmHg	0.604	0.531
	5-second Squeeze Increment	**0.762**[†]	0.066	0.005	0.633	0.891	16.500 mmHg	0.818	0.703
	Involuntary Cough Pressure	0.555	0.115	0.606	0.330	0.780	36.500 mmHg	0.625	0.588
	Threshold Volume to distension	0.405	0.071	0.179	0.267	0.544	41.000 ml	0.571	0.253
	Urge Volume to distension	0.354	0.070	0.058	0.216	0.492	52.000 ml	0.294	0.500
	Max Tolerated Volume	0.481	0.136	0.857	0.214	0.747	102.500 ml	0.625	0.446

On ROC curve analysis, the only ARM parameter that had an AUC greater than 0.7 was the 5 second squeeze increment, with an AUC of 0.748. Using the Youden index, the optimum cut-off point for the 5-second squeeze increment in predicting the need for surgical intervention in FI was less than 16.5mmHg. This figure had a sensitivity of 81.8% and a specificity of 70.3%. The graph for this variable is shown below (figure 5.1):

Figure 5.1: ROC curve 5-second squeeze increment



Discussion

This chapter aimed to utilise commonly measured ARM parameters used in the assessment of motor and sensory function of the anal canal in patients presenting with anal incontinence to predict the need for surgical intervention. Compared with the results obtained in chapter 4, which looked at various PROMS and predicting the need for surgery, ARM appeared to be a less sensitive investigation. On initial comparison between surgically versus conservatively managed groups, the maximum resting pressure was the only value which was significantly lower in those undergoing surgery. On multivariate regression analysis, anal canal length, maximum resting pressure and endurance 5-second squeeze were all associated with the need for surgery. Anal canal length did not show any significant correlation on univariate logistic regression (p= 0.168), however was significant on multivariate analysis (p=0.044). This is known as a suppressor effect, where there is zero correlation with the dependent variable, but due to correlation with another predictor, it acts to improve the overall effect of the predictors in the multivariate analysis[192].

When ROC analysis was performed, the majority of ARM measurements taken had a low sensitivity and specificity in the prediction of the need for sphincter repair or SNS

in faecally incontinent patients. The only factor which was considered to be a fair predictor for the need for surgical intervention was a poor endurance squeeze over five seconds. Using Youden's index, this suggested that the inability to maintain a minimum of 16mmHg incremental pressure over the baseline resting pressure over a five second period was the single most important ARM parameter when considering the need for surgery. This had a sensitivity of 81.8% and a specificity of 70.3%. The maximum resting pressure obtained had a lower sensitivity of 63.8% and a specificity of 58.3% in the prediction of surgical intervention, with a corresponding AUC that suggested this was a "poor" indicator of the need for surgery. The sensory parameters had AUCs that indicated failed tests, as did the maximum squeeze pressure increment. Overall, the results indicate that the most useful parameters within ARM testing within this cohort were the 5-second squeeze pressure increment and the maximum resting pressure obtained. This could indicate that these parameters are the most reliable indicators of the need for further surgery and should be the parameters most focussed on during ARM assessment.

This study is relatively unique in current published literature. The only study with a similar objective was one undertaken by Hill et al in 2006[193], which studied a relatively small group of 35 patients referred for investigation of FI. Their aim was to identify the role of ARM and EUS in the prediction of clinical outcomes in faecally incontinent patients. They found no correlation with either ARM or EUS and clinical outcome.

There are however several published studies which attempt to use ARM in the prediction of the presence or severity of AI. Pehl et al[112] studied 144 healthy volunteers and 559 patients with anal incontinence. Included participants suffered from varying severities of anal incontinence to gas, liquid stool and solid stool. The authors compared ARM measurements of motor and sensory function in those with FI to the healthy volunteers. They found significant differences in the mean RP, mean SP and volume to urge in FI patients, and overall showed ARM had a sensitivity of 91.4%, with a specificity of 63.2% and a diagnostic accuracy of 85.8% in prediction of FI. Another cohort of patients studied by Felt-Bersma et al[194] demonstrated the mean squeeze pressure to be the most discriminatory of all ARM measurements when used to predict the presence of FI. However for all measurements, there was almost complete overlap with patients who had been recruited as healthy volunteers. Lam et al[195], in their comprehensive study of 600 patients, found that a reduced mean RP and

mean SP were significantly associated with the presence of FI in both males and females. Additional positive associations in females were a shorter sphincter length and lower rectal capacity.

A few studies attempted to determine whether ARM could be used in order to predict the presence of a sphincter defect. Roos et al[196] in their study of 159 patients with OASI defined a mean resting pressure of 95mmHg and a mean squeeze increment of 53mmHg, to allow for the detection of 90% of sphincter defects. Reddymasau et al[197] in their cohort of 27 patients found that anorectal manometry in combination with the use of endoanal ultrasound was useful in detecting an abnormality in 25/27 patients.

Within this study, Spearman's correlation was used in order to attempt to define whether specific questions from the BBUSQ could be used as a surrogate for ARM testing, with the hypothesis that this may be more accessible in a community or non-tertiary setting, and may help guide referrals. The results showed a significant correlation between BBUSQ Q3 (*can you hold onto your motions for more than five minutes*?) and the maximum squeeze pressure and Q6 of the BBUSQ " *do you leak stool for no obvious reason and without feeling that you want to go to the toilet*?" and the mean resting pressure. This would suggest that the presence of certain features in the clinical history or as assessed by incontinence scoring systems may give an indication as to the likelihood of EAS or IAS injury, and therefore a lack of these specific symptoms in the history could be used as a "rule out" for the presence of significant motor dysfunction of the anal sphincter complex, therefore allowing for primary care practitioners to assess patients within the community and make decisions regarding the appropriateness of direct referral to physiotherapy services rather than to tertiary pelvic floor services.

Limitations

A notable limitation of this study is the large proportion of patients presenting with FI in this patient population have had an OASI; however it is believed that the proportions represented by the study cohort included in this chapter are representative of the general case mix presenting to a tertiary pelvic floor service. An additional observation is that here were only seven patients (2.54%) within the cohort who were documented as having a post-surgical sphincter injury secondary to lateral sphincterotomy. This would seem to be a low number given the high complication rate of the procedure[198]. Another potential limitation is the risk of reporting bias. This

is due to the voluntary nature of patient involvement and completion of PROMS, as it is not inconceivable that those who complete PROMs may be more motivated due to worse symptoms and wanting to relay these more effectively to the clinical team. This is an issue which relates to the majority of the thesis, and this is evidenced by the total numbers of patients held within the database versus the numbers of described patients within this thesis.

As previously been discussed, an air-perfused catheter ARM system was used for all patients both within this study and throughout all patients who went ARM in this thesis, with newer technologies widely available. However the air-perfused systems have shown to be non-inferior previously to other systems[199]. Therefore it was viewed as beneficial to continue to use the same system throughout the duration of the research period in order to ensure consistency of results and to allow for amalgamation and usage of the large database already in existence.

There is also a potential risk of inter-operator variability; however all ARM measurements and interpretation of obtained results were undertaken by, or under the close supervision of, a single pelvic floor colorectal surgeon with extensive experience of performing ARM. In addition the original equipment used and methods utilised were adhered to throughout the lifespan of the database.

5.3 CHAPTER CONCLUSIONS

This chapter has documented the exploration of ARM parameters testing sensory and motor function of the anorectal sphincter complex in patients presenting with FI. In particular, the correlation of specific BBUSQ questions with ARM was explored, in addition to the main focus of this chapter; whether ARM was predictive for the need for surgery.

Whilst the inability to maintain a sustained squeeze pressure was shown to be a fair indicator, other parameters on ARM testing were less predictive of the need for surgery. Looking back at the results from the previous chapter, where predicting the need for surgery was more reliably predicted by the various PROMs used within this thesis, clinical assessment and a robust assessment of PROMS may prove to be a more reliable determinant of the maximal treatment intervention required in faecally incontinent patients compared to ARM measurements. Having said that, there is most definitely still a role for ARM, with sustained squeeze pressure being most useful in

assessing the need for surgery. ARM also comes into its own in assessing response to treatment interventions and allows a documentation of treatment effect, a topic not covered by this research. Additionally, newer models such as HRAM may bear a closer correlation with disease severity and the need for intervention. The caveat to this is that these sophisticated systems are costly and even more scarcely encountered, and therefore the ability to apply a screening process to patients in a community setting will allow for streamlining of services and diverting of patients with less significant symptoms to other primary care services such as biofeedback and pelvic floor physiotherapy, at least in the first instance. Moving forward, with the currently used technology used for ARM assessment within the local unit, greater weighting should be given to the sustained squeeze increment and resting pressure results with regards to decision-making in patients with FI compared to the other ARM parameters used currently.

CHAPTER 6: THE ROLE OF MR DEFECOGRAPHY IN THE DETECTION OF PELVIC FLOOR DYSFUNCTION.

Publications related to this chapter:

1. **Magnetic resonance defecography versus clinical examination and fluoroscopy: a systematic review and meta-analysis.** Ramage L, Simillis C, Yen C, Lutterodt C, Qiu S, Tan E, Kontovounisios C, Tekkis P.Tech Coloproctol. 2017 Dec;21(12):915-927. doi: 10.1007/s10151-017-1704-y.
2. **Can we correlate pelvic floor dysfunction severity on MR defecography with patient-reported symptom severity?** Ramage L, Georgiou P, Qiu S, McLean P, Khan N, Kontnvounisios C, Tekkis P, Tan E Updates Surg. 2017 Dec 19. doi: 10.1007/s13304-017-0506-0. [Epub ahead of print]

6.1 Introduction and aims of chapter

MR-defecography (MRD) is a highly detailed examination that allows for excellent soft tissue differentiation due to its T2-weighted dynamic images. It has certain benefits, such as a lack of ionising radiation, and the ability to visualise all three compartments of the pelvic floor in unison. However, its exact role and clinical significance remains unclear. Few attempts have been previously made to correlate MRD findings with symptom severity or the need for treatment intervention within published literature. The methodology of performing MRD is outlined in chapter 3.

Chapter outline and objectives

This chapter comprises of three studies, and focuses on the role of MR-defecography in the detection of pelvic floor abnormalities and its role in the decision-making process.

The first study employs meta-analytical techniques in order to compare the detection and miss rates of MRD versus clinical examination and also fluoroscopic techniques such as conventional defecography (CD) and colposystodefecography with or without the additional use of small bowel contrast to allow for assessment of the presence of enterocele.

The second study attempts to assess the degree of correlation between various PROMs and different MR variables. It comprises a cohort of 170 patients and takes the form of

a binary logistic regression analysis of numerous MRD variables in addition to patient factors such as age and historical pelvic floor surgery against the several patient-reported outcome measure tools already visited within this thesis.
The final study looks at key MRD variables and whether these can be used to predict the need for surgical intervention for pelvic floor dysfunction in patients presenting with symptoms suggestive of obstructed defecation.

The overall aim of this chapter is to explore the role of MR-defecography in the diagnostic work-up of patients presenting with pelvic floor dysfunction.

The overall chapter objectives are as follows:

1. To explore the role of MRD in comparison to physical examination and conventional fluoroscopy
2. To identify which MRD variables most closely correlate with patient-reported symptom severity
3. To identify which MR variables can be used to predict the need for surgical intervention in patients with obstructed defecation

6.2. Study 1: How does MR-defecography compare to clinical examination and fluoroscopic techniques in the detection of pelvic floor structural abnormalities?

This study was designed to allow comparison of three different methods of assessment of pelvic floor dysfunction in terms of their ability to detect significant pelvic floor abnormality. This study describes meta-analytical methods used in order to uniformly compare papers which focus on the benefits of one test over another, and given an overall impression as to which diagnostic modality has a better detection rate and lower miss rate over the other for each parameter described above.

Methods

As discussed in chapter 3, the following systematic review and meta-analysis was undertaken in accordance with the guidance set out in the PRISMA guidelines.

Search strategy

Two reviewers (LR & CS) working independently from one another undertook a comprehensive literature search of the following databases: MEDLINE, Embase and the Cochrane Central Register of Controlled Trials (CENTRAL). The following search terms were used in various combinations: (MRI OR Magnetic Resonance Imaging) AND (diagnosis OR assessment OR identify OR evaluation) AND (pelvic floor OR rectocele OR cystocele OR rectal intussusception OR outlet obstruction OR pelvic organ prolapse). In order to expand the net as wide as possible, the related articles function in Pubmed was also used; additionally references of included studies were also searched for relevant articles. There were no language restrictions placed on included studies.

Study selection

Studies were selected for inclusion if they reported detection rates with MRD versus EITHER clinical examination AND/OR fluoroscopic techniques of at least one of the seven structural abnormalities listed below:

1. cystocele
2. middle compartment descent (including vaginal vault post-hysterectomy)
3. rectocele
4. intussusception
5. rectal prolapse
6. enterocele
7. perineal descent

Data extraction

Data was extracted by two authors (LR & CY) working independently of one another.

In cases of disagreement, a third opinion was sought from CS.

The term ‘fluoroscopic’ was used as an umbrella term to signify a number of different investigatory methods with a similar underlying principle: dynamic X-ray proctography with or without the use of additional contrast mediums to opacify the small bowel, bladder, and vagina in females. This included a number of terms such as “conventional defecography” and “barium proctography”, which concentrated on the posterior compartment only, and others such as “cystodefecography”,

"colposystodefecography" and "entero-colpocystodefecography" which included other compartmental opacification allowing comparison of detection and miss rates of abnormalities of the anterior and middle compartments. In cases where only the posterior compartment was assessed with fluoroscopy, additional abnormalities outwith the posterior compartment were excluded from this analysis.

For each of the above structural abnormalities of interest, the detection and miss rate was calculated as follows:

Detection rate = number of patients with evidence of abnormality divided by number of patients examined by that modality

Miss rate = number of abnormalities missed by that modality divided by the total number of abnormalities found overall

Statistical analysis

This meta-analysis was performed using the latest version of Review Manager: version 5.3. All variables were dichotomous in nature. The software was used in order to calculate the Odds Ratio (OR) with an associated 95% confidence interval (CI). The Mantel-Haenszel method was used to combine the OR for each of the outcomes of interest through use of a "random effect" meta-analytical technique. The random-effects model calculates a more conservative value when compared to the "fixed effect" model as it makes the assumption that there is a degree of variation between studies secondary to heterogeneity. Therefore, it generates a wider CI than that generated with a fixed effects model[200]. Between-study heterogeneity was assessed using the Chi2 (or $\chi 2$) test. A P value of $p<0.10$ was considered to be statistically significant. Between-study heterogeneity was quantified by "I^2", where the higher the I^2 value, the higher the risk of between-study heterogeneity[201]. In order to assess the quality of the included cohort studies, the Newcastle-Ottawa Scale for cohort studies was employed[202].

Results.

Figure 6.1 shows the details of the literature search. 2435 records were initially returned using the previously described search terms. After extraction of duplicate, 1867 record titles were reviewed. A further 1262 studies were excluded based on title

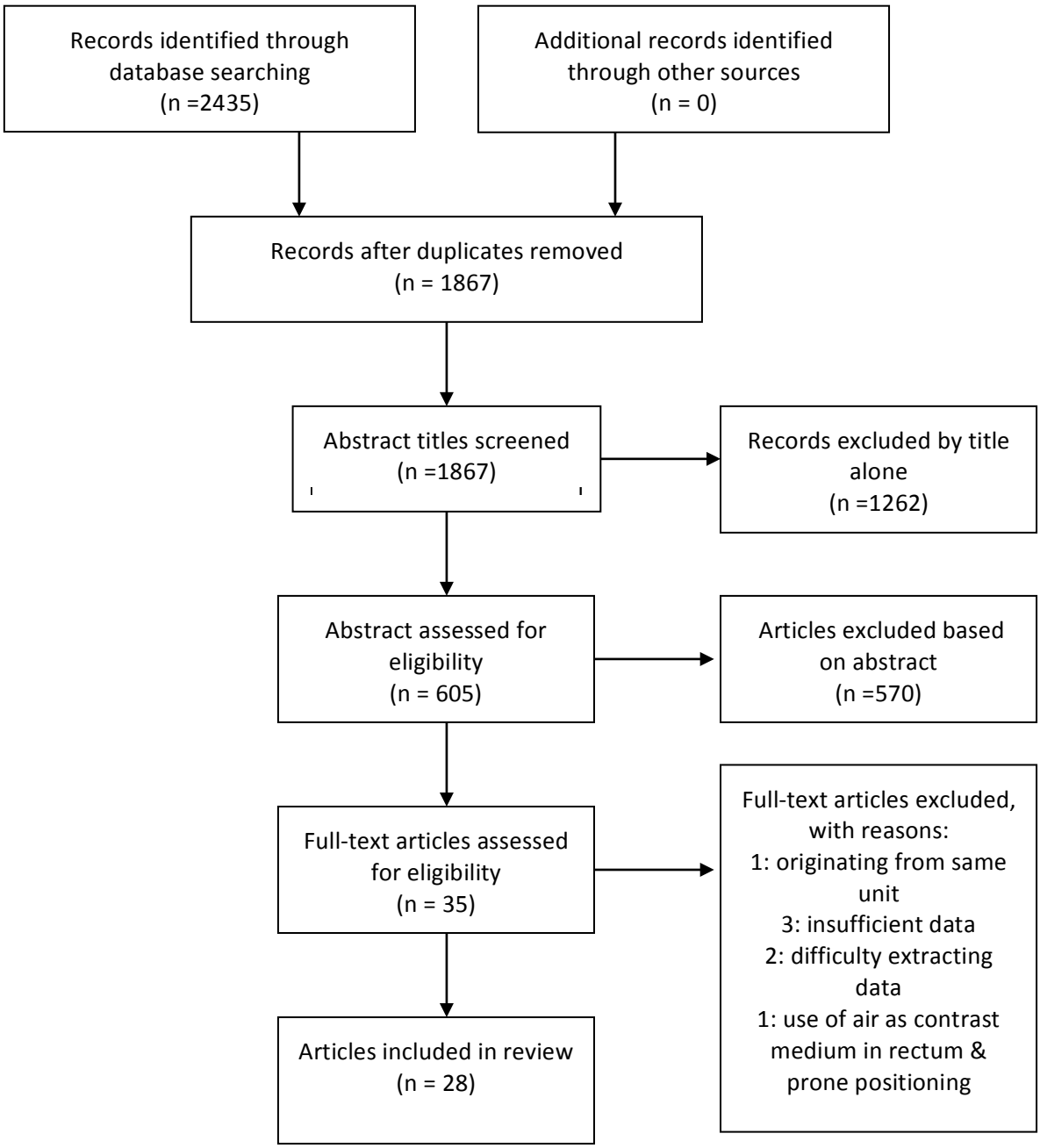
alone. Upon abstract review, 570 more clinical papers were excluded. Therefore, 35 full text manuscripts were analysed.

Upon close review of manuscript contents, the following exclusions were made based on content:

1. Gufler et al[203] was excluded as it originated from the same unit as a more recently published paper. Therefore it was impossible to exclude the possibility of partial data overlap.
2. Pannu et al[204] was excluded as the data was presented according to agreement by two separate reviewers, and therefore it was difficult to ascertain absolute numbers to allow accurate comparison of the two techniques.
3. Matsouka et al[205] was excluded as the authors conducted the study using only air in the rectum as a contrast medium with the patients in a prone position. All other studies used some form of rectal contrast, and therefore it was felt that this study was an unfair comparator to the other included studies.
4. Paetzel et al[206] was excluded as clinical examination was conducted using only proctoscopy.
5. A further two papers[207, 208] were excluded as data was insufficient to allow for the comparison in the manner described in the methods section above.

Overall, twenty-eight papers were included in the final analysis. Fourteen studies compared MRD against clinical examination [120, 126, 209-220]. Sixteen studies compared MRD and different fluoroscopic techniques [123, 214, 221-230]. Two studies compared all three methods, therefore were considered in each separate analysis. Two papers [120, 217] had originated from the same unit. The newer paper considered only two outcomes (rectoceles, enteroceles) and therefore was used for these outcomes alone; the majority of analysed data was extracted from the earlier paper.

Figure 6.1: Study flow diagram



In the manuscript published by Pannu et al[217], data from patients who underwent MRD without rectal contrast was excluded. In the study by Vanbeckevoort et al[123], MRDs were analysed with and without an evacuatory phase. Data was extracted from the MRD series with an evacuation phase in order to as best possible maintain consistency

of technique. In studies where two reference lines were discussed in interpretation of results, the pubococcygeal line (PCL) was used preferentially.
The Newcastle-Ottawa rating for each study is detailed in table 6.1 below.

Table 6.1: Newcastle-Ottawa rating for each study

Study	Selection (max 4)	Comparability (max 2)	Outcome (max 3)	Final score
Attenberger	3	1	2	*****
Azab	3	2	3	********
Bussen	3	2	3	********
Cappabianca	3	2	3	********
Cortes	3	0	3	******
Dvorkin	3	2	3	********
Elshazly	3	1	3	*******
Etlik	4	1	3	********
Faucheron	3	1	3	*******
Foti	3	1	3	*******
Gouse	4	2	2	********
Gufler	3	1	3	*******
Healy	3	1	3	*******
Kaufman	3	1	3	*******
Kelvin	3	1	3	*******
Lineman	4	2	3	*********
Martin	3	1	3	*******
Melchior	3	1	3	*******
Pannu	3	1	3	*******
Pfeifer	3	1	3	*******
Pilkington	3	1	2	******
Rentsch	3	1	3	*******
Song	3	1	3	*******
Vanbeckvoort	3	2	3	********
Vitton	3	2	3	********
Wang	3	1	3	*******
Woodfield	3	2	3	********

MRD versus clinical examination

Results

Fourteen studies compared MRD to clinical examination. There were 602 patients included overall[120, 121, 126, 209-213, 216-219, 231]. The demographics and outcomes reported for each study are given in table 6.2 below. Table 6.3 gives a tabulated version of the meta-analysis results.

Table 6.2: Studies comparing clinical examination versus MRD

Study	Year	Place	Study type	N	Mean age	Sex	Gold standard	MR Position	Outcomes compared[1]
Attenberger[218]	2015	Mannheim Germany	R	50	ND	F	None	Supine	R, E
Azab[209]	2014	Egypt	P	40	(20-65)	F	None	Supine	C, MCD, R, E
Cortes[210]	2004	RFH, London	P	51	64 (40-95)	F	None	Supine	C, MCD, R
Elshazly[211]	2010	Egypt	P	40	48.15+/-14.29	31F	None	Supine	C, MCD, R, E, RI, PD
Etlik[212]	2005	Turkey	P	46	35+/-9	F	None	Supine	C, MCD, R
Faucheron[213]	2014	Grenoble, France	P	50	51	F	None	Supine	RI
Gousse[232]	2000	California, USA	P	65	55 (23-880)	F	None	Supine	C, MCD, E, R
Kaufman[120]	2001	Baltimore, Maryland	P	22	58+/-13		None	Supine	C, S, PD, RI, RP, RI
Lineman[121]	2000	Munich, Germany	P	55	61	F	None	Supine	E
Martin[231]	2012	Valencia, Spain	P	30	60M(23-76)	28F	None	Supine	C, R, E, RI, RP
Melchior[216]	2014	Rouen, France	P	74	60.5M (30-81)	F	None	Unknown	R
Rentsch[219]	2001	Regensburg, Germany	P	20	57M (30-80)	13F	None	Supine	R, RI , RP
Woodfield[126]	2009	Providence USA	P	20	54.9 (41-84)	F	None	Supine	C, MCD, PD
Pannu[217]	2011	Baltimore, Maryland	P	39	58 (34-84)	F	None	Supine	R, E

[1] *C: cystocele; MC: middle compartment descent; R: rectocele; E: enterocele; RI: rectal intussusception; RP: rectal prolapse; PD: perineal descent*

Table 6.3: Summary of meta-analysis: MRD versus clinical examination detection rates and miss rates.

Outcome	No of studies	No of patients	MRI (%)	Clinical (%)	OR	P value	95% confidence interval		Heterogeneity	
							Lower	*Upper*	*I^2 (%)*	*P value*
Detection rates										
Cystocele	8	315	62.22	61.59	1.00	0.99	0.60	1.67	36	0.14
MCD	6	263	44.87	49.43	0.81	0.72	0.26	2.52	83	<0.01
Rectocele	10	439	51.25	53.76	0.94	0.82	0.52	1.69	67	<0.01
PD	3	82	75.61	64.63	1.46	0.69	0.23	9.25	82	0.02
Enterocele	8	323	37.16	25.08	2.23	0.01	1.21	4.11	34	0.16
RI	5	162	27.78	22.84	1.36	0.55	0.50	3.72	62	0.03
RP	2	52	7.69	7.69	0.87	0.91	0.08	9.20	47	0.17
Miss rates										
Cystocele	6	227	13.55	19.35	0.61	0.42	0.18	2.02	59	0.03
MCD	5	197	24.77	16.51	1.41	0.85	0.03	57.96	88	<0.01
Rectocele	9	373	14.08	14.29	0.87	0.83	0.25	3.10	60	<0.01
PD	3	82	4.62	21.54	0.32	0.52	0.01	9.89	74	0.02
Enterocele	7	257	1.20	37.35	0.04	<0.01	0.01	0.20	22	0.27
RI	5	162	28.57	30.16	1.08	0.94	0.13	9.09	62	0.03
RP	2	52	81.63	81.63	1.56	0.86	0.01	213.4	73	0.05

MCD: middle compartment descent; PD: perineal descent; RI: rectoanal intussusception; RP: rectal prolapse

A description of each individual outcome of interest is described below.

Cystoceles

Eight studies discussed detection rates of cystoceles, including 315 patients overall[120, 126, 209-212, 231, 232]. Detection rates between MRD and clinical examination were not significantly different (OR 1.00, 95% CI 0.60-1.67, p =0.99). Overall, MRD detected cystoceles in 62.22% of patients, and clinical examination in 61.59% (figure 6.2). The funnel plot for this outcome is shown as figure 6.3. The graph appears symmetrical and is not typical of publication bias.

Figure 6.2: Detection rate cystocele

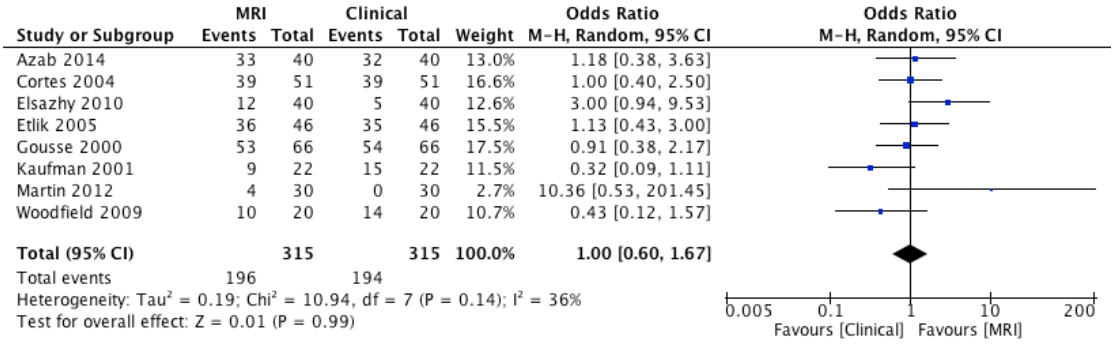
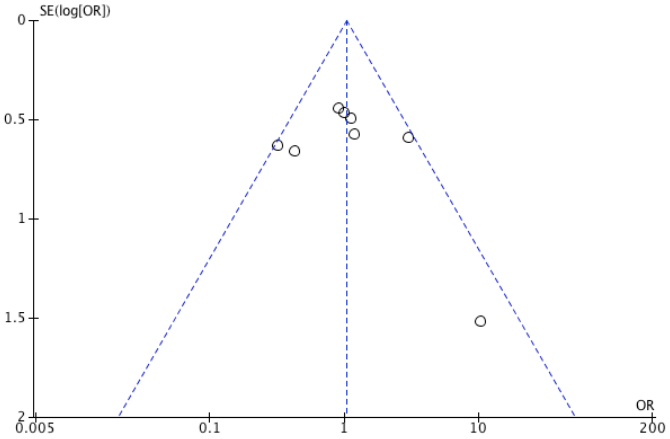


Figure 6.3: Funnel plot: detection rate cystocele



Six studies considered the miss rate of clinical examination versus MRD for cystoceles (n= 227)[126, 209-212, 231] (figure 6.4). The miss rate for MRD was lower at 13.55% compared to 19.35% with clinical examination; however this was not statistically significant (OR 0.61, 95% CI 0.18-2.02, p = 0.42). Heterogeneity between studies however was significant for both detection and miss rates of cystoceles (p= 0.09). The funnel plot appears largely symmetrical, and not suggestive of publication bias (figure 6.5).

Figure 6.4: Miss rate cystocele

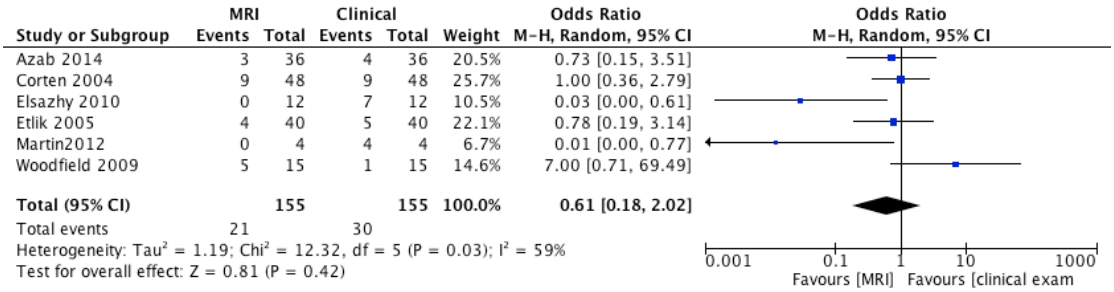
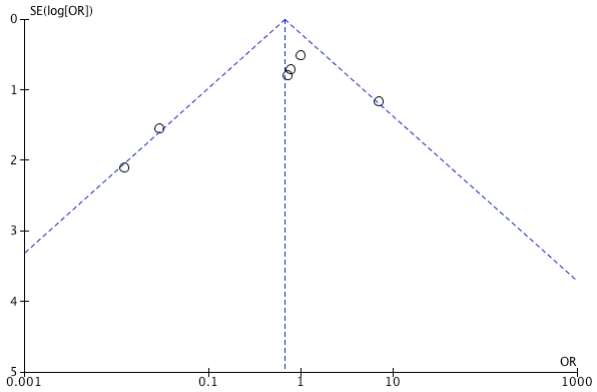


Figure 6.5: Funnel plot: miss rate cystocele



Middle compartment descent

Middle compartment descent detection rates were considered by six studies, which included a total of 263 patients[126, 209-212, 232] (figure 6.6). The detection rate for middle compartment descent was 49.43% with MRD versus 44.87% with clinical examination; this was not statistically significant (OR 0.81 95% CI 0.26-2.52, p = 0.72). The funnel plot was not suggestive of publication bias (figure 6.7), however there were two significant outliers noted Azab et al and Woodfield et al. These were removed and the analysis repeated, however the results did not show any statistically significant detection rates between the groups (p=0.42).

Figure 6.6: Detection rate middle compartment descent

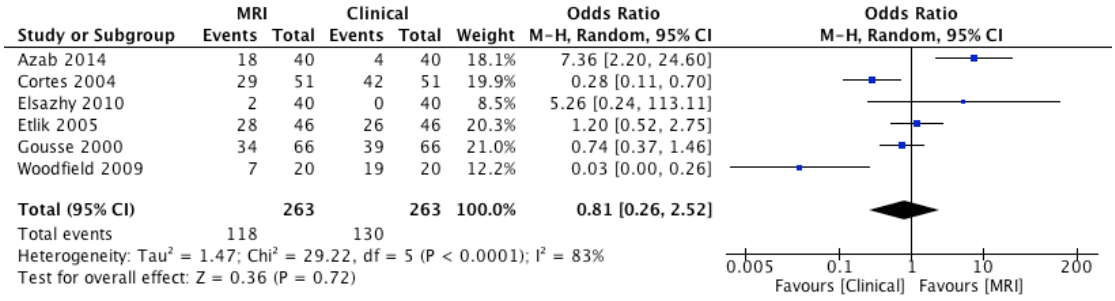
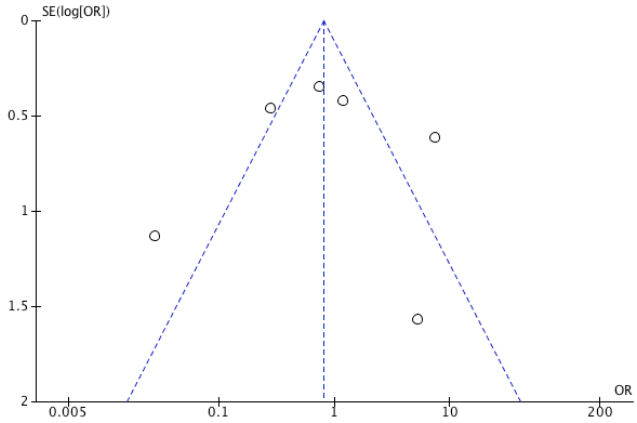


Figure 6.7: Funnel plot: detection rate middle compartment descent



Five studies considered the miss rate of middle compartment descent (figure 6.8). Overall, MRD had a miss rate of 24.77% versus 16.51% with clinical examination (OR 1.41, 95%CI 0.03-57.96, p = 0.85). Between-study heterogeneity was markedly significant for both detection and miss rates (P<0.00001). The funnel plot (figure 6.9) is also indicative of publication bias, with three out of four studies shown to be outliers.

Figure 6.8: Miss rate middle compartment descent

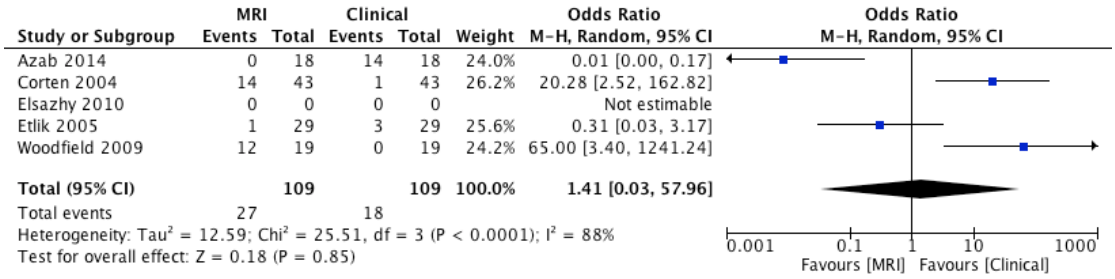
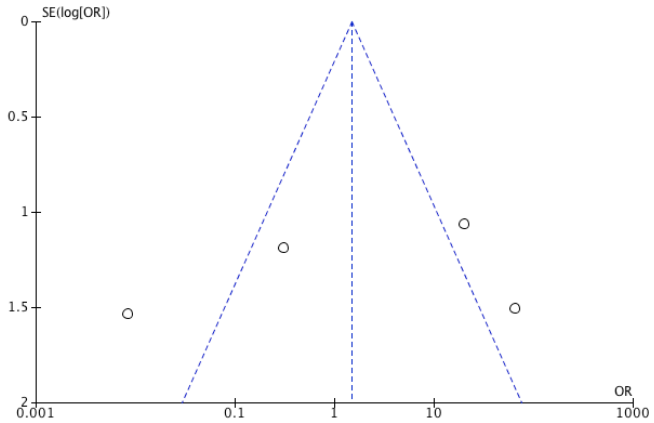


Figure 6.9: Funnel plot middle compartment descent



Rectoceles

Ten studies considered detection rates of rectoceles (n = 439)[120, 209-212, 216, 218, 219, 231, 232]. Detection rates were of 51.25% with MRD versus 53.76% with clinical examination (OR 0.54 95% CI 0.52-1.69, p = 0.94). Between-study heterogeneity was significant (p=0.001). Funnel plot was symmetrical and not indicative of publication bias (figure 6.11).

Figure 6.10: Detection rate rectocele

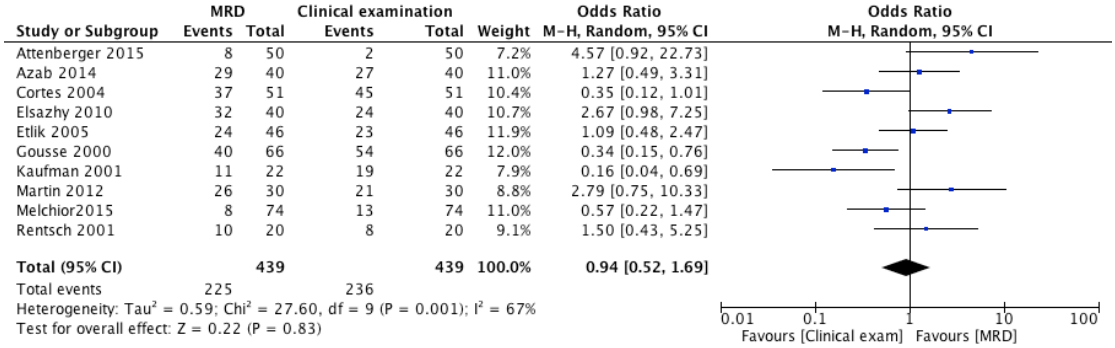
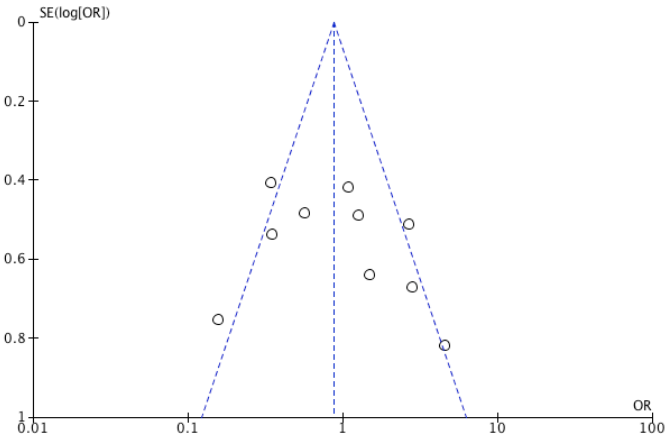


Figure 6.11: Funnel plot detection rate rectocele



Miss rates of rectoceles were calculated for nine studies (figure 6.12). These were also comparable between the two modalities at 14.29% with clinical examination versus 14.08% with MRD (OR 0.87, 95% CI 0.25-3.10, p=0.83). Between-study heterogeneity was significant (p=0.004). The funnel plot is shown below, and is not indicative of publication bias (figure 6.13).

Figure 6.12: Miss rate rectocele

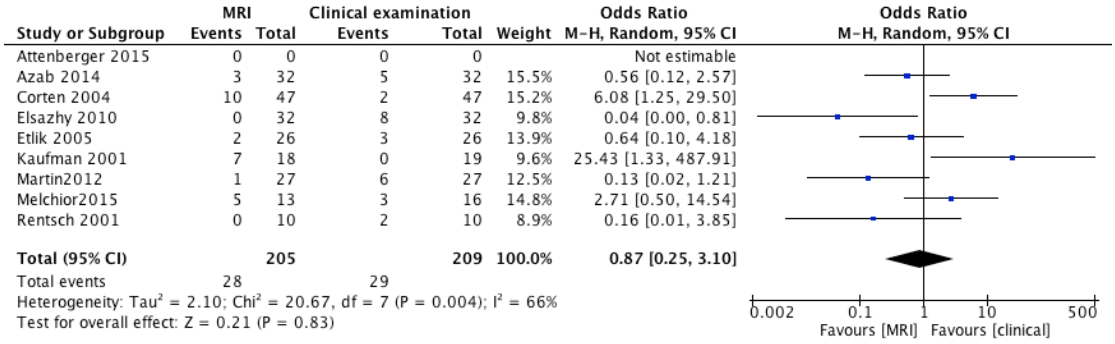
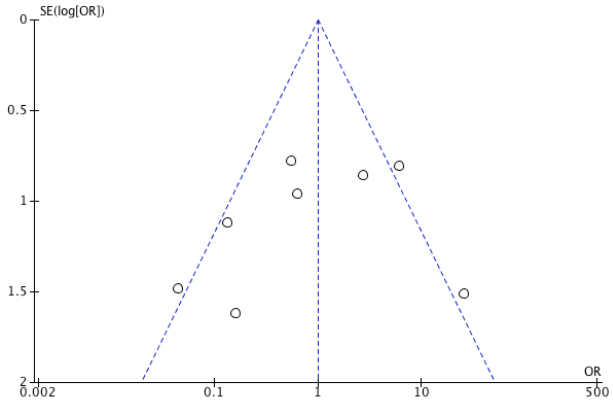


Figure 6.13: Funnel plot miss rate rectocele



Enteroceles

Eight studies (n = 323) considered detection rates of enteroceles[120, 121, 209, 218, 219, 231-233] (figure 6.14). The detection rate was significantly higher with MRD: 37.16% versus 25.08% (OR 2.23, 95% CI 1.21-4.11, p = 0.010). Between-study heterogeneity was not significant. The associated funnel plot was asymmetrical and therefore may indicate publication bias (figure 6.15).

Figure 6.14: Detection rate enterocele

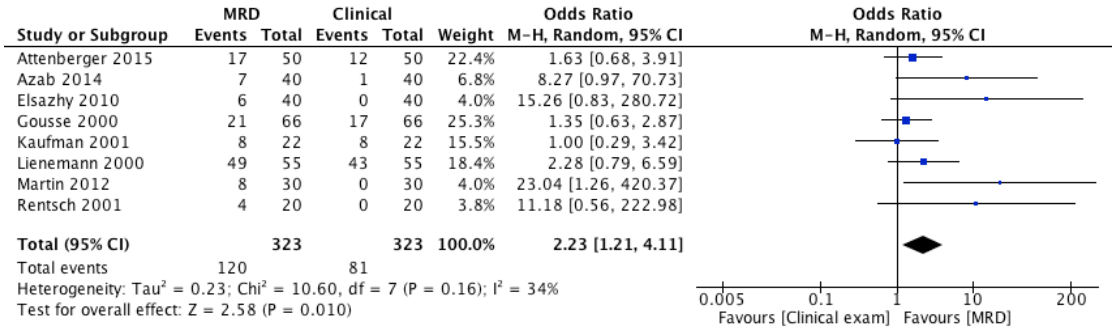
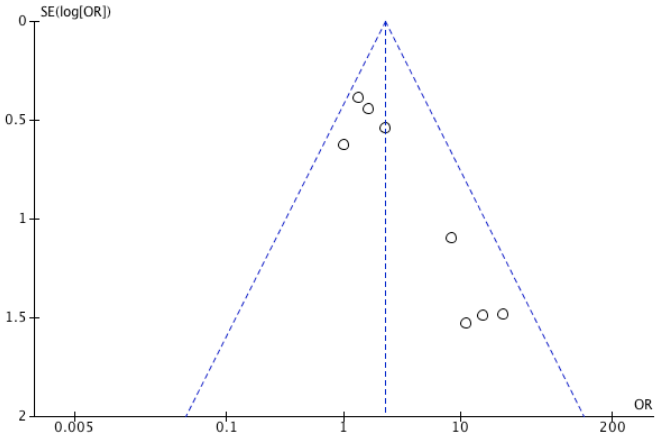


Figure 6.15: Detection rate enterocele funnel plot



Six studies considered miss rates of enteroceles (n=83) (figure 6.16). MRD had a significantly lower miss rate for enteroceles compared to clinical examination 1.20% versus 37.35%, p=0.0001 (OR 0.05, 95% CI 0.01-0.20) (figure 3). Between-study heterogeneity was not significant. Again, the funnel plot (figure 6.17) showed evidence of publication bias.

Figure 6.16: Miss rate enterocele

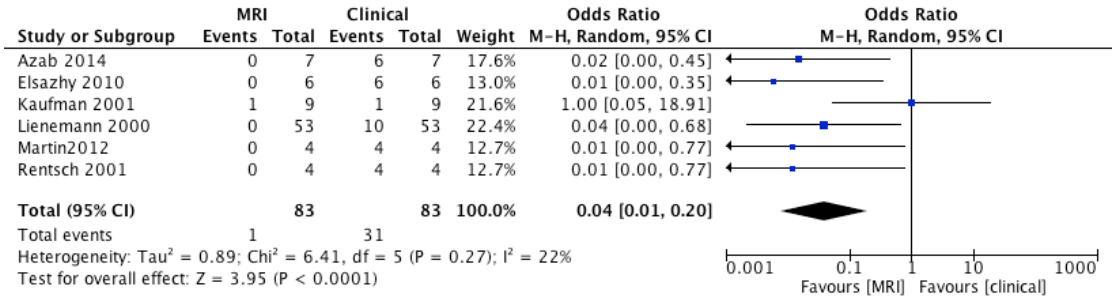
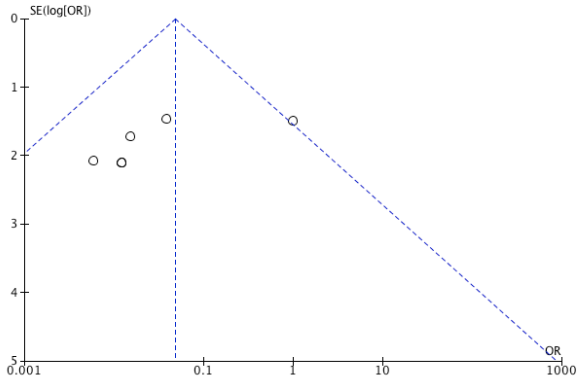


Figure 6.17: Miss rate enterocele funnel plot



Intussusception

Five studies (n=162) considered rectoanal intussusception rates[120, 211, 213, 219, 231] (figure 6.18). Overall, MRD detected intussusception in 27.78% of examined patients, whereas clinical examination detected slightly less (22.84%). This difference was not statistically significant (OR 1.36, 95% CI 0.50-3.72, p = 0.55). Heterogeneity was significant between studies. The funnel plot was fairly symmetrical and not indicative of publication bias (figure 6.19).

Figure 6.18: Detection rates intussusception

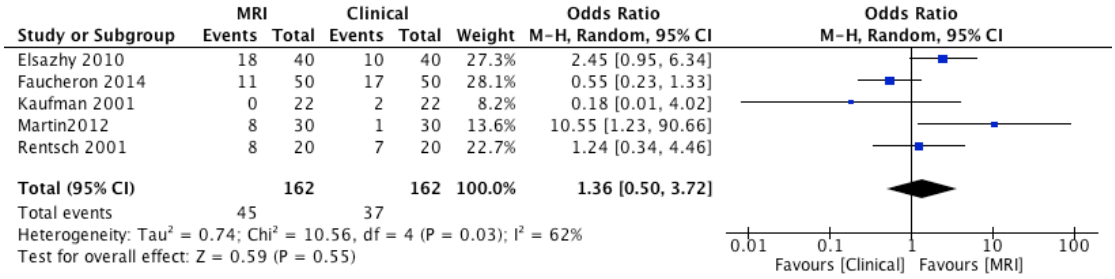
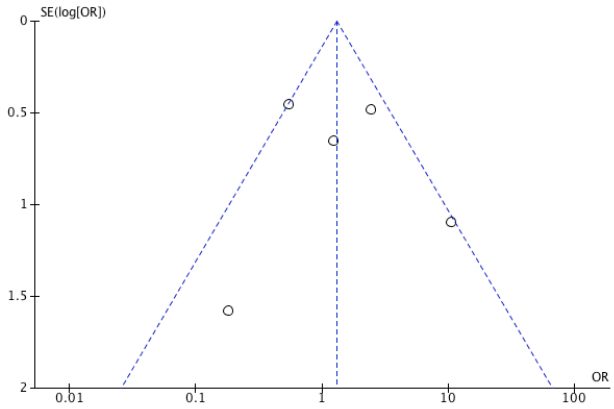


Figure 6.19: Funnel plot detection rate intussusception



Miss rates were 28.57% with MRD versus 30.16% with clinical examination (OR 1.08, 95% CI 0.13-9.09, p = 0.94) (Figure 6.20). Heterogeneity between studies was significant (p = 0.03). The funnel plot (figure 6.21) was not indicative of publication bias.

Figure 6.20: Miss rate intussusception

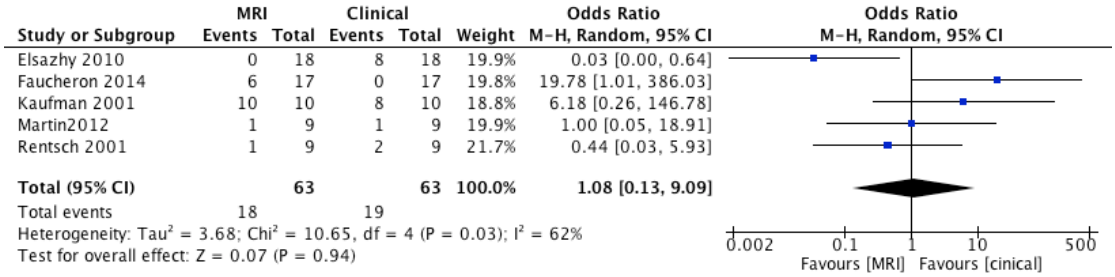
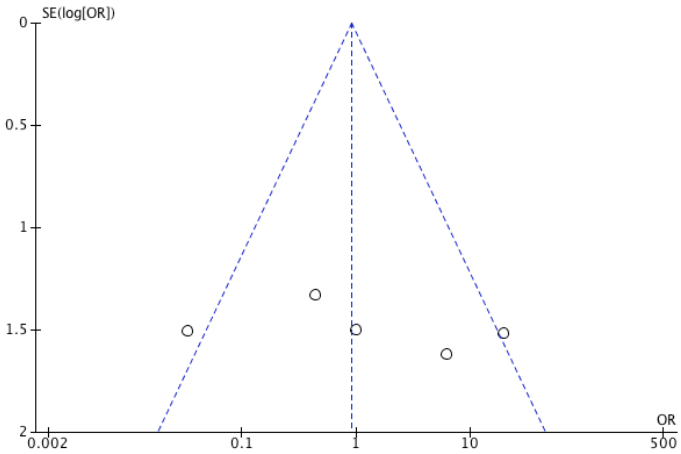


Figure 6.21: Miss rate intussusception funnel plot



Perineal descent

Perineal descent was discussed by three studies (n = 82)[120, 126, 211] (figure 6.22). Perineal descent was detected in 75.61% of patients with MRD. Clinical examination detected fewer cases, at 64.63%, however this difference was not statistically significant. (OR 1.46, 95% CI 0.23-9.25, p = 0.69). Between study heterogeneity was significant (p = 0.02). Given there were only three included studies, it was difficult to make a comment on publication bias (figure 6.23).

Figure 6.22: Perineal descent detection rate

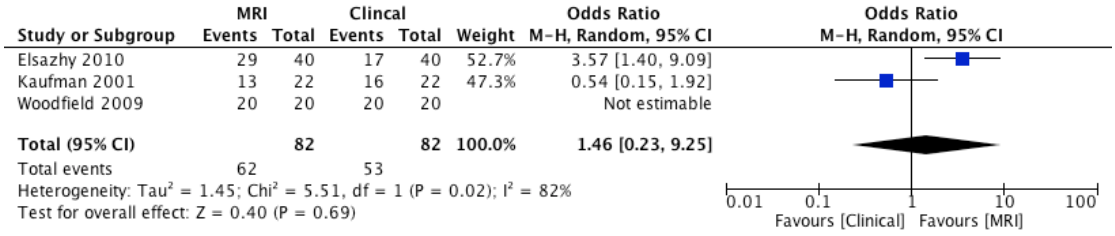
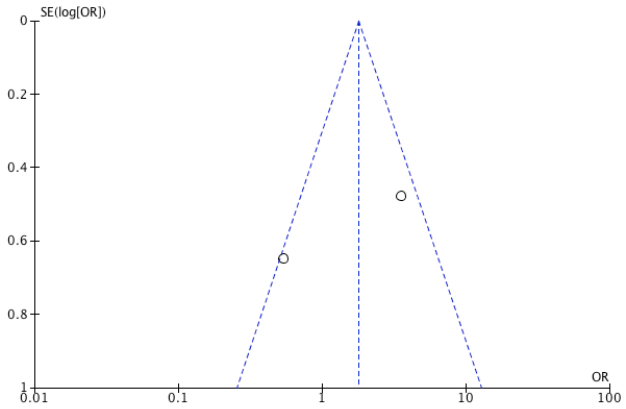


Figure 6.23: Funnel plot: detection rate perineal descent



Miss rates of perineal descent were 4.62% with MRD versus 21.54% with clinical examination (Figure 6.24). This difference however was statistically insignificant using the random effects model (OR 0.32, 95% CI 0.01-9.89, p = 0.52). Between-study heterogeneity was significant with both detection (p = 0.02) and miss (p= 0.02) rates. Again, the funnel plot was difficult to interpret given the low numbers of included studies (figure 6.25).

Figure 6.24: Miss rates perineal descent

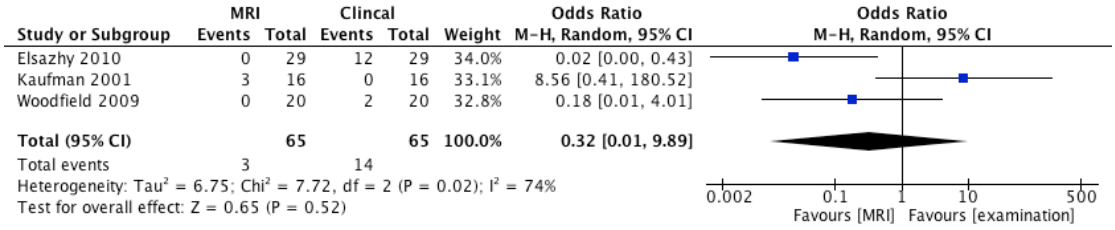
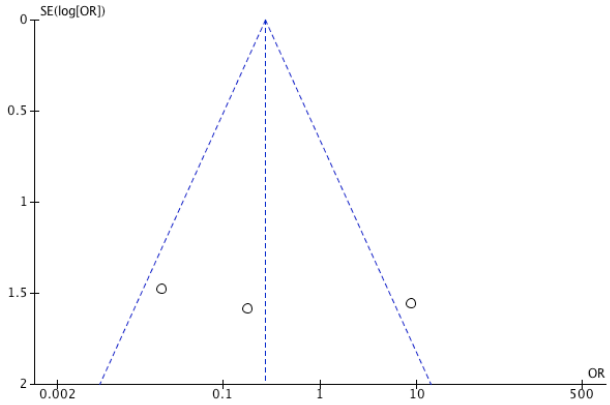


Figure 6.25: Funnel plot: miss rates perineal descent



Rectal prolapse

Only two papers discussed the detection and miss rates of rectal prolapse. Both MRD and clinical examination were able to detect full-thickness rectal prolapse in 7.6% of 52 patients. There was no significant heterogeneity. (figure 6.26-6.27).

Figure 6.26: Detection rates rectal prolapse

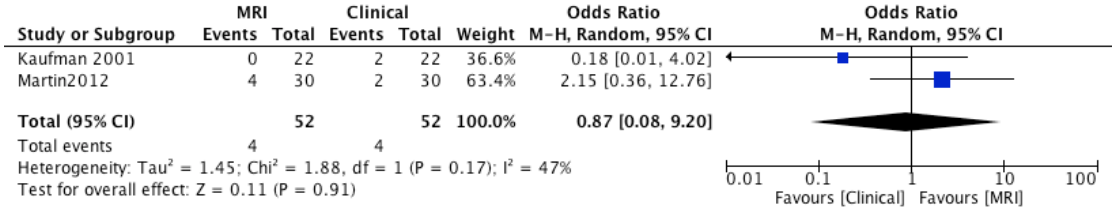
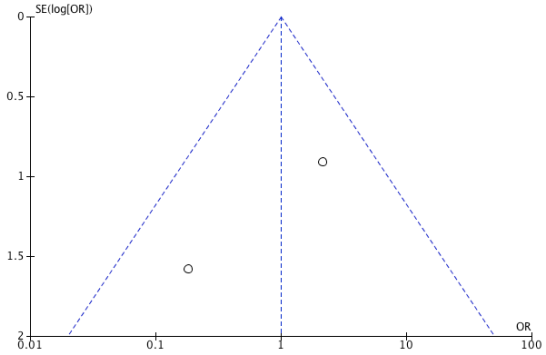


Figure 6.27: funnel plot: detection rates rectal prolapse



Again, miss rates were the same at 81.63% for both clinical examination an MRD, however significant heterogeneity was present (p = 0.05) (Figure 6.28 -6.29).

Figure 6.28: Miss rates rectal prolapse

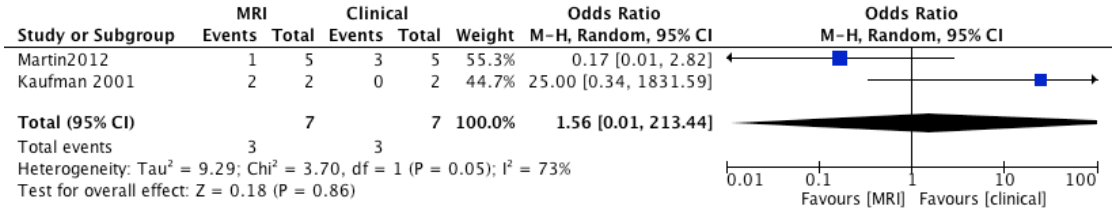
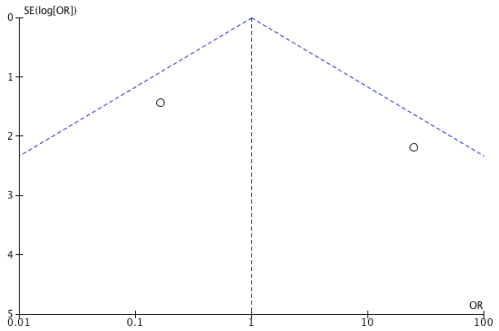


Figure 6.29: Funnel plot miss rates rectal prolapse



MRD versus fluoroscopic examinations.

1703 patients were included across the sixteen studies overall. Table 6.4 demonstrates the overall demographics for each study. Table 6.5 provides a tabulated summary of the meta-analysis for each of the seven outcomes of interest as outlined earlier.

Table 6.4: Studies comparing fluoroscopic techniques and MRD

Study	Year	Place	Study type	Exam[1]	MR position	Gold standard	Sex	N	Mean age	Outcomes compared [2]
Gufler[225]	2004	Rostock, Germany	P	CCD	Supine	CCD	F	7	57 (48-68)	R, E, C
Foti[224]	2013	Cantania, Italy	P	CD	Supine	CD	17F	19	54 (36-77)	R, RP, E
Cappabianca[223]	2011	Naples, Italy	P	ECCD	Supine	ECCD	F	1,142	52.47+/-13.71	E,
Dvorkin[234]	2004	St Marys, London	P	CD	Sitting	None	6F	10	43M(30-65)	R, PD, RI,
Healy[226]	1997	London, UK	P	CD	Supine	CD	F	10	61M (38-82)	R
Kaufman[120]	2001	Baltimore, Maryland	P	CCD	Supine	None	F	22	58+/-13	C, R, E, PD, RI, RP
Kelvin[235]	1999	Indianna	P	ECCD	Supine	None	F	10	65(44-79)	C, MCD, E, R
Lieneman[121]	2000	Munich, Germany	P	CCD	Supine	None	F	55	61	E
Pilkington[227]	2012	Southampton, UK	P	ECD	Supine	None	38F	42	59 (37-76)	R, E, RI
Faucheron[213]	2014	Grenoble, France	P	CD	Supine	None	F	22	68 (21-85)	RI
Vanbeckvoort[123]	1999	Leuven, Belgium	P	ECCD	ND	ECCD	F	35	65.4 (44-83)	C, MCD, E, R, PD
Vitton[229]	2011	Marseille, France	P	ECCD	Supine	CD	F	56	50.7 +/-12.5	R, PD, E
Bussen[222]	2003	Wurzberg, Germany	P	CD	Supine	None	F	30	58.4 +/-11.9	RI, R
Wang[230]	2005	Chong quing, China	P	CCD	Supine	ND	F	33	52 (34-71)	C, R, MCD, PD
Song[236]	2009	Bejing, China	P	CD	ND	ND	F	109	56 (24-79)	R
Pfeifer[237]	1999	Kronach, Germany	P	CCD	Supine	ND	55F	56	59+/-14.5	RI

[1]: CD: conventional defecography; ECCD: entero-colpo-cysto-defecography; CCD: colpocystodefecography
[2]C: cystocele; MC: middle compartment descent; R: rectocele; E: enterocele; RI: rectal intussusception; RP: rectal prolapse; S: sigmoidocele; PD: perineal descent

Table 6.5: Summary of meta-analysis: MRD versus fluoroscopy detection rates and miss rates

Outcome	No of studies	No of patients	MRI (%)	Clinical (%)	OR	P value	95% confidence interval		Heterogeneity	
							Lower	*Upper*	*I^2 (%)*	*P value*
Detection rates										
Cystocele	5	104	51.92	65.38	0.51	0.41	0.17	2.03	58	0.05
MCD	3	75	40.0	72.0	0.21	0.11	0.03	1.47	76	0.01
Rectocele	12	380	61.84	73.68	0.48	<0.01	0.30	0.76	33	0.14
PD	5	153	52.29	74.51	0.36	<0.01	0.17	0.74	38	0.17
Enterocele	9	1367	42.94	62.98	0.81	0.57	0.40	1.66	74	<0.01
RI	6	182	37.91	57.14	0.32	<0.01	0.16	0.66	26	0.24
RP	2	41	21.95	29.27	0.65	0.48	0.20	2.12	0	0.38
Miss rates										
Cystocele	5	104	27.02	8.11	2.49	0.57	0.11	56.93	73	0.02
MCD	3	75	44.44	0	20.53	0.03	1.42	297.28	55	0.11
Rectocele	12	380	15.96	0	15.74	<0.01	5.34	46.40	0	0.87
PD	5	153	32.11	0.92	12.30	<0.01	3.38	44.76	0	0.45
Enterocele	8	225	16.88	19.48	2.66	0.43	0.24	29.46	71	<0.01
RI	6	182	36.11	3.70	10.52	<0.01	3.25	34.03	24	0.26
RP	2	41	25.0	0	7.06	0.14	0.15	97.52	0	0.47

MCD: middle compartment descent; PD: perineal descent; RI: rectoanal intussusception; RP: rectal prolapse

Below is a description of each individual outcome of interest with the corresponding figures.

Cystoceles

Five studies discussed cystocele detection rates, including 104 patients overall (figure 6.30). Detection rates with MRD were 51.92% versus 65.38% with fluoroscopy (OR 0.51, 95% CI 0.17-2.03, p = 0.51). However, heterogeneity was significant (P= 0.05). Between-study heterogeneity was found to be significant between studies (p=0.05). The associated funnel plot was also suggestive of publication bias (figure 6.31).

Figure 6.30: Detection rates cystocele

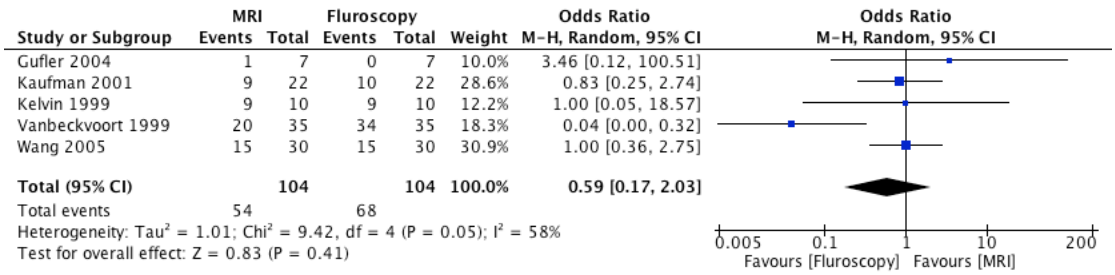
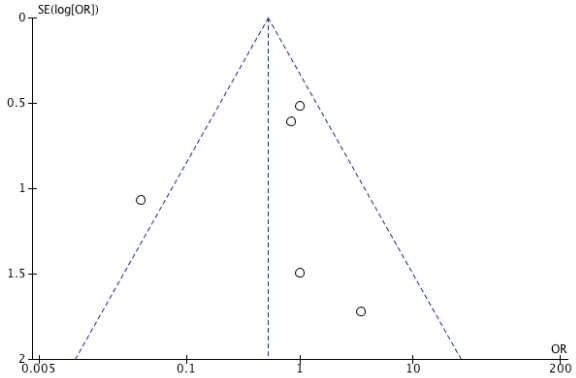


Figure 6.31: Funnel plot detection rates cystocele



When comparing miss rates, MRD had a higher miss rate compared to fluoroscopy (27.02% versus 8.11%), but this difference was not significant (OR 2.49, 95% CI 0.11-56.93, p = 0.57) (figure 6.32). Again, between-study heterogeneity was significant. It was difficult to comment on publication bias (figure 6.33).

Figure 6.32: Miss rate cystocele

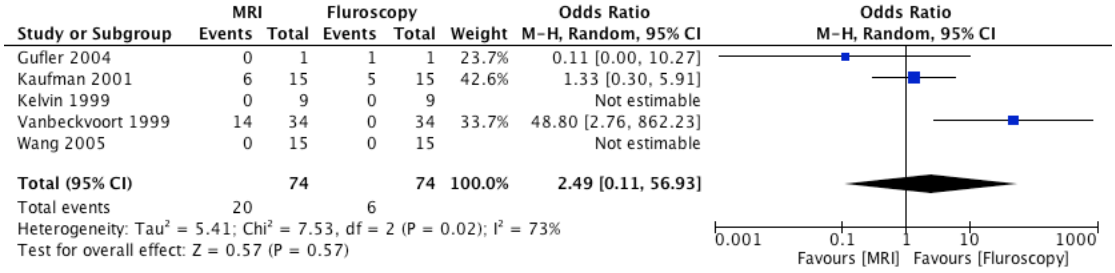
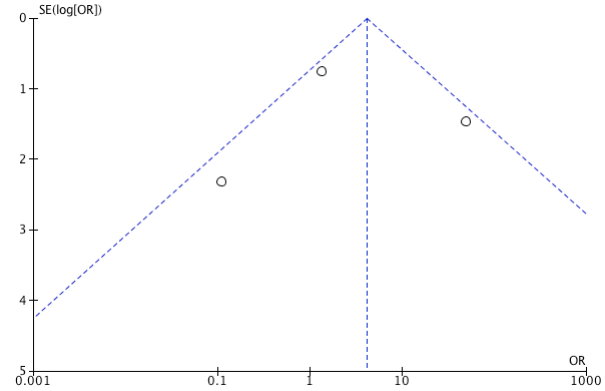


Figure 6.33: Funnel plot miss rate cystocele



Middle compartment descent

There were three studies which considered middle compartment descent totalling 75 patients[122, 123, 230] (figure 6.34). The detection rate was 40% with MRD versus 72%

with fluoroscopy (OR 0.21 95% CI 0.03-1.47, p = 0.11). Between-study heterogeneity was significant (p= 0.01). Figure 6.35 shows the funnel plot for these studies.

Figure 6.34: Detection rates middle compartment descent

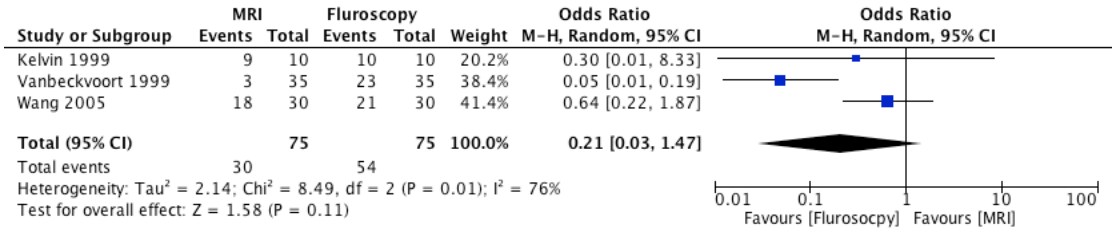
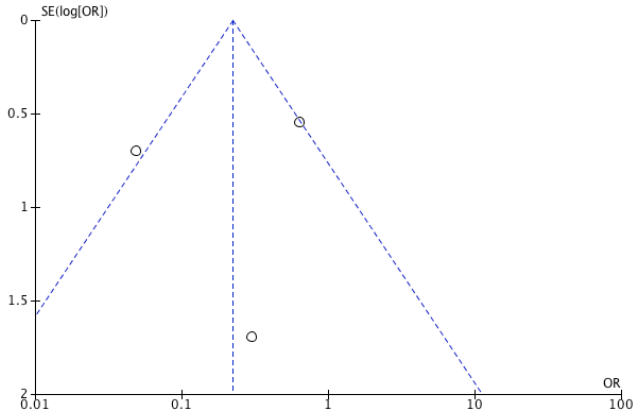


Figure 6.35: funnel plot detection rate middle compartment descent



The miss rate was statistically significantly different between the two tests: 44.44% with MRD versus 0% with fluoroscopy (OR 20.53, 95% CI 1.42-297.28, p = 0.03) (Figure 6.36). Between-study heterogeneity was not significant (p= 0.11). The associated funnel plot is shown in figure 6.37.

Figure 6.36: Miss rates middle compartment descent

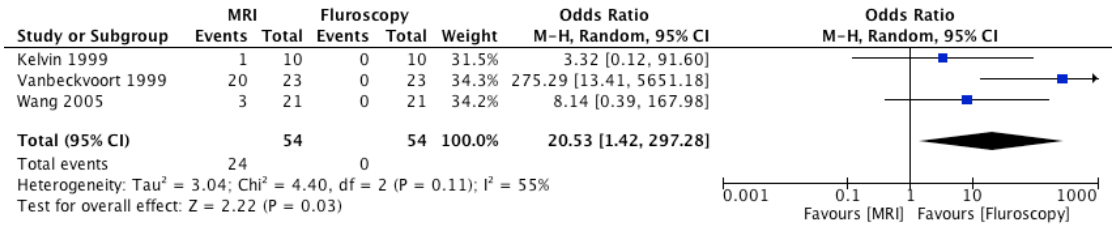
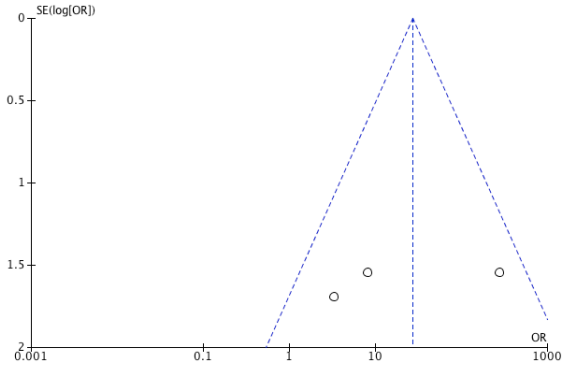


Figure 6.37: Funnel plot miss rates middle compartment descent



Rectoceles

Twelve studies considered detection and miss rates of rectoceles. The detection rate of rectoceles was significantly higher with fluoroscopy: 73.68% versus 61.84% with MRD (OR 0.48 95% CI 0.30-0.76, p = 0.002) (figure 6.38). There was no significant between study heterogeneity detected. The funnel plot shown in figure 6.39 showed reasonable symmetry and was not indicative of publication bias.

Figure 6.38: Detection rates rectocele

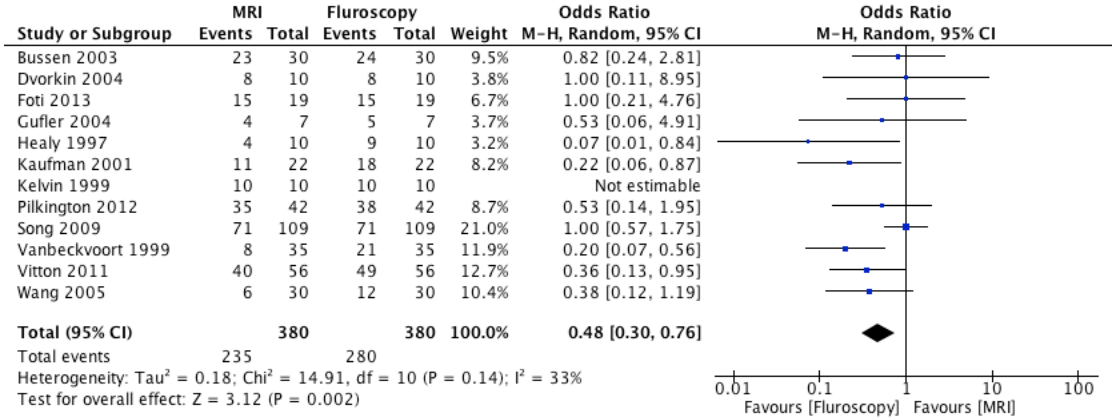
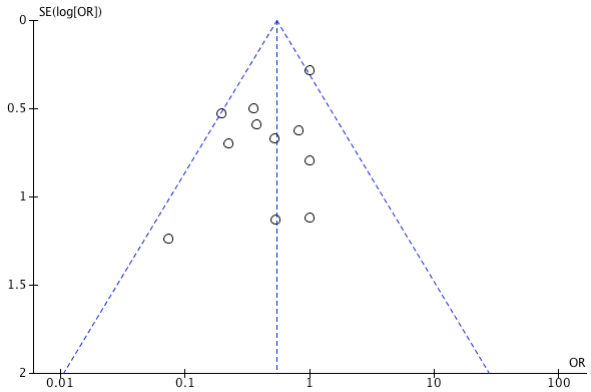


Figure 6.39: Funnel plot detection rate rectocele



None of the 12 studies reported a missed rectocele on fluoroscopy. By comparison, the miss rate for MRD was 15.96% (OR 15.74, 95% CI 5.34-46.40, P<0.00001)(figure 6.40). Heterogeneity was non-significant between included studies. The funnel plot was also symmetrical and not indicative of publication bias (figure 6.41)

Figure 6.40: Miss rate rectocele

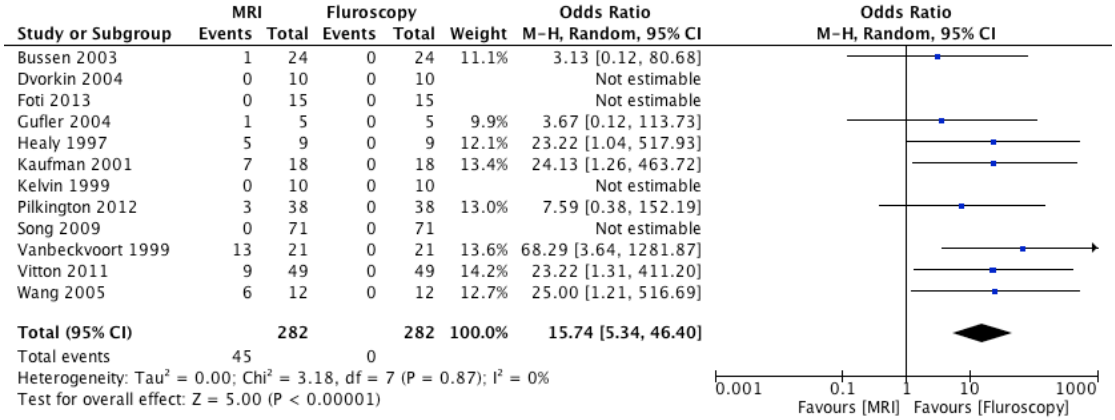
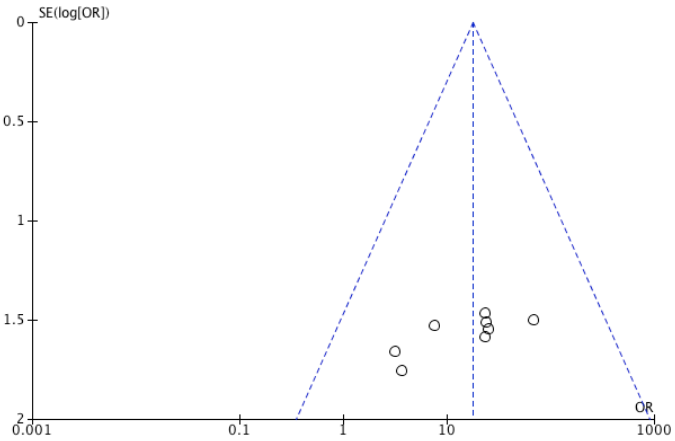


Figure 6.41: Funnel plot: miss rate rectocele



Enteroceles

Nine studies considered the detection rate of enteroceles with MRD and fluoroscopy (n= 1367) (figure 6.42). The detection rate of MRI was 42.17% versus 61.93% with fluoroscopy and there was no statistically significant difference between tests (OR 0.81, 95% CI 0.40-1.66, p = 0.57). Heterogeneity however was found to be significant at 75% p= 0.0001). The funnel plot shown in figure 6.43 does suggest a degree of publication bias.

Figure 6.42: Detection rate enterocele

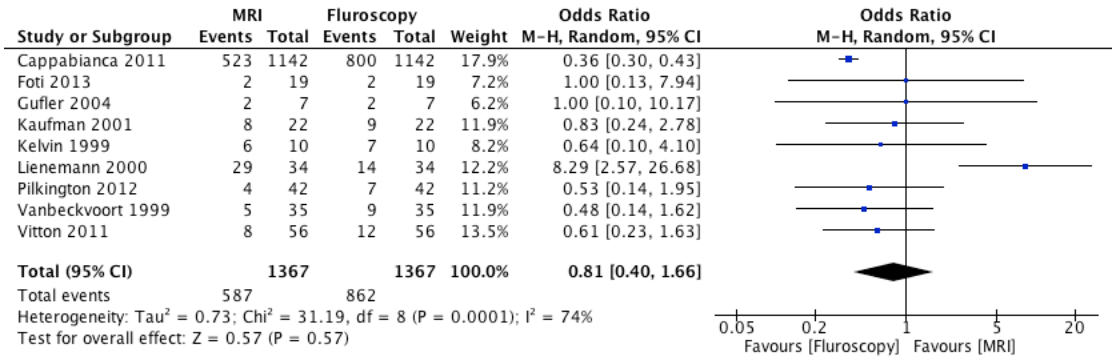
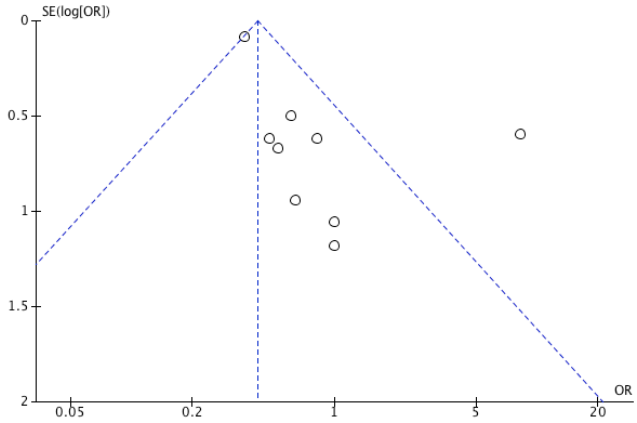


Figure 6.43: Funnel plot detection rate enterocele



Eight studies considered miss rates of enteroceles with MRD versus fluoroscopy (n = 225), giving an overall miss rate of 16.88% with MRD versus 19.48% with fluoroscopy (OR 2.66, 95% CI 0.24-29.46, p = 0.43) (figure 6.44). Heterogeneity was significant at 71% (p = 0.004). Publication bias was again demonstrated (figure 6.45).

Figure 6.44: Miss rate enterocele

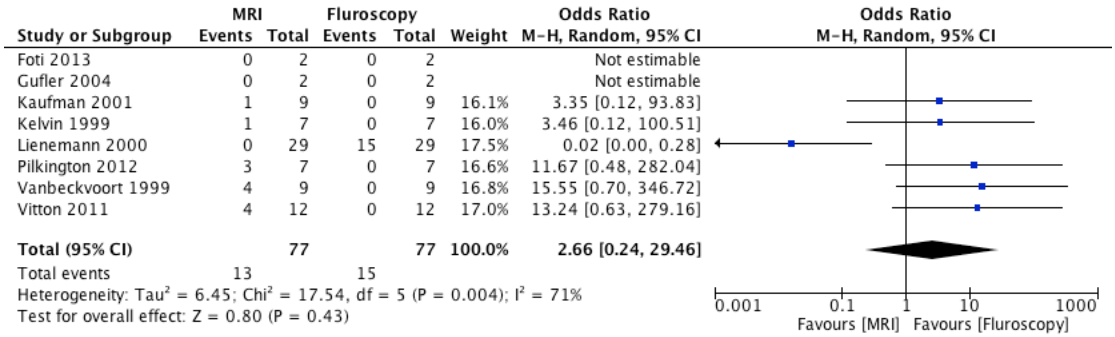
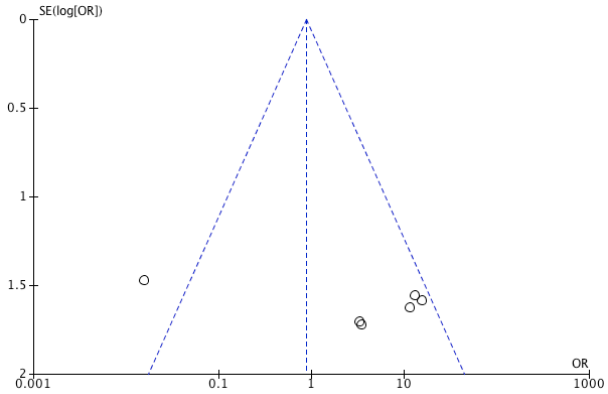


Figure 6.45: Funnel plot miss rate enterocele



Intussusception

Six studies considered rectoanal intussusception, which included a total of 182 patients. MRD detected intussusception in 37.91% of patients. By comparison, fluoroscopy had an overall detection rate of 57.14% (OR 0.32, 95% CI 0.16-0.66, p = 0.002) (figure 6.46). Between-study heterogeneity was significant. The funnel plot was also suggestive of publication bias (figure 6.47).

Figure 6.46: Detection rates rectoanal intussusception

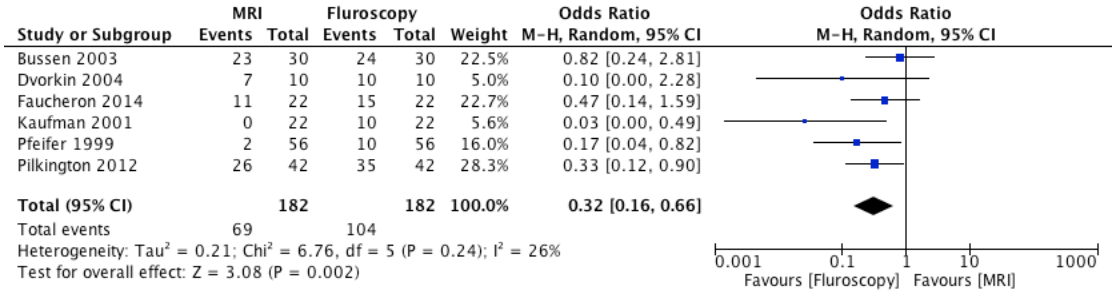
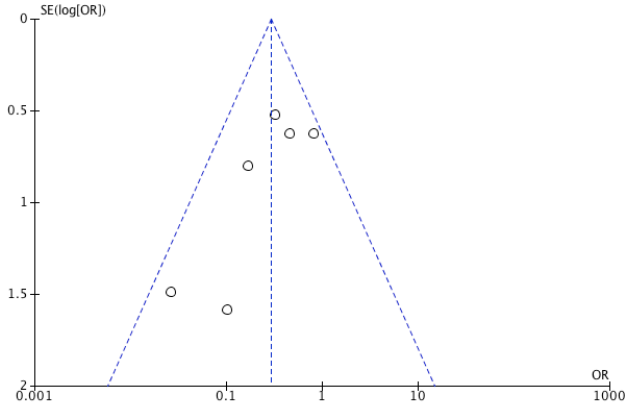


Figure 6.47: Funnel pot detection rate rectoanal intussusception



Miss rates were also significantly higher in with MRD, at 36.11% versus 3.70% with fluoroscopy (OR 10.52, 95% CI 3.25-34.03, p = 0.0001) (figure 6.48). Heterogeneity was non-significant in both cases. The associated funnel plot is demonstrated in figure 6.49, with reasonably symmetrical distribution.

Figure 6.48: Miss rates rectoanal intussusception

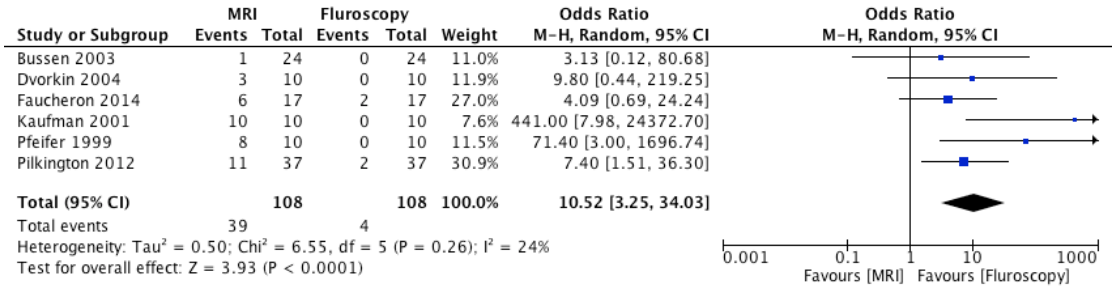
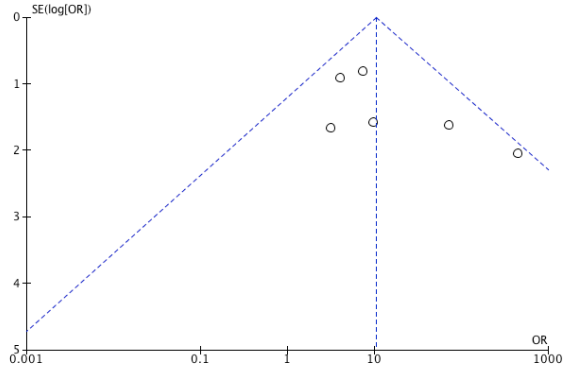


Figure 6.49: Funnel plot miss rates rectoanal intussusception



Perineal descent

Five studies discussed perineal descent (n = 153), shown in figure 6.50. Detection rates with MRD were 65.29% versus 74.51% (OR 0.36, 95% CI 0.17-0.74, p = 0.006). Heterogeneity was non-significant (p = 0.17). The funnel plot was not suggestive of publication bias (figure 6.51)

Figure 6.50: Detection rate perineal descent

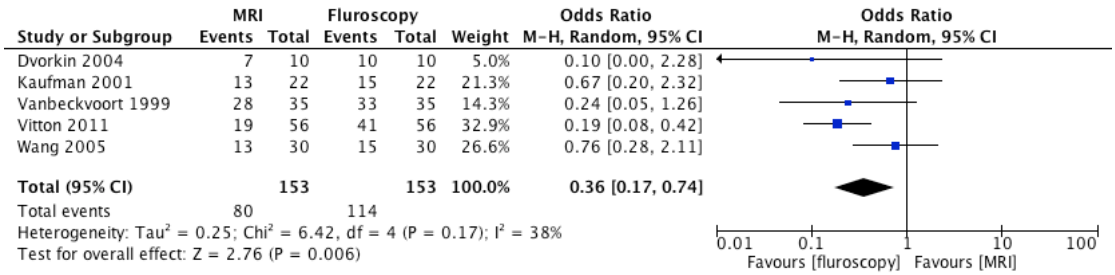
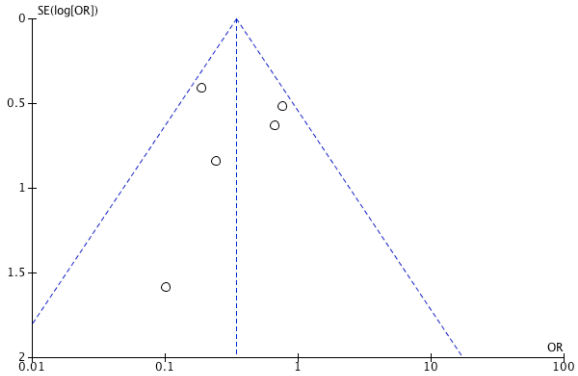


Figure 6.51: Funnel plot detection rate perineal descent



Miss rates were 32.11% with MRD versus only 0.92% with fluoroscopic techniques (OR 12.30, 95% CI 3.38-44.76, p = 0.0001) (figure 6.52). Again, between-study heterogeneity was not significant. The funnel plot, shown in figure 6.53 was largely symmetrical.

Figure 6.52: Miss rate perineal descent

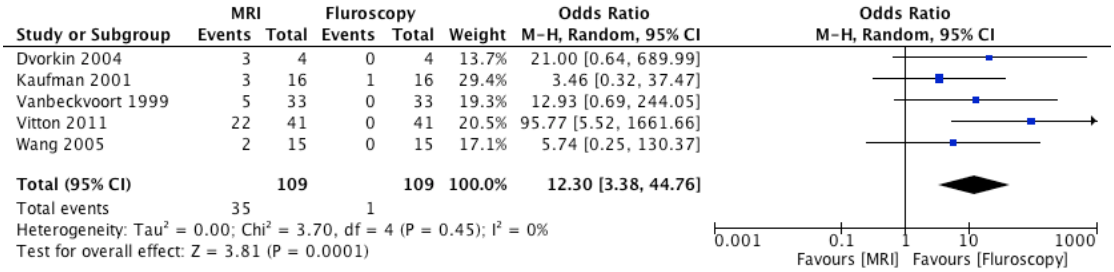
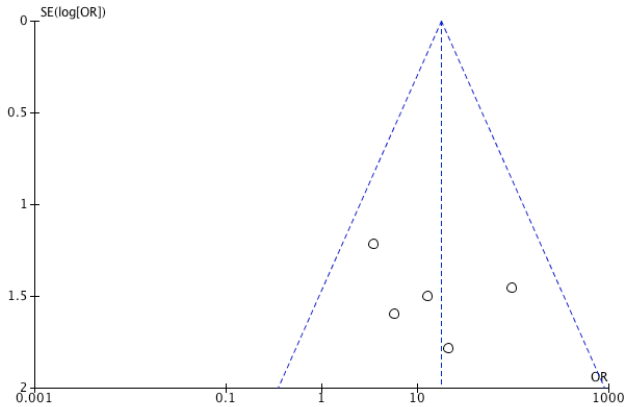


Figure 6.53: Funnel plot miss rate perineal descent



Rectal prolapse

Only two studies considered rectal prolapse, including only 41 patients overall. Detection rates were not significantly different (21.95% versus 29.27%) between both imaging modalities (OR 0.65, 95% CI 0.20-2.12, p = 0.48) (figures 6.54-6.55).

Figure 6.54: Detection rate rectal prolapse

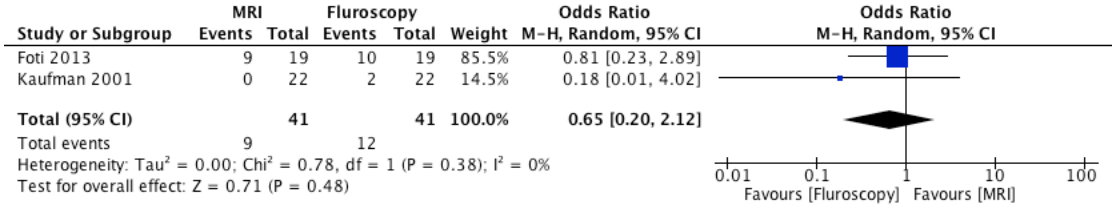
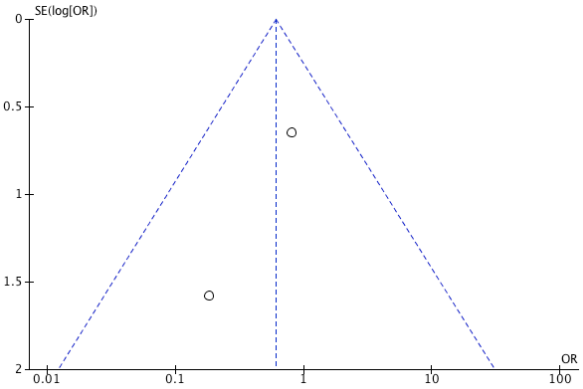


Figure 6.55: Funnel plot detection rate rectal prolapse



Miss rates were also found to be not significantly different between MRD and Fluoroscopy (OR 7.06, 95% CI 0.15-97.52, p = 0.14) at 25% with MRD versus 0% with fluoroscopy. Heterogeneity was non-significant (figures 6.56-6.57).

Figure 6.56: Miss rates rectal prolapse

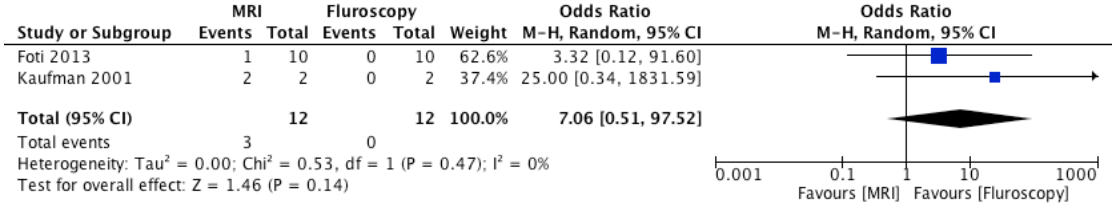
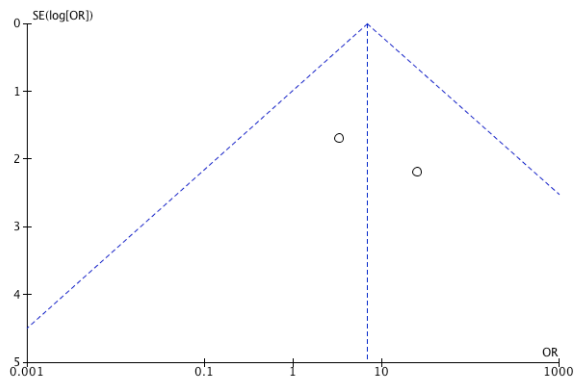


Figure 6.57: Funnel plot miss rate rectal prolapse



Discussion

The meta-analysis explored the ability of MRD to detect the presence of structural pelvic floor abnormalities compared to both clinical examination and various fluoroscopic techniques. The results showed no real advantage of MRD over clinical examination when attempting to detect abnormalities of the anterior or middle compartments. However, MRD fared significantly better in the detection of the presence of enterocele than clinical examination in both detection rates and miss rates.

Fluoroscopic techniques fared better overall in terms of better detection rates and lower missed rates compared to MRD; on no outcome of interest did MRD have a better detection rate or lower miss rate of a structural abnormality than fluoroscopy. It should be noted however that there is a possibility of reporting bias, in particular with regards to the miss rates of fluoroscopy. This is due to a number of studies that considered fluoroscopy to be the gold standard of diagnostic test. Observed results in each study are also dependent on the experience of the reporting radiologist.

In considering cost of one test over another, the NHS national tariff was accessed. The cost for a contrast fluoroscopic procedure lasting under 20 minutes was £78, and for an MRI of one area with post contrast views only this was £163 according to 2017/18 data[238]. The MRD cost is a conservative estimate given the number of runs in succession required to get sufficient elevation and strain views, and so MRD costs are at least double that of fluoroscopic examinations.

Another factor worth discussion is that of between-study heterogeneity. On numerous occasions, this was proven to be significant. The underlying reasons for this may be secondary to a multitude of factors such as variations in techniques used, patient positioning, and imaging reporting methods. To counteract this, a network meta-analysis could have been undertaken; however this would have been outwith the scope of this thesis due to the sheer scale of the required works and complex methodology.

Image sequences for MRD are usually performed with the patient lying in a supine position, in comparison to fluoroscopy, where the patient is positioned in a sitting position. Conceivably, this must have an impact on the sensitivity of MRD, in particular when relying on this imaging modality to detect more subtle structural abnormalities. This concept has previously been investigated. Bertsinger et al[239], undertook a study which found that found both supine and sitting positions permitted evaluation of all three compartments during MRD. However they confirmed the above

in that they noted that supine positioning tended to underestimate structural abnormalities. Therefore less severe abnormalities such as small rectoceles and lesser degrees of vaginal vault descent were less likely to be detected. Fielding et al conducted a similar study[240], and concluded that although either position could detect abnormalities in pelvic floor laxity, changes were less well detected with the patient in a supine position. Another point worthy of discussion was the use of rectal contrast during MRD. Although the majority of studies did employ rectal contrast with or without additional vaginal and bladder opacification, there were several that did not. Healy et al[241] used rubber tubing within the vagina and rectum as a luminal marker. Five other included studies did not employ any contrast during MRD[120, 212, 225, 230, 232]. This may be accounted for, at least in part, by the degree of between study heterogeneity observed in the results section of this chapter.

Another important point of discussion is the employment of an evacuatory phase during the examination. In seven studies, [120, 126, 209, 210, 212, 225, 226], only maximal strain views were obtained. The rest performed full defecatory views in order to mimic defecation as best possible. This is also the technique used within our own study, detailed next in this chapter. Cappabianca et al, in their study[223] concluded that complete defecation was vital in order to allow for complete dynamic evaluation.

Considering the results as a whole, there was a notably large discrepancy in the miss rates of rectal prolapse with MRD compared to clinical examination (87%,) and fluoroscopy (25%). The reasons behind this may be multiple in nature, with some of the factors as described above playing a part, such as lack of defecation phase, positioning of the patient and contrast mediums used. Additionally, image reporting carried out by non-specialist radiologists and the potential presence of a learning curve in understanding the dynamics of the study may have contributed further.

Patient satisfaction rates with the examination modality used were discussed within two studies. Pilkington et al[227] found that patients generally preferred MRD to proctography as embarrassment was felt to be less during the procedure.

Interestingly however, some participants stated awareness that the supine positioning during MRD had underestimated their abnormality compared to if the exam had been performed in a more physiologically correct defecatory position. On the other hand, Vitton et al[229] found no difference in satisfaction rates between conventional defecography and MRD.

If perhaps unsurprising that MRD is not as sensitive as fluoroscopy in detecting pelvic floor structural abnormalities, it is somewhat surprising that it had no significant benefits over clinical examination with the exception of the presence of enteroceles. It should be emphasised that this meta-analysis only explores the ability of each test to detect or miss the presence of an abnormality, and does not examine how the estimates of severity of abnormality vary between them. It is not unreasonable to presume that experienced clinicians examining patients are able to detect abnormalities in the pelvic floor with a good success rate, and so perhaps MRD has been underestimated in this study where the ability to predict degree of severity has not been explored.

Although less sensitive than fluoroscopy, MRD does convey certain benefits. This is seen in particular with women of childbearing age: the radiation dose to the ovaries is significant with ECCD, 15+/-5mSv[242].

Dvorkin et al[234] stated that MRD was particularly useful when planning surgery; similarly, Attenberger et al[218] felt MRD did impact on treatment strategy. Kaufman et al[120] stated MRD was particularly useful in follow-up of patients who had undergone pelvic floor reconstruction.

Limitations

Limitations of this meta-analysis are largely secondary to the significant variation in techniques employed when carrying out MRD by different units. In particular some studies did not use contrast or an evacuatory phase, and techniques of fluoroscopy also varied from study to study.

As already mentioned, another limitation of this meta-analysis is that only detection and miss rates have been explored. Any future work should consider a comparison of severity grading.

Study conclusions

Extrapolating from the results above, MRD does have a role in the diagnostic work-up of pelvic floor disease. This is particularly the case for women of childbearing age, where enterocele is suspected, or where postoperative assessment of pelvic floor reconstructive surgery is required. Where performed, studies should include a full evacuatory phase. MRD does not replace clinical examination, and in cases where MRD is not fruitful in its findings and a structural abnormality is still suspected, then other imaging modalities should be considered, such as barium proctography. Clinicians must also bear in mind that there is the possibility of a degree of

underestimation of the severity of an abnormality with MRD. Given that estimated costs of MRD are approximately 10 times higher than those of video proctography [205], it may be prudent to suggest careful patient selection for MRD studies, with male patients who have not undergone prior pelvic floor surgery being considered for fluoroscopy in the first instance.

6.3 Study 2: Can we correlate patient reported symptom severity with severity of abnormalities seen on MR-defecography?

Introduction

The following study represents the second part of an evaluation as to the clinical usefulness of MR-defecography in dealing with patients who present with pelvic floor disturbance. It considers all-comers to the pelvic floor unit, and therefore no exclusions were made on the basis of type of reported symptoms. This analysis takes the form of univariate and multivariate logistic regression analysis of multiple MRD factors against various patient-reported scoring systems.

As discussed previously, there have been a few various previous attempts to quantify the exact role of MRD in the decision-making process for surgery. There exists very little information in existing literature with regards to how MR-defecography correlates with patient-reported symptom severity. One study, undertaken by Piloni et al[243] discussed an attempt to correlate MRI with the Altomere clinical ODS score[244], and found no correlation.

This study aims to identify which factors, as seen on MR-defecography, correlate with patient-reported symptom severity which have been assessed through the use of various patient-reported outcome measure tools, namely the Birmingham Bowel, Bladder & Urinary Symptom Score, the Wexner Incontinence Score and the ODS score.

The primary objective is to detect whether there is any statistically significant relationship between MRD features of anterior, middle and posterior compartment and each scoring system on univariate and then multivariate analysis. The secondary objective is to determine whether a scoring system for MRD can be devised which relates to the severity of experienced symptoms and can help guide management.

Methods

Patients who had undergone MR-defecography within a single unit between January 2012 and April 2015 were retrospectively identified from a prospectively-maintained pelvic floor database of all attendees to the pelvic floor services within the trust for consultation with a pelvic floor colorectal surgeon. The aforementioned questionnaires were routinely given out during each outpatient clinic attendance to capture data at each clinic visit (BBUSQ, WIS, ODS score).

Inclusion criteria

Patients were included in the study if they had prospectively completed at least one questionnaire within 12 months of undergoing the MRD and prior to any further treatment intervention.

PROMs

As previously described in chapter 3, (general methods), the four domains of the BBUSQ were considered separately alongside the Wexner Incontinence Score and ODS score. All patient scores were coded into a binary system, with "0" indicating a normal score and "1" indicating an abnormal score. For the BBUSQ the cut-off scores for an abnormal score were based on the original validation criteria. A Wexner Incontinence Score of 10 or more was considered to be indicative of significant symptoms of faecal incontinence, and an ODS score of 8 or more was considered to be indicative of significant symptoms of obstructed defecation: these cut-offs as definition of an abnormal score were decided upon consultation with a consultant colorectal surgeon with a specialist interest in pelvic floor disorders (ET) who routinely uses both the ODS and WIS as part of the clinical assessment of patients presenting with pelvic floor dysfunction.

MRD features

As previously described in the general methods section, MRD features were assessed as according to a set of predefined criteria on two separate occasions by two examiners. Features were similarly coded into "0" indicating normal and "1" indicating abnormal findings. Additionally, where feasible, MRD variables were coded into the presence of a moderate/severe abnormality (1) versus the presence of no/mild abnormality (0). Inter-observer variability was considered using Cohen's kappa, statistic. For each variable, agreement between reviewers regarding the presence or absence of that abnormality was considered. A kappa value of >0.41 was considered to indicate fair agreement between reviewers. For variables with a kappa value of <0.60, a third opinion was sought from a separate reviewer (ET).

Statistical analysis

Pearson Chi-squared test was applied to compare sex and age distributions in those reporting a normal versus abnormal score. For each of the aforementioned BBUSQ domains, WIS and ODS score, binomial logistic regression analysis was performed for each of the MRD covariates against each functional score. Factors with a $p<0.2$ on univariate analysis were included in multivariate analysis. $P<0.05$ was considered to be statistically significant.

Results

Over a thirty-nine month period between January 2012 and April 2015, a total of 302 MR proctograms were performed within a single unit. This time period was chosen to allow for sufficient follow-up post imaging to allow identification of those who underwent surgery. Of these, 191 (63.25%) had documented functional data with one or more of the required functional outcomes as described above measured within 12 months of imaging and undertaken prior to any treatment intervention taking place.

21 patients were excluded during initial analysis: 8 – no/little pelvic floor movement during evacuatory phase; 1 – image improperly centred therefore difficult to interpret; 8: functional scores completed more than 12 months from date of MRI scan; 1: MRI improperly coded, performed in context of suspected fistulous disease rather than PFD; 3- insufficient data collection to allow for accurate analysis.

Therefore, a total of 170 patients were included in this study. Table 6.6 gives the study demographics. Of the 25 patients who had undergone prior pelvic floor surgery, 10 had undergone stapled transanal resection of the rectum, (STARR); 4 had undergone anterior resection; 1 had undergone total colectomy and J-pouch formation; 3 had undergone ventral mesh rectopexy, (VMR); 2 had undergone rectocele repair, and 5 had either anterior or posterior vaginal repair.

With regards to inter-observer variability, agreement was almost perfect for the presence or absence of an abnormality in the following variables: M line (k=0.91), cystocele (k= 0.89) and middle compartment descent (k= 0.81). Agreement was substantial between reviewers for the presence or absence of enteroceles (k= 0.79), rectoceles (k= 0.76), and moderate for the presence of an abnormal H line (k 0.50), pelvic floor elevation (k= 0.41), urethral hypermobility (k= 0.54) and intussusception (k= 0.54). Only slight agreement was seen for measurements of the change in

anorectal angle (k=0.183); therefore these measurements were reassessed on a third occasion with a separate reviewer

It is worth noting that only 31 patients (18.2%) were able to successfully expel 80% or more of the rectal contents on attempted evacuation. In fact, 107 (62.9%) patients demonstrated little to no evacuation of rectal jelly during the procedure.

Table 6.6: Study demographics

	No of patients (%)
Median Age	**55 (17-105)***
Over 50 years	**97 (57.1%)**
Females	**151 (88.1%)**
Prior hysterectomy	**30 (19.9%)**
Other pelvic floor surgery:	**25 (14.7%)**

** expressed as median (range)*

Results for the four domains of the BBUSQ univariate analysis are shown in the table below (table 6.7). Only MRD variables with a $p<0.2$ on multivariate analysis have been shown.

Univariate analysis BBUSQ

BBUSQ: constipation

The BBUSQ constipation score was available for 157 participants (92.3%). An abnormal score was reported by 29.9% of patients. (i.e. ≥64%). Significantly more females than males reported an abnormal score (p=0.045, 33.1% versus 10.5%) 37.7% of patients under 50 versus 23.9% over 50 years of age had an abnormal score (p=0.061).

Only one factor was associated with an abnormal constipation score on univariate analysis: the inability to evacuate 80% of rectal contrast (p = 0.039, OR 3.235; 95% CI 1.059-9.881). Age >50 (p = 0.062, OR 0.518; 95% CI 0.260-1.034) and female sex (p = 0.062, OR 4.204; 95% CI 0.931-18.978) were approaching statistical significance.

Table 6.7: BBUSQ: univariate analysis

Covariate	Odds ratio	95% Confidence Limit Lower	Upper	P value
Constipation				
Age >50	0.518	0.260	1.034	0.062
Sex	4.204	0.931	18.978	0.062
Rectocele >2cm	1.574	0.795	3.119	0.193
<80% rectal evacuation	3.235	1.059	9.881	**0.039**
Incontinence				
Previous pelvic floor surgery	0.485	0.202	1.162	0.104
Elevation	1.686	0.806	3.529	0.166
M line >2cm	2.049	0.901	4.656	0.087
H line >6cm	2.411	1.203	4.834	**0.013**
<80% rectal evacuation	0.452	0.189	1.081	0.074
Age >50	1.983	1.047	3.759	**0.036**
Evacuation				
Age >50	0.164	0.047	0.577	**0.05**
ARA binary	0.459	0.187	1.127	0.089
Presence of cystocele	2.219	0.859	5.737	0.100
Urethral Hypermobility	3.400	1.186	9.746	**0.023**
Rectoanal intususseption	0.377	0.120	1.185	0.095
Urinary				
Prior hysterectomy	2.050	0.765	5.494	0.154
Abnormal elevation	2.271	1.012	5.097	**0.047**
M line >4cm	1.655	0.855	3.200	0.135
H line >6 cm	2.460	1.211	4.998	**0.013**
Presence of cystocele	2.191	1.120	4.289	**0.022**
Presence of cystocele >3cm	2.381	0.838	6.765	0.104
Presence of rectocele >2cm	1.950	1.001	3.798	**0.049**
Urethral Hypermobility	1.955	0.989	3.864	0.054
Female sex	0.586	0.192	1.385	0.189
Previous pelvic floor surgery	0.500	0.208	1.201	0.121

BBUSQ incontinence

Data was available for 96.5% of patients. 61.0% were considered to have an abnormal score. 67.7% of patients over the age of 50 had an abnormal score, which was significantly higher than those under 50 (51.4%, p=0.035). There was no significant

difference in scores between male and females (p=0.770). The presence of an abnormal H line, i.e. greater than 6cm (p = 0.013, OR 2.411; 95% CI 1.23-4.834) and age of more than 50 (p = 0.036, OR 1.983; 95% CI 1.047-3.759) were the only factors found to be of statistical significance on univariate regression analysis. Descent of the anorectal junction of more than 2cm below the pubococcygeal line on strain views (M line) (p = 0.087, OR 2.049; 95% CI 0.901-4.656) and an inability to evacuate >20% of the rectal contents evacuation (p = 0.074, OR 0.452; 95% CI 0.189-1.081) approached but did not reach statistical significance.

BBUSQ Evacuation

Data was available for 94.1% of patients. The majority of patients – 85.7% had a score that was considered to be abnormal as according to the validation criteria. There was no significant difference in proportions of abnormal scores between sexes (p=0.769). Significantly more patients under 50 reported an abnormal score (95.6% versus 78.0%, p = 0.002). On univariate analysis, age of more than 50 (p = 0.05, OR 0.164; 95%CI 0.047-0.577); 0.187-1.127) and the presence of urethral hypermobility (p = 0.023, OR 3.40, 95% CI 1.186-9.746) were statistically significant for the prediction of an abnormal score. Showing a trend towards statistical significance were failure to change the anorectal angle by 15 degrees or more on attempted rectal evacuation (p= 0.089, OR 0.459, 95% CI and the presence of rectoanal intussusception or rectal prolapse (p = 0.095, OR 0.377; 95% CI 0.120-1.185).

BBUSQ Urinary

93.5% of patients had completed the urinary domain portion of the BBUSQ. An abnormal score was reported by 64.1%. There were no significant differences in the frequency of abnormal scores between older and younger patients (p = 0.226) or males and females (p=0.184). On univariate analysis, abnormal pelvic floor contraction and elevation (p = 0.047; OR 2.050 95% CI 0.765-5.494), an H line of >6cm, indicating significant hiatal widening (p = 0.013; OR 2.460 95% CI 1.211-4.998), presence of a cystocele (p = 0.022; OR 2.191 95% CI 1.120-4.289) and presence of a rectocele greater than 2cm in size (p = 0.049; OR 1.950 95% CI 1.001-3.798) were associated with an abnormal urinary domain score.

Multivariate analysis: BBUSQ

Table 6.8 shows the results of the multivariate analysis of the BBUSQ factors that had a p value of <0.2 on univariate analysis.

BBUSQ Constipation

On multivariate analysis, the inability to evacuate more than 20% of the rectal contents was the only covariate found to be statistically significant in the prediction of an abnormal score. These patients were 3.6 times more likely to have an abnormal constipation score (p = 0.027, OR 3.602; 95% CI 1.159-11.197).

BBUSQ Incontinence

When multivariate analysis was undertaken, patients over 50 were 2.2 times more likely to have an abnormal BBUSQ faecal incontinence domain score (p = 0.027, OR 2.204 95% CI 1.092-4.447). A history of prior pelvic floor surgery was negatively associated with an abnormal score: patients were 0.36 times as likely to have an abnormal faecal incontinence score if they had previously undergone prior corrective pelvic floor surgery (p = 0.042, OR 0.359; 95% CI 0.134-0.962).

BBUSQ Evacuation

On multivariate analysis, only two factors were found to be predictive of an abnormal evacuation score: age >50 (p = 0.07, OR 0.156; 95% CI 0.041-0.600) and the presence of rectoanal intussusception or rectal prolapse (p= 0.010, OR 0.138; 95% CI 0.031-0.623)

BBUSQ Urinary

On multivariate analysis, only one factor was statistically correlated with an abnormal BBUSQ urinary domain score: prior pelvic floor surgery; Patients were 0.27 times as likely to have urinary symptoms following prior pelvic floor surgery (p = 0.026; OR 0.271 (95% CI 0.086-0.855) than those who had not had surgery.

Table 6.8: multivariate analysis BBUSQ

Covariate	Odds ratio	95% Confidence Limit		P value
		Lower	Upper	
Constipation				
<80% rectal evacuation	3.602	1.159	11.197	**0.027**
Age >50	0.573	0.278	1.178	0.130
Female sex	0.236	0.049	1.149	0.074
Rectocele >2cm	1.243	0.585	2.638	0.572
Incontinence				
Age >50	2.204	1.092	4.447	**0.027**
Previous PF surgery	0.359	0.134	0.962	**0.042**
Abnormal elevation	1.349	0.612	2.975	0.458
M line >2cm	0.864	0.242	3.085	0.822
H line >6cm	2.637	0.868	8.011	0.087
<80% rectal evacuation	0.514	0.191	1.383	0.188
Evacuation				
Age >50	0.156	0.041	0.600	**0.007**
Abnormal change in ARA	0.792	0.261	2.406	0.681
Presence of cystocele	2.419	0.434	13.476	0.314
Presence of urethral hypermobility (UH)	2.446	0.408	14.661	0.328
Presence of recto-anal intussusception	0.138	0.031	0.623	**0.010**
Urinary				
Previous pelvic floor surgery	0.271	0.086	0.855	**0.026**
Urethral hypermobility	1.255	.439	3.589	0.672
H line >6 cm	2.267	0.671	7.667	0.188
Abnormal elevation	2.462	0.918	6.602	0.073
Prior hysterectomy	1.858	0.617	5.597	0.271
M line >4cm	0.566	0.188	1.704	0.311
Presence of rectocele >2cm	1.995	0.708	5.621	0.191
Cystocele >3cm	2.039	0.530	7.839	0.300

ODS score

One hundred and thirty six (80.0%) patients had a documented ODS score. 77 patients (66%) had scored 8 or more, indicating clinically significant symptoms. Significantly

more females than males had an abnormal score (72.7% versus 46.7%, p= 0.038). There was no significant difference in older versus younger patients (p=0.225). On univariate analysis, a rectocele of 2cm or greater (p= 0.001; OR 4.007 95%CI 1.763-9.109), and female sex (p = 0.045; OR 3.048 95% CI 1.024-9.068) were found to be significantly correlated with an abnormal ODS score. The presence of a cystocele (p = 0.058; OR 2.109 95% CI 0.975-4.559) and MRD evidence suggestive of puborectalis syndrome (p = 0.096; OR 3.656 95% CI 0.796-16.788) were found to be approaching statistical significance (table 6.9). Again, only variables with a p<0.2 are shown.

Table 6.9: Univariate analysis ODS score

Covariate	Odds Ratio	95% Confidence Interval Lower	Upper	P value
ARA binary	1.839	0.805	4.202	0.148
M line >4cm	1.888	0.883	4.040	0.101
H line >8cm	1.892	0.808	4.435	0.142
Presence of cystocele	2.109	0.975	4.559	0.058
Rectocele >2cm	4.007	1.763	9.109	**0.001**
Puborectalis syndrome	3.656	0.796	16.788	0.096
Female sex	3.048	1.024	9.068	0.045
Previous pelvic floor surgery	2.761	0.762	10.001	0.122

On multivariate analysis, a rectocele of 2cm or more in size (p = 0.003; OR 5.756 95% CI 1.829-18.112) was significantly associated with a higher ODS score. Similarly those who had features suggestive of puborectalis syndrome were 8.6 times more likely to report a higher ODS score (p = 0.025; OR 8.602 95% CI 1.318-56.158). Results are shown in table 6.10.

Table 6.10: Multivariate analysis ODS score

Covariate	Odds Ratio	95% Confidence Interval		P value
		Lower	Upper	
Rectocele >2cm	5.756	1.829	18.112	**0.003**
Anorectal angle binary	2.032	0.669	6.172	0.211
M line >4cm	0.633	0.172	2.333	0.492
H line >8cm	0.929	0.236	3.663	0.916
Puborectalis syndrome	8.602	1.318	56.158	**0.025**
Female sex	2.758	0.616	12.356	0.185
Previous pelvic floor surgery	2.421	0.556	10.549	0.239
Presence of cystocele	2.231	0.781	6.370	0.134

Wexner incontinence score

One hundred and fifty three patients (90.0%) completed the WIS. 30.1% had a score of 10 or greater. The proportion of patients with a WIS of 10 or more was not significant between males and females (p=0.822) and older and younger patients (p=0.176). On univariate analysis, the following features were correlated with an abnormal WIS: prior hysterectomy (p = 0.006; OR 3.446 95% CI 1.432-8.295), presence of enterocele (p = 0.003; OR 5.667, 95% CI 1.815-17.697) and inability to evacuate the rectum during MRD (p = 0.001; OR 0.237 95% CI 0.101-0.556) (table 6.11). Again, only MRD valuables with a p<0.2 are shown.

On multivariate analysis, only a lack of rectal evacuation was significantly associated with an abnormal WIS (p = 0.007; OR 0.228 95% CI 0.079-0.664). (Table 6.12)

Table 6.11: Univariate analysis Wexner incontinence score

Covariate	Odds Ratio	95% Confidence Interval		P value
		Lower	Upper	
Hysterectomy	3.446	1.432	8.295	**0.006**
Elevation	2.026	0.936	4.385	0.073
Enterocele	5.667	1.815	17.697	**0.003**
Mucosal binary	1.861	0.908	3.814	0.090
Evacuation <80%	0.237	0.101	0.556	**0.001**
Age >50	1.644	0.979	3.402	0.178

Table 6.12: Multivariate analysis Wexner incontinence score

Covariate	Odds Ratio	95% Confidence Interval		P value
		Lower	Upper	
Age >50	1.851	0.700	4.896	0.215
Hysterectomy	1.575	0.515	4.811	0.425
Evacuation <80%	0.228	0.079	0.664	**0.007**
Mucosal binary	0.884	0.327	2.390	0.808
Presence of enterocele	2.952	0.719	12.113	0.133
Abnormal pelvic floor elevation	1.411	0.542	3.670	0.480

DISCUSSION

This study aimed to assess how well various MRD factors commonly reported on by radiologists in the assessment of the severity of structural abnormalities correlated with PROMs. Overall, with the exception of a few MRD variables as discussed above, there appeared to be little to no correlation between MRD factors and the PROMS used within this paper. Several patient factors had also been explored as part of this regression analysis. On multivariate analysis, these factors seemed to have closer correlation with PROMs than the majority of MRD variables. For example, patients older than 50 were 2.2 times more likely to have an abnormal faecal incontinence domain score.

Apart from those discussed above, on multivariate analysis no other MRD variables seemed to have any significant correlation with significant symptom burden. This seems surprising when considering certain factors such as the presence of anorectal junction descent. However, on closer scrutiny of the data obtained, only 28 patients (16.5%) demonstrated anorectal junction descent of less than 2cm on strain, and 80 patients (47.1%) had M line descent which was considered to be either moderate or severe (>4cm), therefore this may have confounded the results. Additionally, as this study was undertaken as a retrospective review of obtained MRDs in a population who were attendees to a colorectal pelvic floor clinic, and there was no control group, it may be reasonable to conclude that this radiological feature is a common and early sign of pelvic floor laxity, and may be present radiologically prior to any clinical indication of significant symptoms.

To date, there are a handful of studies that have considered the relationship between patient-reported symptom severity and MRD. In 2009, Broekhuis et al [245] analysed POP-Q results and MRD findings against symptoms of pelvic organ prolapse in a cohort of 69 patients. They reported similar findings, in that MRD findings were largely not predictive of symptom severity. The only factor that correlated with symptoms was being able to see or feel a bulge in the vagina. In a similar vein, Lakeman et al[246] attempted to correlate MRD findings in three groups of ten patients: one group of asymptomatic nulliparous women, another with only mild symptoms and stage 1 POP, and a third group with significant symptoms and at least stage 2 POP. They used a variety of questionnaires: the Urogenital Distress inventory, Defecation Distress Inventory and the Incontinence Impact Questionnaire. None of the three patient groups showed any positive correlation between MRD staging of prolapse severity and questionnaire results. A study undertaken by Piloni et al[243] attempted to compile scoring criteria to be used in the interpretation of MRD in patients with ODS order to guide patient management. Rather than identify individual factors, they classified generalised MRD findings into grades 1-5, with higher grades indicating worse severity on MRD: Grade 1: considered to have a functional disturbance only; grade 2: as above, with additional minor anatomical defects (e.g. rectocele <2cm or 1st degree intussusception); grade 3: presence of major posterior compartment defects; grade 4: major defects in all three compartments present; grade 5: patients who had evidence of previous surgical failure (e.g. ODS recurrence after

STARR/stapled haemorrhoidectomy). Grades 1-2 were felt suitable for pelvic floor rehabilitation, with surgical intervention reserved for grades 3-5. In a similar vein to this work, they had attempted to correlate the ODS[79] score with MRD findings, and were also unable to find any significant correlation.

In another small study conducted by Hubner et al[247] which consisted of only 16 patients, where participants underwent MRD both pre and post rectocele repair, that there was a strong association between the perceived sensation of incomplete evacuation of the rectum and stool trapping on MRD. However they also corroborated the above findings that PROMS did not correlate with preoperative rectocele size, nor with postoperative morphology of the corrected rectocele.

When considering the likely reasons for a lack of robust correlation between MRD findings and PROMs, these are likely to be multifactorial. The supine positioning of the patient within the MRI scanner is likely to have an impact on the degree of abnormality detected and therefore MRD likely underestimates the structural severity of present disease. This phenomenon has already been alluded to earlier in this chapter. Anticipation of this likely underestimation of the degree of anatomical deformation of the rectum and adjacent organs during straining and defecation makes the measurements of H and M lines even more vital. Additionally, it is vital that patients are well schooled as to the need to really engage with the examination and strain as maximally as they can in order to bring about defecation whilst on the scanner, in order to optimise the diagnostic gains of performing the examination. This has been demonstrated as another potential issue within this study, given that 70.9% of patients had little to no evacuation of their rectum during the defecatory phase. These findings were replicated by Pilkington et al[227], where there was an under-reporting of abnormalities with MRD compared to barium proctography. This was a problem in particular when there was lack of rectal evacuation, with only 2% of included participants being able to fully empty the rectum during MRD.

Flusberg et al[116], in their study of 85 patients, highlighted the importance of a defecatory phase during MRD. They found that severity scores were significantly higher in the defecatory phase than in rest, squeeze and strain phases. More rectoceles, enteroceles and intussusceptions were identified, and the degree of bladder, uterovaginal and anorectal descent was more marked.

Looking again at the low incidence of defecation within this study, reasons may include patient embarrassment, poor instruction by the radiographer and too few

attempts at defecation. Additionally, the use of a jelly-like medium as a contrast agent within the rectum is not representative of true stool consistency, which may be an additional contributory factor – this would be easier to expel and unlikely to replicate stool trapping within a rectocele.

Limitations

As already discussed, one of the major limitations within this study is the lack of proper evacuation of the rectum, which is likely to have caused an under-representation of the true severity of structural deformation during defecation. Ways in which to improve this have already been alluded to, with good patient communication and maintenance of privacy as best able being key in optimising performance of the examination. Perhaps even use of a video demonstration pre procedure might be of use in optimisation or results, or inclusion of a pre-procedure questionnaire, which would enable the patient to highlight the areas of main concern to the radiologist interpreting the results.

Included patients were heterogeneous in terms of symptomology and pathological diagnosis, with some patients having undergone previous pelvic floor surgery. Ideally, a group of healthy volunteers should have been recruited to allow for comparison of normal versus abnormal. To counteract this, universally accepted definitions of normal and abnormal were used in image interpretation.

Conclusion

This study has demonstrated that whilst there were certain features on MRD in addition to patient factors which were associated with significantly abnormal PROM scores which were used throughout this thesis, there was a lack of demonstrable robust evidence of specific and consistent MRD features which would allow for the development of a scoring system to aid management decisions. As with all benign conditions, the decision to operate centres heavily on the patient's wishes and also their perception as to the severity of symptoms. Therefore if radiology imaging and patient both indicate severe disease, then this combination would allow for justification of a more invasive treatment strategy. When PROMs and MRD do not equate, then careful consideration has to be given, firstly to the adequacy of the performed tests, and whether further imaging is needed to corroborate patient symptoms (such as fluoroscopy), and secondly to whether every conceivable

conservative intervention has been performed, including where needed psychological support.

6.4 Study 3: Can MR defecography be used as a tool to predict the need for surgical intervention in patients with symptoms of obstructed defecation?

Introduction

The previous study in this chapter focussed on the degree of correlation between MRD and patient's experience of symptoms. This next study focuses on the ability of MR defecography to predict the need for surgery based on the radiological severity of findings. Included patients are those who have presented with a history of symptoms of obstructed defecation; this includes patients who also have symptoms of passive faecal incontinence that is likely secondary to a structural cause, for example rectoanal intussusception causing passive FI.

The main aim of this study was to attempt to delineate the role of MR-defecography in determining the need for surgical intervention through the analysis of each of the MRD variables described previously in the context of a final outcome of surgical intervention.

Methods

Patients included in this study were identified from a similar cohort to those examined in the previous MRD study. Inclusion and exclusion criteria were as follows:

Inclusion criteria:

1. Patients who had undergone MRD and had documented final treatment outcome data
2. Patients who reported symptoms of obstructed defecation

Exclusion criteria:

1. Patients who reported a history of isolated faecal urgency or urge faecal incontinence and who had no identifiable structural abnormality found on MRD.
2. In cases where no final treatment data was available.

The primary outcome measure was to determine whether there was any relationship between the various MRD variables already discussed within this thesis and the need for surgical intervention, performed using binomial logistic regression analysis.
The secondary outcome measure was to identify the predictive value of these MRD factors in determining the need for surgery through ROC curve analysis.

Statistical methods

Patient demographic data from patients who were managed conservatively was compared with those who underwent surgery using Chi Squared tests for categorical data, unpaired T-test for parametric variables and Man-Whitney U test for non-parametric variables.
Next, univariate binary logistic regression analysis was performed for each MRD variable of interest as categorical binary data based on the HMO classification system previously described. Multivariate analysis was then performed with factors with a $P<0.2$.
The final analysis comprised a separate analysis of the predictive ability of each MRD variable using ROC curves. The methodology for this has been described in detail in the general methods chapter. Variables with an AUC of 0.7 or more were considered to be fair discriminators.
For this study, in addition, an attempt to improve diagnostic accuracy was made through the combination of two MRD factors that separately had an AUC of 0.6 or greater. In order to do this, the optimum cut-offs for each MRD variable as defined by the Youden index were used to code each variable into a binary score. Two MRD variables were then combined so that the combination scored '1' if a patient dataset had values above this cut-off for both variables, and a '0' if only one or neither were above the cut-off value. ROC curve analysis was then performed again, giving a single coordinate with its corresponding AUC, sensitivity and specificity.

Results

Of the 170 patients who underwent MRD and had additional functional and follow-up data available twenty-nine were excluded as they did not have symptoms that were suggestive of obstructed defecation. A further twelve patients were excluded as their maximal treatment outcome was unknown. For the most part this was because these

patients had been specifically referred in for specialist diagnostic testing alone, and therefore there was no follow-up data available.

Therefore, 129 patients were included in the analysis: 21.6% were males. The study demographics are displayed in table 6.13 Sex, age and history of prior hysterectomy or pelvic floor surgery were not significantly different between groups.

Table 6.13: Study demographics

	Overall	Conservative	Surgery	P value
Females	114 (88.4%)	88	25	0.437
Mean age+/-SD	53.30+/-16.79	54.5+/-17.7	48.8+/-12.06	0.054
Age >50	73 (56.59%)	40	15	0.150
Prior hysterectomy	20 (15.50%)	16	4	0.514
Previous pelvic floor surgery (other)	17 (13.18%)	12	5	0.088
Maximal treatment outcome	None: 19 Medical: 9 Biofeedback: 59 Rectal irrigation:15 Surgery: 27	NA	NA	NA

The majority of patients completed a course of Biofeedback as a maximum treatment outcome. The majority of these were then discharged back to the community with the advice to seek a re-referral via their primary care practitioner if they felt they warranted surgical intervention in the future.

27 patients (20.9%) of patients underwent pelvic floor surgery as their maximal treatment outcome:

- 15 underwent ventral (mesh) rectopexy
- 4 had combined anterior/posterior repairs with Tension-free Vaginal Tape (TVT) insertion (performed by urogynaecologists)
- 2 had Stapled Transanal Rectal Resection (STARR)
- 4 had anterior or posterior vaginal repair (performed by urogynaecologists)
- 2 had sacrospinous fixation

Logistic regression analysis

Table 6.14 shows the results of the univariate logistic regression analysis for all MRD variables.

Table 6.14: Results of univariate logistic regression analysis

MRI variable	Odds Ratio	95% confidence interval		P value
		Lower	Upper	
Failure to elevate PF on contraction	1.121	0.431	2.912	0.815
Abnormal H line >6cm on strain	5.536	1.234	24.836	**0.025**
Abnormal M line >2cm strain	7.667	0.986	59.597	0.052
ARA change <15 degrees on defecation	0.389	0.144	1.050	0.062
Presence of urethral hypermobility	3.360	1.342	8.412	**0.010**
Presence of cystocele	1.884	0.795	4.464	0.150
Presence of cystocele >3cm	4.091	1.481	11.299	**0.007**
Presence of middle compartment descent	2.519	1.002	6.328	**0.049**
Presence of enterocele	1.679	0.404	6.978	0.476
Presence of rectocele	5.246	0.696	3.q2990	**0.010**
Presence of rectocele >2cm	1.667	0.696	3.990	0.251
Evacuation of <80% of rectal contents	0.517	0.176	1.520	0.230
Evacuation of <50% of rectal contents	0.845	0.341	2.093	0.716
Presence of rectal-anal intussusception or external rectal prolapse	0.728	0.150	3.539	0.694

On univariate logistic regression analysis using binary data, MRD factors predictive for the need for surgery were as follows: hiatal widening (H line) >6cm (p =0.025), cystocele >3cm (p= 0.007), presence of a rectocele (p = 0.010), presence of urethral hypermobility (p=0.010) and presence of middle compartment descent (p = 0.049). Approaching statistical significance was the presence of anorectal junction descent (M line) >2cm (p = 0.052) and failure to adequately increase the anorectal angle on defecation (p=0.062).

On multivariate analysis (table 6.15) of factors with a p<0.2 there were none found to be statistically significant correlated with the requirement for surgery.

Table 6.15: Multivariate analysis

MRD variable	Odds Ratio	95% Confidence Interval		P value
		Lower	Upper	
Abnormal H line >6cm on strain	0.784	0.074	8.306	0.840
Abnormal M lie >2cm	0.000	0.000	0.000	0.999
ARA change <15 degrees on defecation	1.367	0.430	4.351	0.596
Presence of urethral hypermobility	0.759	0.204	2.823	0.681
Presence of cystocele >3cm	0.450	0.136	1.484	0.190
Presence of middle compartment descent	1.198	0.359	3.994	0.769
Presence of rectocele	0.253	0.028	2.289	0.222

ROC curve analysis

The results of the ROC curve analysis of all individual MRD variables are shown below (table 6.16).

Table 6.16: Results of ROC curve analysis

	AUC	SE	Sig	Lower	Upper	Optimal Cut-off	Sensitivity	Specificity	Youdens
Difference ARA	0.387	0.056	0.063	0.273	0.493	13.5 degrees	0.475	0.775	0.253
M line strain	0.646	0.061	0.020	0.527	0.765	47.15mm	0.593	0.703	0.296
Change in M line rest to strain	0.640	0.057	0.025	0.529	0.752	38.05mm	0.556	0.713	0.269
H line strain	0.679	0.058	0.004	0.566	0.792	82.9 mm	0.481	0.84	0.321
Rectocele size	0.651	0.058	0.016	0.538	0.764	27.75	0.593	0.653	0.246
Cystocele size	0.654	0.065	0.014	0.526	0.782	18.25mm	0.593	0.743	0.268
Degree of evacuation	0.560	0.062	0.338	0.439	0.682	<2.5%	0.556	0.574	0.13
Middle compartment descent (binary) – females only[§]	0.613	0.064	0.086	0.488	0.738	N/A	0.640	0.586	N/A
Presence of rectal mucosal prolapse or intussusception[§]	0.552	0.063	0.406	0.428	0.676	N/A	0.444	0.660	N/A
Presence of urethral hypermobility[§]	0.645	0.059	0.021	0.529	0.760	N/A	0.704	0.586	N/A
Hysterectomy (females only) [§]	0.486	0.065	0.831	0.358	0.614	N/A	0.160	0.812	N/A
Presence of enterocele[§]	0.521	0.064	0.739	0.396	0.646	N/A	0.111	0.031	N/A

[§]: *Binary data*

ROC curve analysis of all MR variables individually demonstrated none with an AUC of >0.7. The majority of MR variables showed only a poor ability in predicting the need for surgical intervention (i.e. AUC 0.6-0.7). Changes in the anorectal angle, the degree of rectal evacuation, prior hysterectomy and presence of rectal mucosal prolapse or intussusception were considered to have failed AUC tests.

Each MR factor with an AUC >0.6 was combined with another in order to attempt to improve the diagnostic accuracy of the MRD in predicting the need for surgical intervention. Table 6.17 shows the results.

Table 6.17: Results: dual combination of MRD factors with individual AUC >0.6

	AUC	SE	Sig	Lower	Upper	Sensitivity	Specificity
H line + M Line	0.686	0.064	0.003	0.561	0.812	0.481	0.891
H line+ cystocele	0.677	0.065	0.005	0.550	0.804	0.444	0.910
H line+ rectocele	0.622	0.066	0.053	0.492	0.751	0.333	0.910
H line +Delta M line	0.696	0.064	0.002	0.570	0.821	0.482	0.910
H line+ Urethral hypermobility	0.680	0.064	0.005	0.555	0.805	0.481	0.879
M line + cystocele	**0.700**	**0.063**	**0.002**	**0.576**	**0.823**	**0.519**	**0.881**
M line + rectocele	0.618	0.064	0.060	0.493	0.744	0.444	0.792
M line + delta M line	0.622	0.063	0.052	0.498	0.746	0.481	0.762
M line + urethral hypermobility	0.669	0.062	0.007	0.547	0.790	0.557	0.782
Cystocele + rectocele	0.626	0.065	0.045	0.498	0.754	0.370	0.881
Cystocele + delta M line	0.663	0.065	0.010	0.536	0.784	0.444	0.882
Cystocele + urethral hypermobility	0.680	0.061	0.004	0.560	0.800	0.593	0.768
Delta M line + urethral hypermobility	0.641	0.064	0.025	0.516	0.765	0.481	0.800
Delta M line + rectocele	0.617	0.065	0.063	0.489	0.744	0.370	0.863
Rectocele + urethral hypermobility	0.631	0.063	0.038	0.506	0.755	0.481	0.780

AUC= area under the curve.
H line >82.9mm; M line >47.15mm; rectocele >27.75mm; cystocele >18.25mm; delta M line >38.05mm

On dual combination of MRD factors with an AUC >0.6, evidence of an M line of >47.15mm on strain combined with a cystocele of >18.25mm on straining was the only combination which was a "fair" predictor of the need for surgery (AUC = 0.7) (figure 6.58). Approaching statistical significance was the combination of an H line of >82.9mm with a change in the level of the anorectal junction (delta M line) on defecation of >38.05mm (AUC 0.696) (figure 6.59). Despite improvements in AUC

values compared to individually, all other combinations were only "poor" predictors of the need for surgery.

Figure 6.58: An M line of >47.15mm combined with a cystocele of >18.25mm is a fair predictor of the need for surgery.

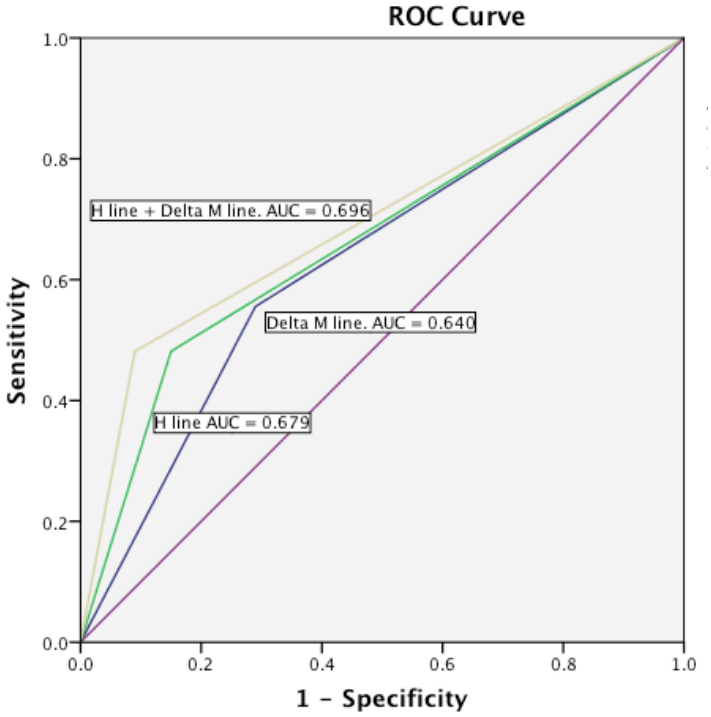
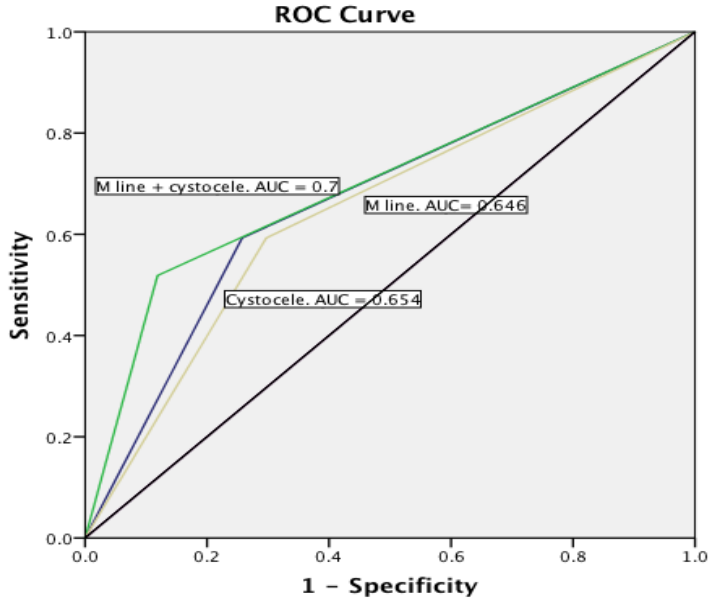


Figure 6.59: An H line of >82.9mm combined with a change in M line on strain by >38.05 gives an AUC of 0.696.



Discussion

This is the first study in published literature which attempts to identify specific MRD features or combinations of features which, if present may predict the need for surgery. Since being introduced as a means of assessment of pelvic floor dynamics in 1991[248], the role of MRD within the diagnostic framework for pelvic floor disorders has been relatively difficult to define. Our results show that in isolation, indicators of pelvic organ dysfunction seen on MRD were poor predictors of the need for surgical intervention. When binary univariate logistic regression analysis was performed, multiple MRD factors were found to be significantly related to the need for surgical intervention: hiatal widening >6cm (p =0.025), cystocele >3cm (p= 0.007), rectocele (p = 0.010), urethral hypermobility (p=0.010) and presence of middle compartment descent (p = 0.049). Presence of anorectal junction descent >2cm (p = 0.052) and failure to adequately increase the anorectal angle on defecation (p=0.062) were approaching statistical significance. However, when multivariate analysis was performed, these factors were not found to be statistically significant. This may, be explained, at least in part, by the tri-compartmental nature of the pelvic floor, and that some patients suffer from unicompartmental rather than global pelvic floor dysfunction, and therefore multivariate analysis of factors across all three compartments may not be representative of true disease states in all patients. Additionally, as already discussed within this chapter, decisions surrounding operative intervention in patients with obstructed defecation are complex, with many factors coming into play that take into consideration the benign nature of the problem.
On ROC curve analysis the combination of an M line of >47.15mm on strain with a cystocele of >18.25mm was the only "fair" predictor of the need for surgery. An H line of >82.9mm with a change in the level of the anorectal junction on defecation (M line) of >38.05mm was close to being considered significant. Therefore these factors in particular could be focussed on during MRD evaluation. It should be noted however, that in reality it may be challenging to accurately identify such small measurements when interpreting MRD without a degree of reporting error.
Several other authors have attempted to define this role in the decision-making process, some of which has been visited earlier in this chapter. Attenberger et al[218] retrospectively examined outcomes with 63 female patients presenting with pelvic floor dysfunction. They found that MRD had acted as an essential examination for

diagnosis in 44% of patients. In particular, the role of MRD was clear when enterocele was suspected. In 13/22 (59%) of cases where MRD was deemed essential for diagnosis, management plans were altered as a result of the scan results. In a similar fashion, Hetzer et al[117] retrospectively studied 50 patients presenting with FI and found that MRD changed operative planning in 67% of cases. Kamal [249], in their series of 30 patients, demonstrated a change in management of patient care in 40% of cases when MRD findings were discussed in an MDT environment. They also identified a significant correlation between MRD and operative findings in terms of enterocele, cystourethrocele, vaginal cuff prolapse and uterine prolapse. This was not replicated with rectoceles. Kaufman et al[120], whose study formed part of the earlier meta-analysis, found that the use of MR defecography altered surgical management plans in 41% of patients. They had compared clinical examination and ECCD against MRD, and concluded that there was no "best test" to indicate management, rather that each had its own strengths which were complimentary to one another.

Limitations

The main limitation of this study is the use of ROC curve analysis to predict the need for surgery rather than its traditional use as a predictor of the presence or absence of a disease state. However, it could be argued that the need for surgery indicates the presence of moderate-severe pelvic floor dysfunction, and therefore the use of a ROC curve in this situation is a valid means of assessing the relationship between surgery and specific MRD features. Additionally, as no post treatment ODS scores were available for these patients, there was no way of truly predicting whether the proposed surgery had been of real clinical value, or whether the correct decision to intervene surgically had been made.

Conclusion

MR-defecography can act as a useful adjunct in identifying the need for surgery in patients with ODS symptoms, with a few factors in combination, if present may aid this decision. In isolation, MRD alone does not accurately predict the need for surgery. However, the literature does consistently demonstrate that a role for MRD does exist and that its use has influenced treatment decisions at least in part.

6.5 Chapter conclusions

This chapter has comprised three individual studies, including a meta-analysis and two clinical studies, all of which explored the role of MRD in pelvic floor dysfunction. The meta-analysis demonstrated some advantages with MRD, namely better identification of enteroceles compared to clinical examination and in the assessment of complex pelvic floor disease. However, MRD did fall short in detection and miss rates of all described abnormalities compared to the fluoroscopic techniques described. There was no robust and consistent relationship with symptom severity as reported by patients with symptoms of obstructed defecation, and in isolation was generally poor at predicting the need for surgical intervention. Therefore, it would be wise to ensure that all patients undertake some form of questionnaire-based assessment prior to scheduling for imaging, as this may identify who is most likely to benefit from MRD versus those who may benefit from a different imaging modality.

The underlying challenge relates to the complexity of pelvic floor dysfunction, which can effect one or all three of the compartments, and the fact that this is a benign condition, and therefore treatment decisions cannot be simplified into a one size fits all rule. Often, patients who have clinically significant abnormalities detected on MRD choose not to proceed with invasive surgical treatments for a number of reasons, such as having not yet completed their families, or have a desire to 'hold out' as long as possible in the knowledge that with time symptoms may worsen to a point that they wish to proceed as benefit then outweighs any perceived risks of surgery.

MRD does have a role in the diagnostic work-up of a patient, and as with the already visited PROMS and ARM, can aid the MDT process in making treatment decisions. Ultimately decisions must be individualised according to each patient rather than based on any single investigation result.

Part 3: The exploration of commonly encountered disease states in a colorectal pelvic floor service

CHAPTER 7: OBSTETRIC ANAL SPHINCTER INJURIES

Publications related to this chapter:

1. Does a missed obstetric anal sphincter injury at time of delivery affect short-term functional outcome? Ramage L, Yen C, Qiu S, Simillis C, Kontovounisios C, Tan E, Tekkis P. Ann R Coll Surg Engl. 2017 Sep 15:1-7. doi: 10.1308/rcsann.2017.0140.

2. Functional and quality of life outcomes following obstetric anal sphincter injury (OASI): does the grade of injury affect outcomes? Ramage L, Yen C, Qiu S, Simillis C, Kontovounisios C, Tekkis P, Tan E. Int Urogynecol J. 2017 May 18. doi: 10.1007/s00192-017-3334-3.

7.1 Introduction and aims of chapter

Obstetric anal sphincter injuries (OASI) represent a major cause of faecal incontinence, both in the short and longer term, and therefore a significant population presenting to a tertiary pelvic floor service. This chapter explores a group of patients who have sustained an OASI and who have been followed up within a specialist pelvic floor clinic with capabilities for both anorectal physiology and endoanal ultrasound scanning.

Outline and objectives

This chapter comprises two separate studies. The first study analyses the impact of a missed OASI on the short-term (<24 months) function of the anal sphincter, and whether there are any detectable differences in PROMs, manometry, quality of life and sexual function between OASIs undergoing primary repair versus those who have been subsequently detected. The aim of the first study was to identify whether there were any demonstrable functional differences between patients who had undergone primary repair of an OASI and those who had initially been missed.

The second study analyses patient functional data according to grade of obstetric injury. Analysis is performed using the distinct OASI grades as defined previously.

Again, similar outcomes are compared, namely PROMs, anorectal manometry, QoL parameters and sexual function.

The aim of the second study was to assess whether increasing severity of OASI had any impact on function, Quality of life (QoL), anorectal manometry and sexual function during early stages of follow-up (<24 months) following delivery.

7.2 Chapter methods

Patients were identified from the pelvis floor database. Following vaginal delivery, it is current practice within the local trust for all patients who have sustained perineal trauma to be followed up in a perineal clinic, which is run by the obstetric service. This includes review of wound healing, and bowel and urinary function. In the initial years since the database was commenced, patients were traditionally reviewed at 6 weeks postpartum, and if an OASI had been sustained, then patients were offered a consultation within the colorectal pelvic floor clinic in order to discuss symptomology, undergo endoanal assessment, and to discuss future mode of delivery. Equally, if patients who had either sustained a 2nd degree tear or had undergone an episiotomy and were symptomatic in terms of bowel function, then they were also referred on for further assessment by a coloproctologist in order to assess for occult sphincter injury. More recently, the service was amended and only those with significant OASI or those who were displaying symptoms related to anal sphincter integrity were referred for full assessment. All patients managed in the perineal clinic were given advice and guidance as to the performance of pelvic floor exercises, and may have had additional physiotherapy input if required prior to referral.

The majority of assessments within the colorectal clinic took place at 3-12 months from the date of delivery. There is no national predefined optimal timeframe for anal sphincter assessment, however standard practice within the local unit was to allow an absolute minimum of three months between delivery and initial assessment.

Symptomatic patients were initially sent for Biofeedback physiotherapy unless they had already had input from a physiotherapist. If needed, they were subsequently followed up on a 6-12 monthly basis. In cases refractory to non-invasive treatment methods, secondary sphincter repair or SNS was considered.

As with the previous studies within this thesis, PROMs assessment was through the use of the Birmingham Bowel, Bladder & Urinary Symptom Questionnaire (BBUSQ)[173], and Wexner Incontinence Score (WIS)[174]. Quality of life (QoL) outcomes were measured using the SF-36[177]. The Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12)[250] was used in the assessment of sexual function post delivery. Anorectal manometry was performed as previously described.
EUS was performed within clinic; additionally this was performed by an experienced radiologist within the postpartum follow-up period. The final grade of tear was defined based on ultrasonic evidence of the degree of sphincter involvement as described earlier within this thesis[157].
Patients who did not undergo EUS for final grading of OASI or had an unclear initial diagnosis were excluded from analysis.

Statistical methods: missed OASI

2:1 propensity matching was performed for the missed OASIs using three criteria: parity, time from delivery to assessment and final grade of OASI. This was performed using SPSS statistical software.
The paired T test was used for parametric data, and the Mann-Whitney U test was used for non-parametric data. Normality of data was tested using the Shapiro-Wilk test. Pearson chi-square was used for proportional analysis.

Statistical methods: grade analysis of OASI

All statistical analysis was performed using SPSS version 21.0 and conducted at 95% confidence intervals. The Shapiro-Wilk test was used on continuous data to test for normality. Subsequently, for non-parametric data, the Kruksal-Wallis and Mann-Whitney U test were employed. For parametric data, the one-way ANOVA was used with post-hoc Tukey honesty of significance test and the unpaired student's t-test. The Chi-square test and post-hoc analysis of standard residual was used in order to analyse categorical data.

7.3: Study 1: Does a missed sphincter injury at the time of injury impact on short-term functional outcomes?

Results

Overall, there were 107 OASIs and 34 missed OASIs identified with at least one functional outcome reported. Using the matching criteria above, it was possible to match 32 missed OASIs with 62 patients who underwent primary repair. Table 7.1 shows the study demographics.

Table 7.1: Study demographics

		Missed OASI	Primary Repair	P value
No of Patients		32	62	-
Age at delivery*[a]		33.8± 0.8 ± 5.0	32.7 ± 0.6 ±5	0.34
Parity	**1**	24	48	0.88
	2	7	13	
	3	1	1	
Episiotomy[b]		18/28 (64.3%)	15/49 (30.6%)	**0.004**
Instrumental Delivery[b]		18/29 (62.1%)	35/52 (67.3%)	0.64
Previous Tears[b]		1/32 (3.1%)	1/61 (1.6%)	0.64
Final Grade	**3A**	21	42	0.73
	3B	11	19	
	4	0	1	
Mean time to Assessment		10.0±1.2 ± 7.0	8.9 ± 0.9 ±6.7	0.47

**Mean ± Standard Error ± Standard Deviation [a] Mann-Whitney U test [b]Pearson Chi-square test*

There were no significant differences in parity (p =0.88), age (p = 0.34), instrumental delivery rates (p = 0.64), history of prior tear (p = 0.64) or time to follow up (p = 0.47) between the two groups. However, there was a significantly higher incidence of episiotomies performed in the missed OASI group (64.3% versus 30.6%, p = 0.004).

1. Functional outcomes

Table 7.2 shows the functional outcomes as measured using PROMs.

Table 7.2: Results of functional scores

	Missed OASI			Primary repair			P value[b]
	N	Mean	SD	N	Mean	SD	
BBUSQ Incontinence	24	30.56	14.41	50	19.75	15.65	**0.002**
BBUSQ Evacuation	24	18.23	15.15	50	10.82	9.60	0.052
BBUSQ Urinary	22	28.25	14.90	44	17.01	13.87	**0.001**
BBUSQ constipation	24	54.72	13.49	50	54.90	11.59	0.896
Wexner Score	17	6.00	3.76	42	3.67	4.06	**0.009**

N: number of responses. SD = Standard Deviation. [b]Mann-Whitney U Test

Patients with a repaired OASI had a significantly better BBUSQ incontinence scores (19.75± 15.65 versus 30.56± 14.41%; p = 0.002) and Wexner incontinence scores (3.67±4.06 versus 6.00±3.76; p = 0.009). Patients with a repaired OASI also had significantly better BBUSQ urinary domain scores (17.01±13.87% versus 28.25± 14.9%; p = 0.001). The patients with a detected and repaired OASI had a normal urinary incontinence score.

BBUSQ evacuation scores were 18.23± 15.15% in the missed versus 10.82± 9.60% in the repaired groups (p = 0.052), although this was only slightly out with the normal range (defined as <17% according to validation criteria). Neither group were found to have an abnormal constipation score.

2. Quality of life (QoL): SF-36

Table 7.3 shows the results of the eight domains of the SF-36 across both groups.

Table 7.3: Results of SF-36

	Missed OASI			Primary Repair			P value[b]
	N	Mean	SD	N	Mean	SD	
Physical Functioning	23	80.00	22.11	43	88.31	20.74	**0.045**
Role physical	22	81.82	22.57	41	83.99	24.88	0.428
Body Pain	23	73.37	25.09	43	78.49	22.87	0.511
General Health	21	72.14	19.34	41	74.21	17.40	0.828
Vitality	23	53.26	11.13	43	52.62	10.36	0.886
Social Functioning	23	73.38	28.53	42	82.44	23.11	0.167
Role Emotional	22	85.60	23.02	41	85.77	24.17	0.823
Mental Health	23	69.78	13.77	43	69.07	11.18	0.571

N: number of responses. SD = Standard Deviation; [b]Mann-Whitney U Test

Patients with a repaired OASI scored significantly better in the 'physical function' domain of the SF-36 (88.31± 20.14 versus 80±22.11; p = 0.045) Otherwise, there were no significant differences between groups.

3. *Anorectal physiology*

Table 7.4 gives the anorectal manometry results. Overall, there were no statistical differences found between the two groups. The maximum tolerated volume, which was higher in those who had a primary repair of OASI was approaching statistical significance (124.19±59ml versus 87.69±27.51ml; p = 0.070).

Table 7.4: Anorectal physiology missed versus primary repair OASIs

	Missed OASI			Primary repair			P value
	N	Mean	SD	N	Mean	SD	
Maximum resting pressure (mmHg)[a]	24	65.75	18.24	53	61.96	15.06	0.342
Maximum squeeze pressure (mmHg)[a]	24	99.17	29.34	52	89.23	24.48	0.127
Mean squeeze increment (mmHg)[a]	25	32.56	19.20	52	27.27	18.06	0.242
Mean 5 second squeeze increment (mmHg)[b]	15	32.27	20.22	20	27.05	25.71	0.191
Mean involuntary cough pressure (mmHg)[b]	13	51.92	28.58	20	39.65	23.82	0.158
Threshold volume (ml)[b]	14	29.27	12.84	26	33.12	19.30	0.790
Urge volume (ml)[b]	14	53.21	19.47	26	64.50	31.13	0.361
Maximum tolerated volume (ml)[b]	13	87.69	27.51	21	124.19	59.00	0.070

[a] Mann-Whitney U test [b]Pearson Chi-square test

4. Sexual function: PISQ-12

PISQ-12 scores were available for 24 (38.71%) of patients who had undergone primary repair, and 10 (31.25%) of patients who had a missed OASI (table 7.5). The mean overall score was 33.13± 8.14 in the repaired versus 34.7±6.96 in the missed OASI group. The scores were not found to be statistically different between the two groups (p= 0.597).

Table 7.5: results of PISQ-12.

	n	Mean PISQ-12 score	Standard deviation	P value*
Primary repair	24	33.13	8.14	0.597
Missed OASI	10	34.70	6.96	

*Max score = 48. *Unpaired T test*

Discussion

The above study aimed to identify any apparent difference in early functional results following a missed OASI. The pertinent findings were that incontinence scores were significantly worse in patients who had a missed sphincter injury, as was early urinary function. The latter finding may occur due to a generalised reduction in pelvic floor muscle strength and the ability to control urinary flow secondary to the significant perineal trauma sustained during childbirth. An interesting finding was that the episiotomy rates were significantly higher in those with a missed OASI. Verghese et al [251], undertook a large meta-analysis of 651,114 women and found that a mediolateral episiotomy was protective against OASI (RR 0.67, 95% CI 0.49-0.92). The reasons behind this higher demonstrated episiotomy rate within the missed OASI group may include a belief that the performance of an episiotomy has been protective against anal sphincter damage and therefore the attending midwife or clinician may not assess the sphincter complex integrity as thoroughly as in cases where there has been a natural perineal tear.

The quantification of the true incidence of missed OASI is challenging, as unless endoanal ultrasound assessment is uniformly carried out on all women post delivery who have sustained a G2 injury or above, then patients are unlikely to undergo full endoanal assessment unless they present with symptoms of faecal urgency, reduced deferral time or flatal or faecal incontinence. Therefore it is conceivable that occult lesions may go undetected initially, only to be discovered later in life where the patient becomes more symptomatic, perhaps after subsequent deliveries or in the postmenopausal period.

Some researchers have suggested the use of endoanal ultrasound in the immediate post-delivery period with the aim of improving detection rates of OASI. Faltin et al [252] conducted a randomised control trial, which recruited 752 primiparous women. Study participants had no clinical evidence of anal sphincter tear on perineal inspection. Included patients were randomised to either undergo endoanal ultrasound scan prior

to any perineal wound suturing to allow identification of the presence of an occult sphincter injury and permit repair as appropriate, or to receive standard care. They demonstrated a 5.6% rate of OASI detection in the treatment arm which would have been otherwise missed. At 3 and 12 months postpartum, significant differences in the observed rates of severe faecal incontinence were noted between groups (3.3% versus 8.7% at 3 months and 3.2% versus 6.7% at 12 months). They concluded that their results favoured use of endoanal ultrasound assessment for all G2 tears to facilitate better detection and subsequent appropriate management of any sphincter involvement. Similarly, Ozyart et al screened 201 women who had undergone a mediolateral episiotomy prior to hospital discharge, and found occult sphincter injuries not detected on clinical examination in 11.5% of study participants[253].

The utilisation of endoanal ultrasound post G2 tear or following episiotomy in order to identify those injuries not detected through clinical examination is, in theory at least, a means of ensuring patients receive the best possible standard of care, which means primary repair of their sphincter injury. However, in reality, this would be incredibly labour intensive – it is estimated that approximately 77% of primiparous women require an episiotomy[254]. In addition, a clinician who is appropriately trained to interpret the images would need to be available, and it is likely that imaging would be difficult to interpret within the immediate post-delivery phase given the likelihood of significant tissue plane distortion due to oedema and haematoma formation. Therefore, this currently remains a research area[166] and further studies would be needed in order to further stratify the risk/benefit ratio and to more accurately define the patient cohort who would benefit most from post-delivery endoanal sphincter assessment.

The presence of an occult OASI missed at the time of delivery has the potential for significant implications on bowel function. Fatlin et al[252] demonstrated that women with clinically undetected and unrepaired OASIs were 8.8 times (95% CI 2.9-26.5) more likely to report symptoms of AI than those without a demonstrable sphincter injury on endoanal ultrasound. A further study documented 71.5% of patients who had a clinically undetected (and hence unrepaired) OASI demonstrated symptoms of at least moderate FI during the early postpartum phase[253]. Oberwalder et al[255] performed a comprehensive meta-analysis using Bayesian statistical methods of five studies which examined rates of OASI detected through postpartum endoanal ultrasound. They demonstrated an incidence of OASI in primiparous women of 26.9%

and 8.5% in multiparous women. They concluded that in those presenting with AI, there was a prevalence of OASI in 76.8% of primiparous and 82.8% of multiparous women. Sultan et al[256] prospectively examined women at both 6 weeks prior to delivery and at 6 weeks postpartum. They were examined again at 6 months post-partum if they were symptomatic. Within a cohort of 127 women, they found 35% had evidence of sphincter disruption. Presence of a sphincter defect on endoanal ultrasound was significantly associated with symptoms of faecal urgency and urge incontinence.

Limitations

The predominant limitation encountered within this study is the potential for selection bias, as only women who had presented with clinical symptoms suggestive of anal sphincter compromise were referred for full anorectal assessment. However, this is hard to negate unless all patients with a G2 tear or episiotomy undergo endoanal ultrasound assessment pre-discharge or within the early post-delivery period. Therefore it is feasible that there are significant numbers of OASIs that go undetected in this early stage only to present some time later following further insult to the anal sphincter complex or as a consequence of advancing age. However, it could be argued that nearly all patients with OASI are expected to have at least some evidence of AI symptoms, this is apparent within the data presented in the following study; therefore it is unlikely that large numbers have remained unidentified.

In addition, the length of follow-up within this study is relatively short, and only at a single time point for each patient. Therefore, propensity matching was undertaken to allow for a likewise comparison. Finally, the effect of a misdiagnosis with regards to the degree of OASI sustained was not explored within this work - rather these patients were excluded from analysis. It was felt that it would be challenging to determine whether misclassification of the OASI was secondary to under-recognition of the degree of injury sustained, or whether the injury was appropriately repaired but under- or over- estimated due to limited understanding of the grading system.

Conclusions

The risk of an occult OASI at delivery is significant. The data presented within this thesis demonstrates the potential for worse short-term outcomes within the early post-delivery period in those who have had an occult injury that has not undergone primary

repair. Occult injuries can be targeted with interventions such as Biofeedback physiotherapy in order to improve function as best possible. Alternatives include consideration for a delayed sphincter repair, or sacral nerve stimulation. If left undetected and unrepaired, over time, the risk of anal incontinence will increase. Therefore it is likely that those with a missed OASI may have a higher risk of problems relating to anal continence later in life. A greater index of suspicion must be maintained in those with risk factors for OASI including a baby >4kg, instrumental delivery and nulliparity. A thorough examination of the perineum must take place following delivery in order to maximise detection rates, especially when an episiotomy has been performed. If an occult injury is suspected, then patients should undergo early endoanal assessment to give an opportunity for aggressive management in terms of Biofeedback physiotherapy and counselling regarding future mode of delivery. Further studies are suggested in order to quantify the longer-term functional consequences as a result of occult sphincter injuries.

7.4: Study two: Does the grade of obstetric anal sphincter injury impact short-term functional outcomes?

The aims, objectives and methods have already been outlined in section 7.1&7.2 of this chapter.

Results

A total of 177 patients were included within this study: 29 (16.38%) had a final diagnosis of 3Ga, 55 (31.07%) were G3b, 77 (43.5%) were classified as G3c injuries, and 16 (9.04%) were G4 injuries. Table 7.6 gives the breakdown of the time point of assessment for each patient by grade of severity (range 3-24 months).

Table 7.6: Number of patients with each OASI grade in time cohorts 3-6 months, 6-12 months, 12-24 months.

	Total	3-6 months	6-12months	12-24 months
3a	29	6	20	3
3b	55	18	29	8
3c	77	31	38	8
4	16	7	7	2
	177	**62**	**94**	**21**

The majority of patients (n= 99) were seen at 6-12 months post delivery with only 21 patients between 12-24 months and 62 at 3-6 months. Comparing baseline characteristics of these patients, there were no differences in age at delivery, parity, the need for episiotomy or an instrumental delivery, history of previous tears and the final grade as defined by EUS. As expected, there was a significant difference between time of assessment between the three predefined time points, ($p<0.001$), validating any comparisons made between these (table 7.7).

Table 7.7: Demographical study data

		Overall	3-6 Months	6-12 Months	12-24 Months	P value
No of Patients		177	62	94	21	-
Age at delivery		32.9 ± 4.6	32.6 ± 4.3	33.0 ± 5.0	33.7 ± 3.7	0.552
Mean time to Assessment		8.1± 4.1	4.5 ± 0.9	8.4 ±1.5	16.9 ± 3.3	**0.000**
Parity	**1**	144 ((81.4%)	49 (79.0%)	78 (82.9%)	17 (81.0%)	0.717
	2	27 (15.2%)	9 (14.5%)	14 (14.9%)	4 (19.0%)	
	3	5 (2.8%)	3 (4.8%)	2 (2.1%)	0	
	4	1 (0.6%)	1 (1.6%)	0	0	
Episiotomy		56 (40.9%)	17 / 53 (32.1%)	32 / 72 (44.4%)	7 / 12 (58.3%)	0.166
Instrumental Delivery		88 (62.9%)	29 / 53 (54.7%)	49 / 74 (66.2%)	10 /13 (76.9%)	0.227
Previous Tears		2 (6.1%)	0/13 (0%)	2/16 (12.5%)	0/4 (0%)	0.323
Final Grade	**3A**	29 (16.4%)	6 (9.6%)	20 (21.3%)	3 (14.2%)	0.529
	3B	55 (31.1%)	18 (29.0%)	29 (30.9%)	8 (38.1%)	
	3C	77 (43.5%)	31 (50%)	38 (40.4%)	8 (38.1%)	
	4	16 (9.0%)	7 (11.3%)	7 (7.4%)	2 (9.5%)	

P-values shown are chi-square comparisons across the 3 pre-defined time frames

Overall analysis

Analysis was performed across all 177 datasets regardless of time from delivery across all parameters. 83.6% of patients experienced symptoms of urgency while 21.9%, 41.1% and 8.2% reported symptoms of faecal incontinence, flatal incontinence or combined faecal/flatal incontinence respectively at least once per week. There were no statistically significant differences in the prevalence of these symptoms across the grades of tears (table 7.8).

When comparing across all 4 grades, maximum squeeze increment (SI) on ARM turned out to be the only significant parameter with G3a having a better squeeze

increment when compared to both G3b and G4 at a mean of 35.6, 24.5 and 20.2 mmHg and p=0.02 and p=0.01 respectively. The other ARM scores were not significant and had no discernable trends.

Table 7.8: Overall analysis per grades

	3a		3b		3c		4		p-value
	N	Mean Score	N	Mean Score	N	Mean Score	N	Mean Score	
Functional Scores									
BBUSQ: Constipation	26	56.0	49	51.8	57	55.0	15	56.7	0.692
BBUSQ: Incontinence	26	21.2	49	22.7	57	24.7	15	26.4	0.483
BBUSQ: Evacuation	25	14.6	49	12.1	55	12.3	13	16.2	0.557
BBUQ: Urinary	21	9.8	47	11.6	51	10.7	15	15.0	0.395
Wexner	19	5.0	37	5.0	38	4.5	10	4.4	0.682
PISQ-2	8	46.3	22	45.5	33	44.6	10	44.3	0.709
SF-36 Quality of life									
Physical Functioning	21	86.3	40	83.6	53	89.2	6	70.8	0.081
Role Physical	20	88.1	38	82.2	52	84.0	7	73.2	0.540
Bodily Pain	21	69.6	41	79.1	52	82.7	7	71.4	0.113
General Health	20	67.5	39	71.5	48	75.1	7	67.1	0.679
Vitality	21	52.7	41	51.7	52	52.2	7	49.4	0.895
Social Functioning	21	78.6	40	78.8	52	79.9	7	73.9	0.707
Role: Emotional	20	86.7	38	90.4	52	84.4	7	82.1	0.925
Mental Health	21	66.3	41	67.7	52	67.8	7	63.9	0.915
Anorectal manometry									
Final RP	23	64.1	44	66.3	61	61.5	13	57.9	0.380
Final SP	23	100.7	42	89.6	61	94.6	12	78.0	0.088
Max SI	24	35.6	42	24.5	61	33.3	12	20.2	**0.033***

**G3a v G3b, p=0.023; G3a vG4, p=0.01*

3-6 Months

The 62 patients in the 3-6 months cohort were seen in clinic at a mean of 4.5 ± 0.9 months after delivery. 89.1% of the patients experienced faecal urgency. 11.9% reported experiencing faecal incontinence, 23.8% experienced flatal incontinence and 7.1% had dual incontinence at least once a week. Analysis revealed a significant difference between BBSUQ-constipation scores of G3b when compared to G3a and G3c, p=0.007 and p=0.008 respectively. G3b had a lower constipation score at 47.2 compared to G3a, 63.9, and G3c 58.4 (Table 7.9). In addition, there was a significantly lower WIS of 1.3 in G3a tears when compared to G3b, (p=0.008), and G4, (p=0.032), with scores of 5.7 and 4.2 respectively. All other scores of the BBSUQ, PISQ-2, SF-36 and ARM results showed no significant differences.

6-12 Months

These 94 patients were seen at a mean of 8.4 ±1.5 months after delivery. 77.5% reported significant faecal urgency while 14.3% experienced faecal incontinence, 32.7% experienced flatal incontinence and 2.0% had dual incontinence. Of the 14.3% of patients experiencing faecal incontinence there was a statistically significant contribution from the group of patients with G3a tear with a standard residual of +2.4 on chi-square analysis. On reviewing the various self-reported scoring methods, the scores were similar across all 4 grades of tears (Table 7.10).

Table 7.9: Functional Scores, SF-36 Quality of Life questionnaire and ARM results for patient seen at 3-6 months post delivery

3-6 Months	3a		3b		3c		4		p-value
	N	Mean Score	N	Mean Score	N	Mean Score	N	Mean Score	
Functional Scores									
BBUSQ: Constipation	6	63.9	17	47.2	26	58.4	6	58.6	**0.015***
BBUSQ: Incontinence	6	22.9	17	25.7	26	23.4	6	22.2	0.946
BBUSQ: Evacuation	6	13.4	17	14.2	25	11.6	5	12.5	0.960
BBUSQ: Urinary	4	10.4	17	13.9	22	11.0	6	14.9	0.663
WIS	4	1.3	16	5.7	19	3.7	5	4.2	**0.039**[#]
PISQ-2	2	43.7	8	46.9	16	45.9	5	46.6	0.569
SF-36 Quality of Life Scoring									
Physical Functioning	3	86.7	14	85.0	22	84.1	3	70	0.779
Role Physical	3	79.2	12	81.25	21	72.9	4	82.8	0.751
Bodily Pain	3	58.3	14	81.7	22	75.6	4	90.6	0.425
General Health	3	48.3	12	76.5	20	78.3	4	75	0.311
Vitality	3	45.8	14	48.1	22	52.3	4	55.2	0.525
Social Functioning	3	70.8	14	77.7	22	75.8	4	100	0.195
Role: Emotional	3	75.0	12	97.2	21	79.7	4	93.8	0.153
Mental Health	3	58.3	14	69.6	22	68.1	4	68.8	0.418
Anorectal Manometry									
Final RP	5	67.0	12	66.8	26	60.7	7	58.4	0.434
Final SP	5	95.8	11	93.8	26	95.5	6	79.5	0.672
Max SI	5	28.8	11	28.5	26	35.3	6	26.2	0.925

N = no. of patients analysed for each outcome. *G3a versus G3b p=0.007; G3b versus G3c p=0.008 [#]G3a versus G3b, p=0.008; G3a versus G4, p = 0.032

Table 7.10: Functional Scores, SF-36 Quality of Life questionnaire and ARM results for patient seen at 6-12 months post delivery

6-12 Months	3a		3b		3c		4		p-value
	N	Mean Score	N	Mean Score	N	Mean Score	N	Mean Score	
Functional Scoring									
BBUSQ: Constipation	18	54.2	24	54.5	24	51.8	7	54.8	0.893
BBUSQ: Incontinence	18	19,7	24	18.9	24	23.5	7	32.7	0.207
BBUSQ: Evacuation	17	15.7	24	10.2	23	14.9	6	21.2	0.127
BBUSQ: Urinary	15	9.6	23	9.4	22	11.7	7	17.0	0.321
WIS	13	5.6	18	4.0	15	3.7	4	4.8	0.712
PISQ-2	6	47.2	11	44.4	14	42.8	4	42.5	0.582
SF-36 Quality of Life Scoring									
Physical Functioning	16	84.8	19	84.2	26	92.9	1	70.0	0.251
Role Physical	15	88.3	19	85.9	26	93.2	1	87.5	0.276
Bodily Pain	16	72.7	20	78.1	25	87.5	1	50	0.076
General Health	15	72.3	20	61.2	24	73.8	1	80	0.720
Vitality	16	53.5	20	55.1	25	53.7	1	43.8	0.607
Social Functioning	16	82.8	19	83.6	25	84.5	1	87.5	0.846
Role: Emotional	15	88.3	19	88.6	26	86.2	1	100	0.750
Mental Health	16	69.2	20	66.1	25	70.0	1	75	0.541
Anorectal Manometry									
Final RP	16	62.9	26	66.1	27	61.9	6	57.3	0.621
Final SP	16	102.1	26	90.0	27	96.4	6	76.5	0.186
Max SI	17	37.6	26	23.9	27	34.5	6	19.2	0.053

N = no. of patients analysed for each outcome.

12-24 Months

Only a small cohort of 21 patients were reviewed at 12-24 months post delivery. They were seen in clinic at a mean time of 16.9 months ± 3.3 months after delivery and

almost all of them (90%) presented with symptoms of faecal urgency. 15.4% of the patients experienced dual incontinence and an equal number of patients had symptoms of faecal and flatal incontinence at 30.8%. There were no significant differences in functional scores between groups (Table 7.11).

Table 7.11: Functional Scores, SF-36 Quality of Life questionnaire and ARM results for patient seen at 12-24 months post delivery

12- 24 Months	3a		3b		3c		4		p-value
	N	Mean Score	N	Mean Score	N	Mean Score	N	Mean Score	
Functional Scoring									
BBUSQ: Constipation	2	48.3	8	53.8	7	53.6	2	57.5	0.802
BBUSQ: Incontinence	2	29.2	8	28.1	7	33.9	2	16.7	0.663
BBUSQ: Evacuation	2	8.3	8	13.3	7	6.3	2	10.4	0.614
BBUSQ: Urinary	2	10.4	7	12.9	7	6.5	2	8.3	0.395
WIS	2	8	5	6.4	4	11.0	1	4	0.510
PISQ-2	0	-	3	45.7	3	46.3	1	40.0	0.319
SF-36 Quality of Life Scoring									
Physical Functioning	2	17.9	7	79.2	5	76.7	2	72.5	0.137
Role Physical	2	100	7	74.1	5	82.5	2	46.9	0.130
Bodily Pain	2	62.5	7	76.8	5	67.1	2	43.8	0.276
General Health	2	60.0	7	68.6	5	56.7	2	45.0	0.866
Vitality	2	56.3	7	59.1	5	45.0	2	40.6	0.372
Social Functioning	2	56.3	7	67.9	5	75.0	2	50.0	0.705
Role: Emotional	2	91.7	7	83.3	5	76.3	2	50.0	0.728
Mental Health	2	55	7	68.6	5	95.0	2	48.75	0.531
Anorectal Manometry									
Final RP	2	67.0	5	59.0	8	63.0	0	-	0.832
Final SP	2	102.0	5	78.0	8	85.9	0	-	0.386
Max SI	2	35.0	5	19.0	8	22.9	0	-	0.694

N = no. of patients analysed for each outcome.

Symptom prevalence per grade

The prevalence of symptoms of faecal urgency, pure flatal or faecal incontinence, and incontinence to both faeces and flatus was compared across grades, both overall and also at the pre-defined time points. Table 7.12 shows the results.

Table 7.12: Prevalence of incontinence symptoms per grade

	3a		3b		3c		4		p-value
	N	Mean Score	N	Mean Score	N	Mean Score	N	Mean Score	
Overall Analysis									
Urgency	26	76.9	48	83.3	57	84.2	15	93.3	0.594
Faecal Incontinence	19	26.3	37	13.5	38	10.5	10	20.0	0.441
Flatal Incontinence	19	21.1	37	29.7	38	28.9	10	40.0	0.757
Dual Incontinence	19	5.2	37	5.4	38	7.9	10	0.0	0.814
3-6 Months									
Urgency	6	83.3	17	82.3	26	92.3	6	100	0.570
Faecal Incontinence	4	0	14	14.3	19	10.5	5	20.0	0.810
Flatal Incontinence	4	0	14	28.6	19	26.4	5	20.0	0.675
Dual Incontinence	4	0	14	7.1	19	10.5	5	0	0.796
6-12 Months									
Urgency	18	72.2	23	82.6	24	70.8	7	85.7	0.702
Faecal Incontinence	13	38.5	18	5.6	15	0	4	25.0	**0.16***
Flatal Incontinence	13	30.8	18	33.3	15	26.7	4	50.0	0.846
Dual Incontinence	13	7.7	18	0	15	0	4	0	0.407
12- 24 Months									
Urgency	2	100	5	87.5	7	100	2	100	0.694
Faecal Incontinence	2	0	5	40.0	4	50.0	1	0	0.552
Flatal Incontinence	2	0	5	20.0	4	25.0	1	100.0	0.272
Dual Incontinence	2	0	5	20.0	4	25.0	1	0	0.840

*N = number of patients analysed for each outcome. *Standard Residual was +2.4 for G3a hence making this the significant contributor*

Discussion

Overall, the above results do not show any major trends with functional decline across increasing severity of grade of OASI. The only exception to this was that at 3-6 months, patients with a G3a tear had a significantly better WIS compared to G3b and G4 OASI, however this trend was not seen in the overall analysis, or in the analysis of

other time points. The mean WIS for G3a OASI in groups with longer period to assessment was 5.6 at 6-12 months and 8 at 12-24 months, suggesting that the lower result observed in the 3-6 month group may be spurious secondary to low numbers (n = 4).

Of the ARM parameters, the squeeze increment was significantly better with G3a than G3b and 4 tears on the overall analysis. Given that lesser involvement of the anal sphincter complex with a G3a tear, this would correlate with expected results. This also suggests that maximum SI is a more sensitive marker than both maximum SP and RP. More importantly, there was a trend of decreasing SI between G3a, G3b and G4 OASIs. G3c injuries however had a higher SI than G3b disrupting the trend. In addition, there was a discernable trend of worsening BBSUQ Incontinence scores with a higher grade of tear, but this difference was not statistically significant.

Within the group of patients seen between 3-6 months, the findings were largely inconsistent with expected results. With regards to the BBUSQ constipation domain scores, although there were demonstrable statistically significant differences, these were incomprehensible. More importantly, these results needs to be analysed with caution given that all the respective mean BBSUQ constipation scores for each grade were below 64%, which was the cut-off value for a normal versus abnormal score as according to the validation criteria [173]. Secondly, while there was a better WIS in G3a tears compared to G4 tears, there seem to be no trend in severity of symptoms with increasing grades. Tears of G3b had a higher, although insignificant, WIS than G3c and G4 tears.

These findings contradict results from other studies, such as the one undertaken by Mahony et al [257], which studied 500 women at 3 months following sphincter repair. They found that a major OASI, (i.e. those extending to involve the internal anal sphincter) was significantly associated with the presence of FI. The difference in findings may relate to the relatively low numbers of G4 injuries (n= 21). Similarly, Nichols et al found that patients presenting with a G4 OASI were significantly more likely to report new bowel symptoms post-delivery than those with a G3 OASI[258]. Visscher et al further replicated these findings, where patients who had combined EAS and IAS tears had worse function five years following delivery[168].

However, several other studies have demonstrated minimal differences with differing grades of OASI in terms of bowel function. Richter et al [170] in their cohort of 343

females found that at 24 weeks post-partum there was no significant differences between FI and AI rates in G3 versus G4 tears, nor between the G3 OASI subtypes, with the exception of flatal incontinence, which was significantly higher with G4 tears. Roos et al [259] studied 531 women with a documented OASI who underwent primary repair. Mean time to follow up was 9 weeks. On a per-grade analysis, they found no significant differences in symptoms between grades. However, when they classified G3A and G3B injuries into minor OASIs and G3C and G4 injuries into major OASIs, they found that those with a major OASI had significantly worse faecal urgency, flatal incontinence and faecal incontinence to liquid stool compared to those with a minor OASI.

All included patients within this study were assessed at a maximum of 24 months since delivery. With longer-term follow up, differences in functional outcome may become more apparent. Sangali et al[171] studied 177 patients: 129 G3 versus 48 G4 OASI. At 13 years follow-up, they described rates of anal incontinence of 25% versus 11.5% in G4 versus G3 injuries. A study into the prevalence of FI undertaken by Barucha et al[260] discovered that the median onset of symptoms tends to be aged 55 years or older, with increasing prevalence with increasing age. They suggested that although many patients who had sustained OASI were initially asymptomatic, their effects became apparent after further insults which could contribute to further deterioration, such as the increase of general pelvic floor laxity that is associated with the ageing process. Therefore it is not unreasonable to suggest that although within this study population there was little discernable trend in deterioration with increasing grade, with long-term follow-up the prevalence of FI and AI is likely to increase, and the differences between grades of insult to the anal sphincter complex are likely to be come far more apparent.

Limitations

The major limitation in this study is that due to its purely observational nature, patients were not followed up at a specific time point following delivery, and therefore there is a wide range in time to consultation. However this was accounted for by the performance of an initial overall analysis, and then separate analyses at 3-6, 6-12 and 12-24 months from delivery; the mean follow-up for these groups was also statistically significantly different from one another. Additionally, only a handful of patients had more than one clinical follow-up, and therefore an analysis of sphincter

recovery over time was not feasible. There may also be a degree of selection bias, as women who were asymptomatic were possibly less likely to seek further colorectal consultation than those who were symptomatic, although all women considering further vaginal delivery were encouraged to attend for assessment and discussion regardless of current symptom burden.

Conclusions

Our results show that with relatively short follow-up, there was no real apparent difference in functional, sexual or QoL outcomes across all grades of tear; with an exception of a lower WIS before 6 months with G3a tears. However, symptom burden across all OASI grades was generally high, particularly faecal urgency and flatal incontinence. Patients who have sustained OASI need appropriate follow-up, aggressive management of symptoms with specialist Biofeedback physiotherapy and clear advice regarding the risk of AI if recurrent OASI was sustained, as it is likely that with time, degree of injury will become more apparent and symptom burden increase. Patients with dual sphincter involvement may benefit from more sustained and aggressive Biofeedback physiotherapy to attempt to counteract the risk of future deterioration. Further work is needed to stratify long term risk according to grade of tear. It is conceivable that asymptomatic lower grades of tear could be managed in a primary care setting, however they would still need access to physiotherapy to help negate future clinical deterioration.

7.5: Chapter conclusions

The purpose of this chapter was to look at the relationship between a missed sphincter injury and grade of OASI and function in a cohort of patients referred to a colorectal pelvic floor service for follow-up after normal or assisted vaginal delivery. Additionally, the impact of differing grades of tear in the long-term has been explored.

The two studies included within this chapter have explored the impact of childbirth on anal continence with a relatively short-term follow up. The risk of a missed sphincter injury is high, and this study demonstrates significantly worse initial functional outcome. However, with a repaired OASI at the time of delivery, initial results are comparable across all grades of injury. Nevertheless, the symptom burden is

significant in terms of symptoms of urgency and flatal incontinence, with over 80% experiencing regular urgency.

Chapter 8: Functional outcomes with handsewn versus stapled anastomosis in the treatment of ultra low rectal cancer.

Publications related to this chapter:

Functional outcomes with handsewn versus stapled anastomoses in the treatment of ultralow rectal cancer. Ramage L, Mclean P, Simillis C, Qiu S, Kontovounisios C, Tan E, Tekkis P. Updates Surg. 2018 Jan 8. doi: 10.1007/s13304-017-0507-z.

8.1 Introduction and aims of chapter

This chapter focuses on a study which aimed to identify any difference in functional outcomes with patients who had undergone rectal resection for malignancy with either a traditional stapled anastomosis, as performed for an anterior resection, or a handsewn coloanal anastomosis (CAA) which was usually performed in conjunction with a partial resection of the internal anal sphincter. Functional bowel disturbance following rectal cancer resection and restoration of normal bowel continuity is common, as previously discussed. With greater emphasis being placed on the need for good functional and QoL outcomes as part of long-term cancer survivorship, the importance of acceptable functional outcomes and quality of life is a key issue in preoperative treatment decisions.

This chapter has been incorporated into the thesis as the subgroup of patients who have had surgery for low rectal cancer account for a significant proportion of those ultimately requiring surgical intervention in the faecal incontinence cohort described throughout (20.8% of all patients with FI ultimately requiring surgery).

8.2 Study: does the method of anastomotic technique used in ultra low anterior resection influence functional outcomes?

Aims and objectives

The aim of this chapter is to identify whether there were any significant differences in functional and QoL outcomes in patients who had undergone sphincter-preserving surgery in the form of ISR, compared to those who had ultra-low anterior resection, performed within 3cm of the dentate line. This performed through the means of an

observational study which received full ethical approval from the Research Ethics Committee, and represents a single-surgeon series.

The objectives were to compare functional outcomes as demonstrated by the Wexner Incontinence Score, BBUSQ and Low anterior resection syndrome (LARS) score, QoL as assessed using the SF-36, and additionally sexual function, assessed using the Male Sexual Health Questionnaire (MSHQ) or the Female Sexual Function Index (FSFI) between patients with handsewn versus low stapled anastomosis.

Methods

Patient identification was initially performed through a prospectively maintained database of all bowel cancer surgeries performed by a single surgeon with extensive experience of complex and recurrent rectal tumour resection. Procedures were performed across multiple sites. Depending on preoperative and intraoperative findings, patients may have also undergone additional neoadjuvant chemoradiotherapy or adjuvant radiotherapy.

Inclusion criteria for the study were as follows:

1. Patient deemed free of active malignancy
2. Oncological treatment completed at least 6 months ago
3. Any diverting stoma reversed at least 6 months ago.
4. Either performance of a handsewn (coloanal) anastomosis OR a stapled anastomosis with anastomotic height no greater than 3cm above the dentate line.

Exclusion criteria were as follows:

1. Evidence of active proctitis
2. Presence of a permanent diverting stoma
3. Evidence of recurrent or distant disease

Eligible participants were identified and contacted via post, and were invited to attend for a one-off assessment within the pelvic floor unit which included patient interview, and the completion of the several validated patient questionnaires which aimed to assess functional outcomes, quality of life (QoL) data and postoperative sexual function: Wexner Incontinence Score[174]; Birmingham Bowel, Bladder & Urinary Symptom Questionnaire, (BBUSQ) [173]; Low Anterior Resection Syndrome (LARS)

score [127]; Short-Form 36 (SF-) 36 [177]. Additionally, patients were asked to complete a sexual function score (Male Sexual Health Questionnaire, MSHQ [261], and Female Sexual Function Index, FSFI)[262]. Completion of the FSFI and MSHQ were entirely voluntary, and a decision to abstain from completion did not preclude study enrolment. Following from this, patients underwent physical examination, which included digital rectal examination (DRE) and ARM assessment of motor and sensory function. ARM assessment was performed as outlined in the general methods chapter.

Surgical methods

A laparoscopically-assisted approach was performed where feasible. Surgical methods employed by the operating surgeon in order to create a handsewn anastomosis have previously been described[145]. Patients who underwent handsewn anastomosis had one of three slightly different approaches depending on the relation of the tumour to the dentate line, as per the classification outlined by Rullier et al[144]. A straight coloanal anastomosis was performed in all cases. For supra-anal tumours more than 2cm above the dentate line, the rectum was divided transabdominally, and transanl mucosecomy was performed above the line. The IAS was preserved in full (CAA-1). Juxta-anal tumours were managed with anal mucosectomy extending from the dentate line for up to 1xm before continuing into the intersphincteric space, allowing partial IAS excision (CAA-2). Intra-anal tumours were close to or either involving the upper IAS. Mucosectomy was performed from 1cm below the dentate line extending cranially. A minimum of 1cm length of IAS was preserved in all cases (CAA-3).

Statistical analysis

Data analysis was performed using SPSS software. Non-parametric data were compared using Mann-Whitney U test. A p value of <0.05 was considered to be statistically significant.

Results

Study demographics

A total of 20 patients were recruited to this study over a 12-month period and attended for a one-off appointment. Nine patients had rectal resection with CAA versus eleven

who had a stapled anastomosis. The demographics of each group are shown in table 8.1. Overall, the mean follow-up was at 3±2 years since the date of surgery.

One patient in the stapled group and three in the handsewn group required the long-term use of rectal irrigation to help control FI symptoms after restoration of normal bowel continuity. Three patients in the handsewn group required sacral nerve stimulation. No patients in the stapled group went on to have SNS.

Table 8.1: Study demographics

	Handsewn (n = 9)	**Stapled (n = 11)**	**P value**
Age*	66.5 +/-5.6	57 +/-13	0.058
M:F ratio	7:2	8:3	0.795
Postoperative staging	T0N0– 1 T1N0 – 3 T2N0 – 4 T2N2 - 1	T2N0 – 3 T2N1 – 1 T3N0 – 3 T3N1 – 2 T3N2a - 1	ND
Preoperative radiotherapy	5	6	0.964
Neoadjuvant/Adjuvant chemotherapy	4	8	0.391
Time surgery to assessment (years)*	3.62 +/-2.59	2..04+/-0.66	0.109
Complications	3 – anastomotic stricture 1 – pelvic collection	2 – anastomotic leak 1 –pelvic collection	N/A
Anastomosis height	CAA 1 – 2 CAA 2 – 6 CAA 3 - 1	3cm from dentate – 3 2cm from dentate – 2 Unknown - 5	N/A

**Values are expressed as mean+/-SD.*

Functional outcomes

The results of the LARS score, Wexner Incontinence Score and Birmingham Bowel, Bladder and Urinary Symptom Questionnaire are shown in table 8.2.

Table 8.2: Functional scores

	Handsewn	Stapled	P value
LARS score	29.4+/-9.57	21.9+/-10.86	0.133
Wexner Incontinence Score	10.9 +/- 4.76	4.6+/- 3.69	**0.0076**
Birmingham Bowel, Bladder & Urinary Symptom Questionnaire			
Constipation Domain	35.37 +/- 19.03	41.0+/- 9.82	0.182
Evacuation Domain	23.58+/-10.65	16.19+/-11.02	0.182
Faecal Incontinence	53.70+/- 27.038	16.67+/-11.79	**0.001**
Urinary Domain	12.96+/-10.04	12.61+/-9.12	0.968

The mean LARS score was not significantly different between groups (21.9+/- 10.86 in the stapled versus 29.4+/-9.57 in the handsewn group, p= 0.133). However, the WIS was significantly higher in the handsewn group (p = 0.0076), with a mean score of 4.6+/-3.69 versus 10.9 +/- 4.76. With regards to the BBUSQ, the only domain which was significantly different between the two groups was the faecal incontinence domain, (p = 0.001), with the handsewn group having a significantly worse score (53.70+/- 27.04 versus 16.67+/- 22.79). Both groups had a score within normal limits for the constipation (p = 0.182) and the urinary (p = 0.968) domain and these were not significantly different from one another. With regards to the evacuation domain, again the results were not significantly different (23.58+/- 10.65 in the handsewn versus 16.19+/- 11.02 in the stapled group, p = 0.182) however those in the handsewn group had a mean score which was slightly higher than the threshold value which was considered normal set out within the validation criteria (>17).

Table 8.3 below shows a breakdown of relevant questionnaire responses from the WIS and the BBUSQ. Scores were divided into never/rarely versus sometimes/usually/always for the WIS and never/occasionally versus usually/always for the BBUSQ and Fishers exact test used to compare the proportions of responses for the two groups. The WIS was available for 19/20 patients. 9/10 (90%) of patients who underwent stapled anastomosis indicated they were never or rarely incontinent to solid stool, 1 (10%) indicated sometimes/usually/always. In the handsewn group, only 4/9 reported that they were never/rarely incontinent to solid stool. This difference was approaching statistical significance (p = 0.0573).

Considering liquid stool, only 3/9 handsewn were never/rarely incontinent to liquid stool. By comparison, 8/10 of patients who underwent stapled anastomosis reported they were never or rarely incontinent to liquid stool. This difference was approaching statistical significance (p = 0.0698).

Complaints of flatal incontinence were similar, with 4/9 handsewn and 5/10 stapled complaining of being sometimes or usually or always incontinent to gas. 5/9 and 5/10 reported being never or rarely incontinent to flatus (p =1.00).

Table 8.3: Differences in specific PROM questions between handsewn and stapled groups

		Never/rarely	Sometimes/Usually/Always	P value*
Solid stool				
	Handsewn	4	5	0.0573
	Stapled	9	1	
Liquid stool				
	Handsewn	3	6	0.0698
	Stapled	8	2	
Gas				
	Handsewn	5	4	1.000
	Stapled	5	5	
		Never/occasionally	**Usually/Always**	
Faecal urgency				
	Handsewn	5	4	0.1698
	Stapled	8	2	
Inability to defer defecation				
	Handsewn	3	6	**0.0031**
	Stapled	10	0	
Urge faecal incontinence				
	Handsewn	7	2	0.2105
	Stapled	10	0	
Passive faecal incontinence				
	Handsewn	7	2	0.2105
	Stapled	10	0	
Incomplete emptying of bowels				
	Handsewn	4	4	0.3213
	Stapled	8	2	
Urge to pass but unable to pass a motion				
	Handsewn	8	0	1.00
	Stapled	10	0	

** Fishers exact test*

Looking at individual responses from the BBUSQ Q3: ability to defer defecation for >5 minutes, and Q4: presence of faecal urgency, there was no significant differences between groups with regards to urgency (p = 0.1698); however significantly less patients from the handsewn group were able to defer defecation more than 5 minutes (p = 0.0031). Likewise, the proportions of patients reporting the presence of frequent passive faecal incontinence, urge faecal incontinence and incomplete evacuation or inability to pass a motion were not statistically different between handsewn and stapled groups.

Quality of life: SF-36 score

The results across the eight domains of the SF-36 are shown in table 8.4. In each of the eight domains, the SF-36 scores were worse in those with a handsewn compared to the patients in the stapled group. However, this was not found to be statistically significant in six domains (physical function, p =0.211; role physical, p = 0.211; bodily pain, p = 0.182; vitality, p = 0.278; role emotional, p = 0.274; mental health, p =0.156). There was a statistically significant difference between groups in the general health domain (56.81+/- 22.18 versus 76.50+/- 14.90, p = 0.035) and the social function domain (63.89 =/- 31.53 versus 91.25+/- 15.65mmHg, p = 0.035).

Table 8.4: SF-36 Scores

SF-36 Domain	Handsewn (n= 9)	Stapled (n= 10)	P value
Physical Function	76.91+/-27.2	92.39 +/- 10.37	0.211
Role Physical	65.28+/-31.73	85.00+/-21.08	0.211
Bodily Pain	70.83+/-27.95	87.50+/-18.63	0.182
General health	56.81+/-22.19	76.50+/-14.90	**0.035**
Vitality	50.69+/-19.38	62.50+/-13.82	0.278
Social Functioning	63.89+/-31.53	91.25+/-15.65	**0.035**
Role Emotional	73.96+/-28.33	88.33+/-18.09	0.274
Mental Health	62.22+/-17.87	74.00+/-7.38	0.156

Anorectal physiology

Anorectal physiology results are displayed in the table below (table 8.5). Looking firstly at parameters that concerned assessment of motor function, there was no significant difference between groups with resting or squeeze pressures, measuring

both IAS and EAS function. Of note, both groups had a mean value for motor pressures that would be considered to be within normal parameters.

On assessment of sensory function, tested through measurement of threshold, urge and maximum distensile volumes, the handsewn group were found to have a reduced threshold volume when compared to the stapled group; however this difference was not statistically different: 16.75+/- 7.32ml versus 30.7+/-28.20ml, p = 0.397). The urge volume to distension and the maximum volume tolerated were both very close to statistical significance, with lower volumes seen in the handsewn group of patients: 36.33+/-36.48 ml versus 70.43+/-65.24 ml urge volume (p = 0.051) and 63.33+/-72.43 ml versus 117.86+/-86.02 ml maximum tolerated volume (p = 0.051).

Table 8.5: Anorectal physiology results

	Handsewn	**Stapled**	**P value**
Motor			
Maximum resting pressure (mmHg)	45.11+/-15.96	55.0+/-12.10	0.299
Mean squeeze pressure increment (mmHg)	68.56+/-60.78	105.39+/-60.75	0.299
Mean five second squeeze increment (mmHg)	82.33+/-65.46	69.69+/-39.76	1.00
Mean cough pressure increment (mmHg)	87.67+/-62.46	92.65+/-64.58	1.00
Sensory			
Threshold volume (ml)	16.75+/-7.32	30.7+/-28.20	0.397
Urge volume (ml)	36.33+/-36.48	70.43+/-65.24	0.051
Maximum tolerated volume (ml)	63.33+/-72.43	117.86+/-86.02	0.051

5. *Sexual function*

Sexual function data was only available for two males in the stapled group, and three males and two females in the handsewn group. Given the low numbers of responders, it was difficult to make any statistical analysis of results. Therefore they are tabulated below on a per patient basis. Of note, all males scored poorly on the erection scale. Table 8.6 gives the results. The results of the Female Sexual Function index are shown in table 8.7. Only two female patients completed the FSFI, both from the handsewn group, and therefore it was not possible to undertake any comparative analysis.

Table 8.6: Male Sexual Health Questionnaire results

Patient No	Group	Erection scale (max = 15)	Ejaculation scale (max = 35)	Satisfaction scale (max = 30)
1	Stapled	3	1	20
2	Stapled	4	32	16
3	Handsewn	3	10	15
4	Handsewn	0	21	18
5	Handsewn	0	15	23

Higher scores are indicative of better sexual function

Table 8.7: Female Sexual Function Index results

Patient No	Group	Desire (max= 6)	Arousal (max= 6)	Lubrication (max= 6)	Orgasm (max= 6)	Satisfaction (max= 6)	Pain (max= 6)
1	Handsewn	6	1.2	1.2	1.2	ND	1.2
2	Handsewn	3.6	4.8	5.4	5.2	2.4	5.6

Higher scores are indicative of better sexual function

Discussion

Currently, ISR with handsewn CAA is a widely accepted alternative to extralevator abdominoperineal excision (ELAPE). Oncological outcomes are comparable, and additionally there is a perceived benefit of the restoration of normal bowel continuity and avoidance of a long-term stoma.

The MERCURY II study group have set out recommendations regarding patient selection for ISR versus ELAPE. To summarise succinctly, ELAPE is considered best treatment where there is evidence of tumour extension on MRI beyond the muscularis propria or internal anal sphincter (IAS) and into the intersphincteric plane[141]. Otherwise, ISR is considered to be a safe and valid alternative. In the majority of cases, ISR with handsewn CAA is performed in cases where there has been a technical failure with a stapling device, or if the tumour is either very close to or is actually involving the IAS. In the latter situation, a cuff of proximal IAS may be resected along with the specimen in order to achieve the recommended standard of a minimum 1cm of disease-free bowel distally for an oncological curative resection to be achieved. As discussed earlier in chapter 2, three CAA techniques have previously been described based on the level of the tumour in relation to the IAS[145] which relates to a classification set out by Rullier et al [144]. Our local study group had also

documented in a group of 71 patients that a R0 resection was achieved in 97.1%. The level of anastomosis was found to have no relation to oncological outcomes. All included patients had received an end-to-end straight anastomosis with no pouch formation. It is from this group of patients that the study recruits for this chapter were identified.

Within published literature exist a number of studies, which validate the use of ISR. First described by Lytle and Parks in 1977, the technique was initially used in resection of IBD[142]. It was not until 1992 that ISR was used in the context of rectal cancer resection [143]. These pioneer authors reported a five-year survival rate with ISR of 62% versus 58% with APER. 85% of patients also reported good postoperative functional results. Another study was undertaken by Rullier and colleagues[132] of 92 patients who underwent ISR; this included 72 patients with T3 and 6 patients with T4 tumours, where there was evidence of invasion of the internal anal sphincter. Median distance of the tumour from the anal verge was 3cm. They recorded R0 resection in 89% of cases, with a local recurrence rate of 2%, and distal recurrence of 19%. At 5 years, disease free survival (DFS) was 70% and overall survival was 81%. They concluded that adjuvant radiotherapy reduced the likelihood of involved circumferential margins, facilitating successful resection in more advanced tumours, and therefore ISR was acceptable in these situations.

The results of the study within this chapter demonstrate significant differences between handsewn and stapled groups with both the WIS and the incontinence domain of the BBUSQ favouring a stapled anastomosis. Despite this significantly worsened function, in six out of eight domains of the SF-36, there was no apparent difference. The two domains found to be statistically different from one another were "general health" and "social functioning". This is not surprising, as significantly worse incontinence rates are likely to impact on an individuals concept of their general health, and frequent accidents and a worsened ability to defer defecation are likely to negatively impact on social function. However, the population size for each study group was small, and therefore it is entirely feasible that with a larger population sample QoL differences may have become more apparent. Additionally, the SF-36 is a generic tool and does not take into consideration the specific symptom burden of rectal cancer survivors; therefore a different QoL assessment tool, such as the Faecal Incontinence Quality of Life (FIQL) tool may have highlighted further differences in QoL outcomes[263]. It is interesting that the WIS and the faecal

incontinence domain of the BBUSQ had a statistically significant difference between the groups but the LARS score did not. On interrogation of both the raw data and the structure of the questionnaires, there appears to be a number of contributory factors. Firstly, the LARS score considers liquid faecal incontinence using a choice of three responses: never/less than once per week/at least once per week. Despite this, the scoring system awards 3 marks for both less and more than once per week, reducing the sensitivity of detecting the differences otherwise noted in the other PROMs. In addition, the LARS score does not consider incontinence to solid stool, pad usage and alterations to daily life, all of which were worse in the handsewn group when comparing mean scores. This was the case for all bar one of the questions, which had a maximum of three possible responses in comparison to the WIS and BBUSQ that had a choice of four to five symptom severity grading responses. Having said this, the mean scores for each question within the LARS score responses were worse in the handsewn group, giving rise to the higher overall score, however this was not statistically significant. The mean score was however encroaching on a diagnosis of major LARS in the handsewn group versus minor LARS in the stapled.

Considering ARM parameters, sphincter motor function was not significantly different. Again, this is likely to be expected given that the EAS should have been largely unaffected across both patient groups. With regards to IAS function, in 8/9 patients, there had been no or a minimal amount of IAS removal, and therefore this has been reflected in the normal mean resting pressure in the handsewn group.

Sexual function was also explored, although there was insufficient response from patients to allow for any analysis; this was doubly confounded by the need to provide separate questionnaires to males and females to account for the differences in male and female sexual functioning. What is noticeable however, is the generally poor trend with regards to erectile dysfunction in men. This is a recognised complication of pelvic surgery, and it is important that this is adequately recognised and addressed in rectal cancer survivors.

Due to the low patient numbers enrolled in this observational study, it was not feasible to make any statistical comparison between the three differing levels of CAA used within this series; only 1 patient had a CAA-3, 6 underwent CAA-2, and 2 underwent CAA-1. One such study which aimed to assess for differences in function between varying levels of ISR resection was undertaken by Tokoro et al[264]. They analysed the results of 30 patients who underwent partial, subtotal or total ISR (i.e.

complete removal of internal anal sphincter) without additional adjuvant chemoradiation. At 3, 6 and 12 months, there was no significant differences demonstrated between groups. However, patients who developed a postoperative stricture had less improvement of WIS from baseline compared to those who did not. The presence of a stricture was notably linked to ongoing nocturnal defecation and urgency. Functional outcomes at 12 months with regards to bowel frequency, fragmentation and urgency were also worse in patients with a stricture. Overall, they concluded that the volume of residual internal anal sphincter was not found to affect bowel function.

Several studies have previously considered levels of postoperative bowel dysfunction following CAA with ISR. For example, a study undertaken by Bittorf et al[265] was published which included a cohort of 31 patients. They underwent ISR and coloanal anastomosis at 2.9 +/- 1.1cm from the dentate line. 12/33 were fashioned a colonic J pouch, whereas the rest were given a straight coloanal anastomosis. Weekly or more frequent incontinence of solid stool was reported by 8/31 patients, and by 17/31 for liquid stool and gas. 7/31 reported regular soiling. 9 patients reported no change in deferral time, whereas 14 had impaired deferral and 8 were completely unable to defer defecation. Interestingly, 7/9 able to defer defecation time had a colonic J pouch. The mean postoperative Wexner score was 12+/- 4.5. A straight anastomosis ($p<0.05$) and the use of additional chemo-radiotherapy ($P = 0.054$) were associated with a worse Wexner score. They also found there to be a reduced maximum and mean resting pressure, reflecting IAS compromise.

Konanz et al[266] compared QoL between low anterior resection (LAR), APER and ISR in a cohort of 41 patients who underwent LAR, 33 who had ISR and 50 who underwent APER. They were unable to demonstrate any statistically significant differences between all three groups in terms of global quality of life, emotional, social and cognitive functioning. Physical functioning scores were significantly higher in patients who had undergone LAR compared to APER ($p= 0.0262$). APER patients also had lower scores than patients who had undergone ISR ($p = 0.0280$). However, ISR patients had significantly higher symptom scores for defecatory dysfunction ($p <0.05$) in addition to higher WIS scores ($p<0.0005$) compared to patients who had undergone LAR. The mean WIS was 9.5 in the LAR versus 12.9 in the ISR group. A similar study, published by Koyama et al[267] compared outcomes with 77 ISR patients, 68 LAR patient and 33 APER patients. They found no

significant differences in local recurrence rates between groups. Faecal urgency was a common problem, experienced by 57% of ISR patients and 47% of LAR patients. There was no difference in frequency of defecation between ISR and LAR patients. A lack of discrimination was seen more frequently in ISR patients (11% versus 3%), however this was not statistically different. The WIS was significantly higher with ISR patients at 8.1 versus 4.9, p = 0.004). Pad usage was also significantly more commonplace amongst ISR patients. Our results showed a WIS score of 10.9 with handsewn versus 4.6 with stapled anastomoses, which are comparable with the examples from the literature described above. Quality of life data was similar between groups.

Limitations

The major limitation of this study was low patient recruitment. Patients identified for inclusion within this study from the CAA group in particular were from a limited resource; these were patients who were operated on as part of a single surgeon series, and as previously documented, the number of survivors within this cohort was 71. In addition, a number of patients resided overseas and therefore were unable to attend for assessment.

The second limitation was the lack of sexual function data, which made comparisons for this outcome impossible. Again this was as a result of low patient numbers in addition to the nature of the questions themselves; patients may have found this embarrassing. As this was an observational series, length to patient follow-up also differed somewhat, with a range of 1.08-8.44 years, however the differences were not found to be statistically different between groups.

8.3 Chapter conclusions

In this small series, there was a demonstrable difference in incontinence rates and deferral times between handsewn CAA and stapled groups. Overall QoL was not statistically significant, with the exception of general health and social functioning, which were worse in handsewn patients. It has been previously proven that ISR and handsewn anastomosis is a safe and oncologically feasible procedure, however it should be performed in specialist centres with experience in the procedure. Additionally, patients need to be carefully selected and carefully counselled with regards to the likelihood of postoperative symptoms. Factors such as patient age, the

presence of pre-existing functional deficit and the potential need for further intervention should be considered when decision-making about the type of surgery to be performed. In particular, full sphincter assessment including ARM and EUS should be considered in women with a prior history of vaginal delivery even in the absence of a known OASI, as has previously been discussed, in order to rule out prior and as yet clinically undetected sphincter injury which may potentiate disastrous function if ISR were chosen as the method of rectal cancer resection. Additionally, due care and attention must be paid to postoperative sexual function, as patients may not necessarily volunteer this information in a general colorectal clinic consultation.

Suggestions for future work include a prospective study which looks at pre- and post-operative evaluation of functional and QoL outcomes with ISR and ultralow coloanal anastomoses.

Part 4: Final remarks and conclusions

CHAPTER 9: CLOSING CHAPTER

9.1 Chapter introduction

This thesis has focussed on a sizable cohort of patients presenting to a pelvic floor tertiary service, and represents the true variety of patients encountered within this service. In particular, the overriding objectives were to ascertain whether the three most commonly applied investigatory modalities: specific PROMs, ARM and MRD were correlated with symptoms and/or the need for surgical intervention (the latter of which was considered to be a marker of significant symptom burden). Additionally, specific groups of patients were identified who make up a large proportion of the pelvic floor clinic attendees and explored in a number of studies.

A brief summary of the overall results follows below.

9.2 Summary of main thesis results

Faecal incontinence

With regards to patients presenting with symptoms of faecal incontinence, ROC analysis demonstrated that the incontinence domain of the BBUSQ and several domains of the SF-36 were fair predictors for the need for surgical intervention (PF, RP, MH, SF, GH). The WIS had an AUC of 0.696 and therefore this was close to significance.

This thesis also considered two particular subsets of patients with symptoms of anal incontinence: those with an OASI, and patients who had undergone ultra low anterior resection. In those with an OASI, initial follow-up did not suggest any major difference in symptoms between varying degrees of injury severity. However, the literature did suggest that follow up over a longer time frame may lead to some differences in function becoming more apparent, with the possibility of worsening function in later years of life in those with more severe sphincter disruption or those who go on to have multiple subsequent pregnancies.

Patients who had presented later with missed OASI and who had therefore missed the period of intensive pelvic floor physiotherapy with the gynaecology team demonstrated worse BBUSQ faecal incontinence scores ($p = 0.002$), WIS ($p = 0.009$) and BBUSQ urinary scores ($p = 0.001$). Those with missed OASI had a significantly worse score for

physical function on the SF-36 (p = 0.045), but otherwise there were no differences in the QoL scores.

The penultimate chapter considered a series of patients who had undergone ultra low anterior resection with either a stapled or handsewn anastomosis. Those who had a handsewn anastomosis were found to have reduced deferral times (p = 0031). Although there were no significant differences with incontinence to gas, approaching statistical significance were increased rates of incontinence to both liquid (p = 0.6698) and solid stool (p= 0.0573) with those who had a handsewn anastomosis. Both the WIS and the faecal incontinence domain of the BBUSQ also were statistically worse in the handsewn group.

Anorectal manometry

ARM results from the patient cohort who had presented with faecal incontinence were analysed with regards to maximal treatment outcomes. On multivariate analysis, the physiological anal canal length (p=0.044), maximum resting pressure (p=0.001) and squeeze endurance (p=0.021) were all correlated with the need for surgery. On AUC analysis, only the squeeze endurance increment was predictive of the need for surgery, with an increment of <16.5mmHg above the resting pressure having a sensitivity of 81.8% and specificity of 70.3% considered to be a fair predictor of the need for surgical intervention.

In addition, Spearman's correlation was used to explore whether specific questions from the BBUSQ could act as a surrogate for ARM testing in the community. There was a significant correlation between the question '*can you hold onto your motions for more than five minutes*?' and the maximum squeeze pressure increment and also '*do you leak stool for no obvious reason and without feeling that you want to go to the toilet*? and the mean resting pressure.

Defecatory disorders

The relationship between the PROMs used throughout this thesis and the need for surgery as a maximal treatment outcome was explored through logistic regression and ROC curve analysis. There were no clear distinct relationships demonstrated by the results yielded.

Magnetic resonance defecography

MRD was initially compared to clinical assessment and fluoroscopy in assessment of the pelvic floor dynamics through the employment of meta-analytical techniques. Overall, MRD was found to have worse detection rates and higher miss rates than fluoroscopy in the detection of most commonly encountered abnormalities of the pelvic floor. With the exception of enteroceles, which were more commonly detected and less commonly missed than with clinical exam, there was no increase in detection rates compared to clinical examination of the various pelvic floor abnormalities. However through review of current literature, it was felt that there were certain benefits with MRD, with its use advocated in complex and recurrent pelvic floor dysfunction.

When considering the relationship between several MRD features and their relation to patient-reported symptom severity, overall results were not supportive of the development of a scoring system based on MRD findings to indicate symptom severity; a finding already encountered in previously published literature. Inability to evacuate more than 80% of rectal contents was associated with an abnormal BBUSQ constipation score ($p = 0.074$). A history of previous pelvic floor surgery was associated with a lower likelihood of an abnormal BBUSQ faecal incontinence score ($p=0.042$). The presence of a rectocele >2cm in size ($p= 0.003$) or evidence of puborectalis syndrome ($p=0.025$) were significantly associated with a high ODS score.

Finally, the chapter explored whether specific features on MRD could be used to predict the need for surgical intervention. Results were disappointing, with all features on MRD having an AUC of <0.7 in isolation. On dual combination of different MRD variables with an AUC of 0.6 or greater, only evidence of an M line of >47.15mm on strain combined with a cystocele of >18.25mm on straining was was a “fair” predictor of the need for surgery (AUC = 0.7)

9.3 Discussion

With an overstretched NHS and chronic underfunding plaguing all clinical services, it is vital now more than ever to consider how our specialist services are run in terms of efficiency. This includes outpatient services; in 2013 there were 75.5 million outpatient attendances; up by 25% from the preceding six years[268]. In the patient series’ which form

this thesis, only 48 of 278 patients (17.27%) with FI and 27 of 129 patients with ODS (20.93%) actually underwent surgery during the follow-up period. The majority of patients underwent Biofeedback as maximal therapy: 54.68% of those with FI predominant symptoms and 45.74% of those with ODS symptoms. Therefore, interest should lie in the development of a decision-making tool that allows for risk stratification based on symptom clusters and aetiology. This could be used to streamline referrals appropriately to tertiary specialist consultant-led services versus physiotherapy service, which could be community-based.

The design of an integrated care pathway for the management of patients with pelvic floor dysfunction between primary and secondary care could help reduce strain on the overstretched system and also reduce waiting list times to see a specialist. Clearly there are patients who need to be followed up directly by a consultant led service – this includes those who have had surgery for ultra low rectal cancer – in fact evidence is growing that these patients need preoperative assessment of sphincter function in order to identify those who may suffer subsequent problems following stoma reversal[269]. Additionally those who have multi-compartment or recurrent pelvic floor dysfunction are best suited to a consultant-led service from the outset to allow for cross-speciality MDT input.

There currently exist many integrated care pathways (ICPs) that act as a streamlined referral system direct to specialist input. The most prolific examples are the urgent suspected cancer referral pathways. Each identifies a set of clinical criteria or symptoms present for a minimum number of weeks that warrant further urgent investigation. With reference to the urgent suspected cancer pathways, there is a set timeline target to be adhered to, with time to see a hospital specialist from the date of GP referral set at a maximum of 14 days[270]. These pathways are not without their problems. Significant variations in their usage have been evidenced between primary care trusts, suggesting differing patterns of interpretations and implementation[271]. With specific reference to the suspected colorectal cancer (CRC) pathway, there is a low predictive value using the predefined criteria, and it is estimated that half of all CRCs diagnosed would not have met the referral criteria[272]. Therefore it would be vital that the design and implementation of any national referral pathway for pelvic floor dysfunction took into consideration potential variations in practice and included an education programme to promote correct and standardised usage.

The decision as to who needs direct referral to a tertiary consultant led service and who could be appropriately and safely managed in the community, at least in the first instance, should be decided upon and standardized nationally, through development of an ICP. As an aside, before considering further the merits of such a pathway, it should be noted that it is imperative general practitioners ensure that any patient presenting with symptoms of posterior compartment dysfunction have had the risk of underlying malignancy considered and ruled out if required. Anecdotally, it is commonplace for new referrals to the pelvic floor service to first undergo endoscopic assessment for a change in bowel function prior to a diagnosis of a functional disorder. It is not inconceivable therefore that there is a chance of delayed diagnosis of a malignancy if this is not considered before referral to a community-based care system.

In recent years there has been a call for more MDT-based care with the utilisation of joint clinics and theatre services between gynaecology and colorectal surgery in order to more efficiently provide patient treatment. However, current provision of pelvic floor dysfunction services across the UK is often fragmented and single compartmentalised, with access to services compromised due to lack of strategy and also the perception of PF dysfunction being of a low priority condition[273]. The current short-fallings in care delivery represent a potential area for nationalised improvement. Outlined suggestions include the development of a national patient database, and patient held documentation, in addition to more community-based care[273]. Rimmer and colleagues, based in the Midlands, UK, developed an ICP that concerns patients presenting with FI[274]. Their new model replaces the traditional care pathway model, where all referrals are made directly to a specialist outpatient consultant-led clinic, and instead sees all patients triaged initially by a bowel function specialist nurse. In addition, with the exception of the consultant clinics, all other clinics took place in the community setting. Finally, they ensured early involvement of the community continence team in the patient care pathway rather than as a last resort when all other treatment options had been exhausted. Results from service user feedback included satisfaction with reduced waiting times to access services, improved accessibility to services in the community, and an improved understanding by their GPs as to the treatment and support available for FI sufferers[274].

As discussed earlier, the vast majority of the patients included in the studies within this thesis required only Biofeedback as a maximal treatment. In addition, it was a prerequisite that any patient who was under consideration for more invasive treatment

was required to have attempted a course of Biofeedback in the first instance. Clearly, this represents a large patient burden on physiotherapy services, as each patient generally attends for a number of sessions. The consensus guidelines outlined by Rao et al[92] give recommendations for the use of Biofeedback for different anorectal disorders. They recommended the use of Biofeedback as both short- and long-term treatment in constipation with dyssenergia and for the treatment of FI. They also found Biofeedback to be a useful treatment measure in the short-tem for puborectalis syndrome and dyssenergic defecation. Given that Biofeedback is a treatment that the majority of patients suffering with posterior compartmental dysfunction will require, either in the short or longer term, then solutions need to be found with regards to its delivery and a move towards a more community-based approach, and the potential for home delivered Biofeedback explored fully[92].

Taking into consideration the results obtained within this thesis, it may be possible to identify distinct symptom clusters which if present, may indicate a high likelihood for the need for more invasive treatment methods. This thesis used previously validated scoring systems to determine symptom burden. With regards to the FI cohort, it was demonstrated that a higher incontinence domain score of the BBUSQ was a fair predictor of the need for surgery, and the WIS was close to being a fair predictor with an AUC of 0.696. Taking this into consideration alongside the SF-36, of which 4/8 domains were also considered as fair predictors of the need for surgical intervention, a useful starting point in the community would be the deployment of these questionnaires, or validated questions in a similar vein, which if all answered positively signify a direct tertiary centre referral is required. There were no similar studies found in currently published literature, making this a potential area for further clinical research.

Future work in this area could consider the predictive role of other scoring systems or symptom clusters in determining those likely to require surgery; this could then be applied in a community setting and form part of the ICP referral process, with those with lower scores and an absence of known underlying pathology (such as previous low anterior resection) being considered appropriate for a trial of community-based Biofeedback in the first instance. Those with a score considered more predictive of needing a more invasive level of intervention or a known high likelihood of sphincter weakness/disruption could be referred directly to a tertiary level service for consultant-based care.

One of the most significant limitations to the entirety of this thesis is the choice of questionnaires used throughout. The chosen PROMs were employed for ongoing data collection as they had been in use since 2008. However, it is acknowledged that a number of potential other questionnaires could have been employed and may have produced more robust results. Identifying the PROM tools that most closely correlate with symptom severity and are most predictive of the need for more invasive treatment is vital in the development of a future pelvic floor ICP. With regards to assessing the degree of AI, two of the most commonly used tools are the WIS, used within this thesis, and also the Vaizey, or St Mark's Incontinence score[175]. The advantage of the Vaizey score is the consideration of deferral time, a key indicator missing within the WIS. It is certainly feasible that the Vaizey score could be more accurately predictive of the need for surgical intervention in patients with FI. This is especially true given that on Spearman's correlation, there was a significant correlation found between ARM testing of the MSPI and deferral time, therefore suggesting that symptoms of urgency and inability to defer defecation may be indicative of an underlying anal sphincter weakness. The Faecal Incontinence Quality of Life Scale (FIQL) measures quality of life in patients with anal incontinence, and has been validated internationally, showing significant correlation between both the SF-36 and Wexner Incontinence Score[263].Specific questionnaires also exist for conditions such as LARS, which should be separately utilised in order to identify unique symptom clusters not typically encountered with other FI aetiologies.

With regards to obstructed defecatory symptoms, the BBUSQ was used for this thesis. This was only validated for females, however the questionnaire was used in both sexes, which could be considered a significant limitation in evaluating its effectiveness in identifying those requiring surgery. However, the modified ODS score was also used which is validated in both sexes. It was more challenging to find any relationship between PROMs and the prediction of the need for surgical intervention in patients with ODS symptoms. This was most likely secondary to the fact that patients often have multi-compartmental and complex pelvic floor dysfunction, and treatment decisions are less predictable than those with frank FI. Again there are innumerable alternative scores which could have been utilized in order to fully explore the relationship between ODS symptoms and the need for surgical intervention. The Cleveland Clinic Constipation Score[275] and the Altomare ODS Score[276]have gained widespread acceptance and would be worthy of further exploration in future work.

The local pelvic floor service has now adopted a different questionnaire bank from those used within this work. The Pelvic Floor Disability Index (PDFI-20)[277] explores symptom severity with regards to urinary dysfunction, pelvic organ prolapse and colorectal/anal dysfunction. In terms of QoL, the Euroquol 5D has replaced the SF-36 as a QoL assessment tool as it has superseded the SF-36 in popularity in recent years[278]. The Pelvic Floor Impact Questionnaire (PFIQ-7)[277] considers the impact of anterior, middle and posterior compartment dysfunction on activities of daily living, relationships and mental wellbeing.

Sexual function is currently assessed locally using the Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire (PISQ-12). This questionnaire has been in use since the origin of the database however its findings were considered out with the scope of this thesis. However, a large series of initial consultation data was published in 2017 documenting 313 female patients[279]. Major sexual impairment was found in 31.9% (PISQ-12 <30). It demonstrated that the mean PISQ-12 score across the population was 5 points lower than quoted values for the general population. On multivariate analysis, predictors of a worse score in FI patients included previous anorectal surgery (OR 15.4), partner ejaculation problems (OR 2.5), reduced sexual arousal (OR 2.1), and orgasm perception (OR 2.1). Therefore further work needs to focus more heavily on the impact of pelvic floor dysfunction on sexual relationships, and perhaps the future development of a pelvic floor ICP could include provision of support and advice with regards to this.

Another important component to this thesis was regarding the different investigatory tests commonly used within the local pelvic floor service, predominantly MRD and ARM. EUS was also employed but its usage and correlation does not form part of this thesis.

MRD was explored initially through meta-analytical techniques, and it became evident that its advantages of a lack of ionizing radiation and the ability to assess all three pelvic floor compartments were at least partially offset by its inferiority in detection and miss rates compared to fluoroscopy. Given that patients can undergo tri-compartmental assessment through ECCD which includes assessment for potential enterocele and has better detection rates, it is important for the ordering clinician to consider carefully which diagnostic test is likely to give the best diagnostic yield with least harm to the patient. Currently, the local policy is that all patients (unless they have a contraindication to

MRD) undergo MRD. If this fails to yield results, then they may be offered a fluoroscopic examination. Again, when considering the limited resources available within the NHS, it may be prudent to consider a more streamlined approach, with MRD offered only to those who are likely to be compliant with the exam and are able to follow the instructions given, or who require multi-compartmental imaging. With the supine positioning in the scanner, the ability of the patient to fully strain and evacuate is limited, and requires full understanding of the purpose of the examination and the desired end point in order to achieve the best results. Even with maximal strain and evacuation views, it is an accepted limitation that there is a discrepancy with detection rates and estimates of severity compared to a sitting examination[239].

With regards to ARM, only the squeeze endurance was found to be a fair predictor of the need for surgery, suggesting it may have a limited role in decision-making for FI patients; however it remains an accurate test for diagnosing FI [111]. With functional defecatory disorders, it has a limited role as it struggles to distinguish between healthy volunteers and those with functional constipation[113]. There need to be clear guidelines as to who requires ARM to avoid unnecessary testing which adds little to the final decision-making process. It is recommended that in patients with ODS and chronic constipation, ARM is performed in those who fail to respond to initial treatment attempts [280].

When considering the scope of work that could potentially be carried on from this thesis, the primary aims should be to further delineate the relationship between PROMs, investigations and the need for surgery with the development of a pelvic floor ICP. Use of the different PROM questionnaires discussed above would be advised, as well as restructuring of current imaging pathways to more heavily incorporate barium proctography and ECCD into the decision-making process, with MRD being considered as the primary investigation of choice for specific patients, such as those with complex and recurrent pelvic floor dysfunction. Following from this, work could include an exploration of symptom clusters specific to ODS and FI patients, with examination of their ability to predict the need for more invasive treatment. Failing the identification of significant relationships between these additional diagnostic tools and the need for surgical intervention, an ICP could see all patients with ODS symptoms being referred directly to community Biofeedback, with those who show failure to improve significantly being referred to a consultant-led service for consideration of more invasive treatment

options. Similarly with FI patients, an ICP could be structured which allowed for earlier and more intensive community-based physiotherapist services, and early involvement of continence specialist nurses in order to tailor care, with referral of those who fail to show improvement. The exception to this would be those with higher grades of OASI, and also those who have had low rectal cancer resection as these patients will likely need more intensive medical input.

9.4 Final Conclusions

This thesis set out to explore a typical pelvic floor tertiary service in terms of common investigation modalities and diagnoses encountered, and how they relate to maximal treatment outcomes. Moving forward, further research needs to be undertaken into how best to streamline referrals to either community-based or tertiary level care. The ultimate aim is to develop a standardised care pathway for patients presenting with symptoms of pelvic floor dysfunction that acts to reduce strain on specialist services and uses specific PROMs as discriminatory measures of who is most likely to require surgical intervention. The work in this thesis forms a base for the development of this pathway, and should promote further research into which diagnostic tools best perform this act and can safely identify those who most likely require only Biofeedback as a maximal treatment outcome and can be managed in the community.

Part 5: References and appendices

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11. APPENDICES

11.1 Birmingham Bowel, Bladder and Urinary Symptom Questionnaire

Please circle the most appropriate answer regarding your symptoms at present

How often do you open your bowels?	More than 3 times a day 2-3 times a day Once a day Every 1-3 days Less than every 3 days Less than once a week
Are your motions usually →	Watery ? Sloppy ? Soft and formed ? Hard ?
Can you hold on to your motions for more than 5 minutes ?	All of the time Most of the time Occasionally Never
Do you ever have to rush to the toilet to open your bowels?	Never Occasionally Most of the time All of the time
Does stool leak before you can get to the toilet?	Never Occasionally Most of the time All of the time
Do you leak stool for no obvious reason and without feeling that you want to go to the toilet?	Never Occasionally Most of the time All of the time
Do you have to strain to open your bowels?	Never Occasionally Most of the time All of the time

How long do you spend in the toilet, on average, for each bowel action?	Less than 5 minutes 5-10 minutes 10-20 minutes More than 20 minutes
Do you feel that you cannot completely empty your bowel ?	Never Occasionally Most of the time All of the time
Do you use a finger or pressure to help open your bowels ?	Never Occasionally Most of the time All of the time
Do you use a finger in your vagina to help open your bowels?	Never Occasionally Most of the time All of the time
Do you have the urge to open your bowels but are unable to pass a motion?	Never Occasionally Most of the time All of the time
Do you find it painful to have your bowels open ?	Never Occasionally Most of the time All of the time
Have you consulted a doctor in the last six months about constipation ?	Yes No
Do you use laxatives ?	Never Once a week More than once a week Everyday
During the day, how many times do you urinate, on average?	1-6 times 7-9 times 10-12 times

	13 times or more
During the night, how many times do you have to get up to urinate, on average?	Never 1 time 2 times 3 times
Do you have to rush to the toilet to urinate?	Never Occasionally Most of the time All of the time
Do you have difficulty completely emptying your bladder?	Never Occasionally Most of the time All of the time
Does urine leak before you can get to the toilet?	Never Occasionally Most of the time All of the time
Does urine leak when you are active, exert yourself, cough or sneeze?	Never Occasionally Most of the time All of the time
Does urine leak for no obvious reason and without feeling that you want to go to the toilet?	Never Occasionally Most of the time All of the time

11.2 Wexner Incontinence Score

	Frequency				
Type of incontinence	**Never**	**Rarely**	**Sometimes**	**Usually**	**Always**
Solid	**0**	**1**	**2**	**3**	**4**
Liquid	**0**	**1**	**2**	**3**	**4**
Gas	**0**	**1**	**2**	**3**	**4**
Wears pad	**0**	**1**	**2**	**3**	**4**
Lifestyle alteration	**0**	**1**	**2**	**3**	**4**

11.3 Longo modified obstructed defecation score

How often do you..?	Never	Rarely	Sometimes	Usually	Always
Strain	**0**	**1**	**2**	**3**	**4**
Incomplete evacuation	**0**	**1**	**2**	**3**	**4**
Medication use	**0**	**1**	**2**	**3**	**4**
Need to interdigitate rectum/vagina or use of perineal support	**0**	**1**	**2**	**3**	**4**
Constipation	**0**	**1**	**2**	**3**	**4**

11.4 UK SF-36 questionnaire

Instructions: This survey asks for your views about your health. This information will help keep track of how you feel and how well you are able to do your usual activities.

Answer every question by marking the answer as indicated. If you are unsure about how to answer a question, please give the best answer you can.

1. In general, would you say your health is:

(circle one)

Excellent ……1
Very good ……..2
Good …….....3
Fair …….. . 4
Poor ……5

2. Compared to one year ago, how would you rate your health in general now?

(circle one)

Much better now than one year ago ……1
Somewhat better now than one year ago …….2
About the same as one year ago ……..3
Somewhat worse now than one year ago ……4
Much worse now than one year ago ……5

3. The following questions are about activities you might do during a typical day. Does your health now limit you these activities? If so, how much?

(circle one number on each line)

ACTIVITIES	Yes, Limited A Lot	Yes Limited A Little	No, Not Limited At All
a. **Vigorous activities**, such as running, lifting heavy objects, participating in strenuous sports	1	2	3
b. **Moderate activities**, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	1	2	3
c. Lifting or carrying groceries	1	2	3
d. Climbing **several** flights of stairs	1	2	3
e. Climbing **one** flight of stairs	1	2	3
f. Bending, kneeling or stooping	1	2	3
g. Walking **more than a mile**	1	2	3
h. Walking **half a mile**	1	2	3
i. Walking **one hundred yards**	1	2	3
j. Bathing or dressing yourself	1	2	3

4. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

(circle one number on each line)

	YES	NO
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Were limited in the **kind** of work or other activities	1	2
d. Had **difficulty** performing the work or other activities (for example, it took extra effort)	1	2

5. During the past 4 weeks, have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

(circle one number on each line)

	YES	NO
a. Cut down on the **amount of time** you spent on work or other activities	1	2
b. **Accomplished less** than you would like	1	2
c. Don't do work or other activities as **carefully** as usual	1	2

6. During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups?

(circle one)

Not at all ……. 1
Slightly …… 2
Moderately …… 3
Quite a bit ……...4
Extremely ……...5

7. How much bodily pain have you had during the past 4 weeks?

(circle one)

None …….. 1
Very mild ……...2
Mild ……3
Moderate ……4
Severe …….5
Very severe …… 6

8. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)?

(circle one)

Not at all …….. 1

A little bit ……. 2

Moderately …… 3

Quite a bit …….. 4

Extremely …….. 5

9. Theses questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closet the way you have been feeling. How much of the time during the past 4 weeks –

(circle one number on each line)

	All of the Time	Most of the Time	A Good bit of the *Time*	Some of the Time	A little of the Time	*None* of the *Time*
a. Did you feel full of life?	1	2	3	4	5	6
b. Have you been a very nervous person?	1	2	3	4	5	6
c. Have you felt so down in the dumps that nothing could cheer you up?	1	2	3	4	5	6
d. Have you felt calm and peaceful?	1	2	3	4	5	6
e. Did you have a lot of energy?	1	2	3	4	5	6
f. Have you felt downhearted and low?	1	2	3	4	5	6
g. Did you feel worn out?	1	2	3	4	5	6
h. Have you been a happy person ?	1	2	3	4	5	6
i. Did you feel tired?	1	2	3	4	5	6

10. During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting with friends, relatives, etc.)?

(circle one)

All of the time ……1
Most of the time ……..2
Some of the time ……3
A little of the time ……..4
None of the time …… 5

11. How TRUE or FALSE in each of the following statements for you?

(circle one number on each line)

	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
a. I seem to get ill more easily than other people	1	2	3	4	5
b. I am as healthy as anybody I know	1	2	3	4	5
c. I expect my health to get worse	1	2	3	4	5
d. My health is excellent	1	2	3	4	5

11.5 Low Anterior Resection Syndrome Score (LARS Score)

The aim of this questionnaire is to assess your bowel function. Please tick only one box for each question. It may be difficult to select only one answer, as we know that for some patients symptoms vary from day to day. We would kindly ask you to choose one answer which best describes your daily life. If you have recently had an infection affecting your bowel function, please do not take this into account and focus on answering questions to reflect your usual daily bowel function.

1. Do you ever have occasions when you cannot control your flatus (wind)?
    - o No, never 0
    - o Yes, less than once per week 4
    - o Yes, at least once per week 7

2. Do you ever have any accidental leakage of liquid stool?
    - o No, never 0
    - o Yes, less than once per week 3
    - o Yes, at least once per week 3

3. How often do you open your bowels?
    - o More than 7 times per day (24 hours) 4
    - o 4-7 times per day (24 hours) 2
    - o 1-3 times per day (24 hours) 0
    - o Less than once per day (24 hours) 5

4. Do you ever have to open your bowels again within one hour of the last bowel opening?
    - o No, never 0
    - o Yes, less than once per week 9
    - o Yes, at least once per week 11

5. Do you ever have such a strong urge to open your bowels that you have to rush to the toilet?
    - o No, never 0
    - o Yes, less than once per week 11
    - o Yes, at least once per week 16

Add the scores to give one final score:
0-20 = No LARS *21-29= Minor LARS* *30-42 = Major LARS*

11.6 Female Sexual Function Index

INSTRUCTIONS: These questions ask about your sexual feelings and responses during the past 4 weeks. Please answer the following questions as honestly and clearly as possible. Your responses will be kept completely confidential. In answering these questions the following definitions apply:

Sexual activity can include caressing, foreplay, masturbation and vaginal intercourse. Sexual intercourse is defined as penile penetration (entry) of the vagina.

Sexual stimulation includes situations like foreplay with a partner, self-stimulation (masturbation), or sexual fantasy.

CHECK ONLY ONE BOX PER QUESTION.

Sexual desire or interest is a feeling that includes wanting to have a sexual experience, feeling receptive to a partner's sexual initiation, and thinking or fantasizing about having sex.

1. Over the past 4 weeks, how often did you feel sexual desire or interest?

Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time) /Almost never or never

2. Over the past 4 weeks, how would you rate your level(degree)of sexual desire or interest?

Very high/High/Moderate Low/Very low or none at all

Sexual arousal is a feeling that includes both physical and mental aspects of sexual excitement. It may include feelings of warmth or tingling in the genitals, lubrication (wetness), or muscle contractions.

3. Over the past 4 weeks, how often did you feel sexually aroused("turned on") during sexual activity or intercourse?

No sexual activity/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

4. Over the past 4 weeks, how would you rate your level of sexual arousal("turn on") during sexual activity or intercourse?

No sexual activity/Very high/High/Moderate/Low/Very low or none at all

5.Over the past 4 weeks, how confident were you about becoming sexually aroused during sexual activity or intercourse?

No sexual activity/Very high confidence/High confidence/Moderate confidence/Low confidence/Very low or no confidence

6. Over the past 4 weeks, how often have you been satisfied with your arousal (excitement) during sexual activity or intercourse?

No sexual activity/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

7.Over the past 4 weeks, how often did you become lubricated ("wet") during sexual activity or intercourse?

No sexual activity/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

8.Over the past 4 weeks, how difficult was it to become lubricated ("wet") during sexual activity or intercourse?

No sexual activity/Extremely difficult or impossible/Very difficult/Difficult/Slightly difficult/Not difficult

9.Over the past 4 weeks, how often did you maintain your lubrication ("wetness") until completion of sexual activity or intercourse?

No sexual activity/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

10.Over the past 4 weeks, how difficult was it to maintain your lubrication ("wetness") until completion of sexual activity or intercourse?

No sexual activity/Extremely difficult or impossible/Very difficult/Difficult/Slightly difficult/Not difficult

11.Over the past 4 weeks, when you had sexual stimulation or intercourse, how often did you reach orgasm (climax)?

No sexual activity/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

12.Over the past 4 weeks, when you had sexual stimulation or intercourse, how difficult was it for you to reach orgasm (climax)?

No sexual activity/Extremely difficult or impossible/Very difficult/Difficult/Slightly difficult/Not difficult

13.Over the past 4 weeks, how satisfied were you with your ability to reach orgasm (climax) during sexual activity or intercourse?

No sexual activity/Very satisfied/Moderately satisfied/About equally satisfied and dissatisfied/Moderately dissatisfied/Very dissatisfied

14.Over the past 4 weeks, how satisfied have you been with the amount of emotional closeness during sexual activity between you and your partner?

No sexual activity/Very satisfied/Moderately satisfied/About equally satisfied and dissatisfied/Moderately dissatisfied/Very dissatisfied

15.Over the past 4 weeks, how satisfied have you been with your sexual relationship with your partner?

Very satisfied/Moderately satisfied/About equally satisfied and dissatisfied/Moderately dissatisfied/Very dissatisfied

16.Over the past 4 weeks, how satisfied have you been with your overall sexual life?

Very satisfied/Moderately satisfied/About equally satisfied and dissatisfied/Moderately dissatisfied/Very dissatisfied

17.Over the past 4 weeks, how often did you experience discomfort or pain during vaginal penetration?

Did not attempt intercourse/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

18.Over the past 4 weeks, how often did you experience discomfort or pain following vaginal penetration?

Did not attempt intercourse/Almost always or always/Most times (more than half the time)/Sometimes (about half the time)/A few times (less than half the time)/Almost never or never

19.Over the past 4 weeks, how would you rate your level (degree) of discomfort or pain during or following vaginal penetration?

Did not attempt intercourse/Very high/High/Moderate/Low/Very low or none at all

11.7 Male Sexual Health Questionnaire (MSHQ)

INTRODUCTION: The following questions concern various aspects of your ability to have sex. In answering these questions, please think about all aspects of the sexual activity you have had with your main partner, with other partners, or masturbating. By sexual activity, we mean any type of sex you may have had, including intercourse, oral sex or other sexual activities that could lead to ejaculation.

Some of these questions might be difficult to answer. Please answer as many as possible, and be as honest as you can when answering them. Please remember that all of your answers are confidential.

The first questions concern your erections, which some people refer to as "hard-ons".

In the last month have you taken Viagra or any similar drugs for problems with your erection? ☐ Yes ☐ No

Erection Scale

1. **In the last month,** without using drugs like Viagra, how often have you been able to get an erection when you wanted to? (Check only one)

   5 ☐ All of the time
   4 ☐ Most of the time
   3 ☐ About half of the time
   2 ☐ Less than half of the time
   1 ☐ None of the time
   0 ☐ Used Viagra or similar drug with every sexual encounter

2. **In the last month,** if you were able to get an erection without using drugs like Viagra, how often were you able to stay hard as long as you wanted to? (Check only one)

   5 ☐ All of the time
   4 ☐ Most of the time
   3 ☐ About half of the time
   2 ☐ Less than half of the time
   1 ☐ None of the time
   0 ☐ Used Viagra or similar drug with every sexual encounter

3. **In the last month,** if you were able to get an erection, without using drugs like Viagra, how would you rate the hardness of your erection? (Check only one)

   5 ☐ Completely hard
   4 ☐ Almost completely hard
   3 ☐ Mostly hard, but can be slightly bent
   2 ☐ A little hard, but bends easily
   1 ☐ Not at all hard
   0 ☐ Used Viagra or similar drug with every sexual encounter

ED Bother Item

4. **In the last month,** if you have had difficulty getting hard or staying hard without using drugs like Viagra, have you been bothered by this problem?… (Check only one)

   5 ☐ Not at all bothered/Did not have a problem with erection
   4 ☐ A little bit bothered
   3 ☐ Moderately bothered
   2 ☐ Very bothered
   1 ☐ Extremely bothered

Ejaculation (Ej) Scale

INTRODUCTION: The next section deals with male ejaculation and the pleasure you have with ejaculation. Ejaculation or "cumming" is the release of semen or "cum" during sexual climax. These questions concern all of your ejaculations when having sexual activity. These could include ejaculations you have had with your main partner, as well as with other partners, or ejaculations you have had when masturbating.

5. **In the last month,** how often have you been able to ejaculate when having sexual activity? (Check only one)

   5 ☐ All of the time
   4 ☐ Most of the time
   3 ☐ About half of the time
   2 ☐ Less than half of the time
   1 ☐ None of the time/Could not ejaculate

6. **In the last month,** when having sexual activity, how often did you feel that you took too long to ejaculate or "cum"? (Check only one)

   5 ☐ None of the time
   4 ☐ Less than half of the time
   3 ☐ About half of the time
   2 ☐ Most of the time
   1 ☐ All of the time
   0 ☐ Could not ejaculate

7. **In the last month,** when having sexual activity, how often have you felt like you were ejaculating ("cumming"), but no fluid came out?

5 ☐ None of the time
4 ☐ Less than half of the time
3 ☐ About half of the time
2 ☐ Most of the time
1 ☐ All of the time
0 ☐ Could not ejaculate

8. **In the last month,** how would you rate the strength or force of your ejaculation?

5 ☐ As strong as it always was
4 ☐ A little less strong than it used to be
3 ☐ Somewhat less strong than it used to be
2 ☐ Much less strong than it used to be
1 ☐ Very much less strong than it used to be
0 ☐ Could not ejaculate

9. **In the last month,** how would you rate the amount or volume of semen when you ejaculate?

5 ☐ As much as it always was
4 ☐ A little less than it used to be
3 ☐ Somewhat less than it used to be
2 ☐ Much less than it used to be
1 ☐ Very much less than it used to be
0 ☐ Could not ejaculate

10. **Compared to ONE month ago,** would you say the physical pleasure you feel when you ejaculate has…

5 ☐ Increased a lot
4 ☐ Increased moderately
3 ☐ Neither increased nor decreased
2 ☐ Decreased moderately
1 ☐ Decreased a lot
0 ☐ Could not ejaculate

11. In the last month, have you experienced any physical pain or discomfort when you ejaculated? Would you say you have…

5 ☐ No pain at all
4 ☐ Slight amount of pain or discomfort
3 ☐ Moderate amount of pain or discomfort
2 ☐ Strong amount of pain or discomfort
1 ☐ Extreme amount of pain or discomfort
0 ☐ Could not ejaculate

(EjD) Bother Item

12. **In the last month,** if you have had any ejaculation difficulties or have been unable to ejaculate, have you been bothered by this?

    5 ☐ Not at all bothered
    4 ☐ A little bit bothered
    3 ☐ Moderately bothered
    2 ☐ Very bothered
    1 ☐ Extremely bothered

Satisfaction Scale

These next few questions ask about your relationship with your main partner over the **last month**. Some of these questions concern your sexual relationship, while others are about your overall relationship.

13. Generally, how satisfied are you with the overall sexual relationship you have with your main partner? (Check only one)

    5 ☐ Extremely Satisfied
    4 ☐ Moderately Satisfied
    3 ☐ Neither Satisfied nor Unsatisfied
    2 ☐ Moderately Unsatisfied
    1 ☐ Extremely Unsatisfied

14. Generally, how satisfied are you with the quality of the sex life you have with your main partner?

    5 ☐ Extremely Satisfied
    4 ☐ Moderately Satisfied
    3 ☐ Neither Satisfied nor Unsatisfied
    2 ☐ Moderately Unsatisfied
    1 ☐ Extremely Unsatisfied

15. Generally, how satisfied are you with the number of times you and your main partner have sex?

    5 ☐ Extremely Satisfied
    4 ☐ Moderately Satisfied
    3 ☐ Neither Satisfied nor Unsatisfied
    2 ☐ Moderately Unsatisfied
    1 ☐ Extremely Unsatisfied

16. Generally, how satisfied are you with the way you and your main partner show affection during sex?

5 ☐ Extremely Satisfied
4 ☐ Moderately Satisfied
3 ☐ Neither Satisfied nor Unsatisfied
2 ☐ Moderately Unsatisfied
1 ☐ Extremely Unsatisfied

17. Generally, how satisfied are you with the way you and your main partner communicate about sex?

5 ☐ Extremely Satisfied
4 ☐ Moderately Satisfied
3 ☐ Neither Satisfied nor Unsatisfied
2 ☐ Moderately Unsatisfied
1 ☐ Extremely Unsatisfied

18. Aside from your sexual relationship, how satisfied are you with all other aspects of the relationship you have with your main partner?

5 ☐ Extremely Satisfied
4 ☐ Moderately Satisfied
3 ☐ Neither Satisfied nor Unsatisfied
2 ☐ Moderately Unsatisfied
1 ☐ Extremely Unsatisfied

Additional Items (Sexual Activity and Desire)

INTRODUCTION: The next set of questions concern the sexual activity you have had **in the last month**. In answering these questions, we want to know about all of the sexual activity you have had with your main partner, with other partners, or masturbating. By sexual activity, we mean any type of sex you may have had, including intercourse, oral sex, or any other sexual activities that could lead to ejaculation.

19. **In the last month,** how often have you had sexual activity, including masturbating, intercourse, oral sex, or any other type of sex? (Check only one)

5 ☐ Daily or almost daily
4 ☐ More than 6 times per month
3 ☐ 4-6 times per month
2 ☐ 1-3 times per month
1 ☐ 0 times per month

If your answer is "0" for item 19, please answer the following questions:

A. When was the last time you had sex? (Check only one)

5 ☐ 1-3 months ago
4 ☐ 4-6 months ago
3 ☐ 7-12 months ago
2 ☐ 13-24 months ago
1 ☐ More than 24 months ago

B. What are the reasons you have not had sex?

I could not have sex because I could not get an erection: ☐ Yes ☐ No

I could not have sex because I could not ejaculate or "cum": ☐ Yes ☐ No

I had no partner: ☐ Yes ☐ No

Other (specify): _____

20. Compared to **ONE month ago,** has the number of times you have had sexual activity increased or decreased?

5 ☐ Increased a lot
4 ☐ Increased moderately
3 ☐ Neither increased nor decreased
2 ☐ Decreased moderately
1 ☐ Decreased a lot

21. In the last month, have you been bothered by these changes in the number of times you have had sexual activity?

5 ☐ Not at all bothered
4 ☐ A little bit bothered
3 ☐ Moderately bothered
2 ☐ Very bothered
1 ☐ Extremely bothered

INTRODUCTION: These next questions ask about your urge or desire to have sex with **your main partner**. Some people refer to this as "feeling horny". These questions concern the sexual urges you have felt toward your main partner, and not whether you actually had sex.

Do you have a "main partner"? ☐ Yes ☐ No
IF YOU DO NOT HAVE A MAIN PARTNER, PLEASE ANSWER ALL QUESTIONS WITHOUT REFERENCE TO A "MAIN PARTNER"

22. **In the last month,** how often have you felt an urge or desire to have sex with your main partner?

    5 ☐ All of the time
    4 ☐ Most of the time
    3 ☐ About half of the time
    2 ☐ Less than half of the time
    1 ☐ None of the time

23. **In the last month,** how would you rate your urge or desire to have sex with your main partner?

    5 ☐ Very high
    4 ☐ High
    3 ☐ Moderate
    2 ☐ Low
    1 ☐ Very low or none at all

24. **In the last month,** have you been bothered by your level of sexual desire? Have you been…

    5 ☐ Not at all bothered
    4 ☐ A little bit bothered
    3 ☐ Moderately bothered
    2 ☐ Very bothered
    1 ☐ Extremely bothered

25. Compared to **ONE month ago,** has your urge or desire for sex with your main partner increased or decreased?

    5 ☐ Increased a lot
    4 ☐ Increased moderately
    3 ☐ Neither increased nor decreased
    2 ☐ Decreased moderately
    1 ☐ Decreased a lot

THANK YOU FOR YOUR COOPERATION.

11.8: PISQ-12

The Pelvic Organ Prolapse/Urinary Incontinence

Sexual Function Questionnaire (PISQ-12)

Instructions: Following is a list of questions about you and your partner's sex life. All information is strictly confidential. Your confidential answers will be used only to help doctors understand what is important to patients about their sex lives. Please check the box that best answers the question for you. While answering the questions, consider your sexuality over the past *six months*. Thank you for your help.

	Always	Usually	Sometimes	Seldom	Never
1. How often do you feel sexual desire? This feeling may include wanting to have sex, planning to have sex, feeling frustrated due to lack of sex, etc.	☐	☐	☐	☐	☐
2. Do you climax (have an orgasm) while having *sexual intercourse* with your partner?	☐	☐	☐	☐	☐
3. Do you feel sexually excited (turned on) when having sexual activity with your partner?	☐	☐	☐	☐	☐
4. How satisfied are you with the variety of sexual activities in your current sex life?	☐	☐	☐	☐	☐
5. Do you feel pain during sexual intercourse?	☐	☐	☐	☐	☐
6. Are you incontinent of urine (leak urine) with sexual activity?	☐	☐	☐	☐	☐
7. Does fear of incontinence (either stool or urine) restrict your sexual activity?	☐	☐	☐	☐	☐
8. Do you avoid sexual intercourse because of bulging in the vagina (either the bladder, rectum or vagina falling out?)	☐	☐	☐	☐	☐
9. When you have sex with your partner, do you have negative emotional reactions such as fear, disgust, shame or guilt?	☐	☐	☐	☐	☐
10. Does your partner have a problem with *erections* that affects your sexual activity?	☐	☐	☐	☐	☐
11. Does your partner have a problem with premature ejaculation that affects your sexual activity?	☐	☐	☐	☐	☐

12. Compared with orgasms you have had in the past, how intense are the orgasms you have had in the past six months?	Much less intense ☐	Less intense ☐	Same intensity ☐	More intense ☐	Much more intense ☐

Scoring: Scores are calculated by totaling the scores for each question with 0 = never, 4 = always. Reverse scoring is used for items 1, 2, 3, and 4. The short-form questionnaire can be used with up to two missing responses. To handle missing values, the sum is calculated by multiplying the number of items by the mean of the answered items. If there are more than two missing responses, the short form no longer accurately predicts long-form scores. Short-form scores can only be reported as total or on an item basis. Although the short form reflects the content of the three factors in the long form, it is not possible to analyze the data at the factor level. To compare long- and short-form scores, multiply the short-form score by 2.58 (12/31).