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REVIEW ARTICLE

A systematic review on radiofrequency assisted laparoscopic liver resection: challenges and window to excel

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Nagy Habib is a shareholder and director of EMcision Limited, which has developed the Habib 4X, one of the devices cited in this article not manufactured or currently marketed by this company

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HIGHLIGHTS

- Laparoscopic liver resection is a safe and effective procedure, although blood loss is still a challenge
- Among different techniques and devices, Radiofrequency (RF) can help in minimizing blood loss in open and laparoscopic liver resection
- Although RF has been used in a small minority of laparoscopic liver resections, it seems to be safe with reduction in blood loss, low morbidity, and lower hospital mortality rates
- With RF, resection and ablation can be combined during same procedure
- Current results support the use of RF as precoagulation device in laparoscopic liver surgery

Abstract

Laparoscopic liver resection has progressively gained acceptance as a safe and effective procedure in the treatment of benign and malignant liver neoplasms. However, blood loss remains the major challenge in liver surgery. Several techniques and devices have been introduced in liver surgery in order to minimize intraoperative haemorrhage during parenchymal transection. Radiofrequency (RF)-assisted liver resection has been shown to be an effective method to minimise bleeding in open and laparoscopic liver resection. A number of RF devices for parenchymal transection have been designed to assist laparoscopic liver resections. Here we have reviewed the results of various RF devices in laparoscopic liver resection. A total 15 article were considered relevant for the evaluation of technical aspects and outcomes of RF-assisted liver resections in laparoscopic procedures. In these studies, 176 patients had laparoscopic liver resection using RF-assisted parenchymal coagulation. Two monopolar and three bipolar devices were employed. Blood loss was limited in most of the studies. The need of blood transfusions was limited to two cases in all the series. Conversion was necessary due to bleeding in 3 cases. Operative and transection times varied between studies. However, RF-assisted resection with bipolar devices appeared to have taken less time in comparison to other RF devices. RF-related complications were minimum, and only one case of in-hospital death due to hepatic failure was reported. Although RF has been used in a small minority of laparoscopic liver resections, laparoscopic RF-assisted liver resection for benign and malignant disease is a safe and feasible procedure associated with reduction in blood loss, low morbidity, and lower hospital mortality rates.

Key words: laparoscopic; liver resection; radiofrequency-assisted.

Introduction

Laparoscopic surgery has transformed many surgical procedures, by reducing morbidity and achieving results comparable to open procedures. Current evidences on the safety and efficacy of laparoscopic hepatic resection appears adequate to support its routine use in the management of liver neoplasm. [1] In last few decades laparoscopic hepatic resection has attained an equivalent status of safety on a par with conventional open surgeries, particularly in specialized centres with skilled surgical teams, experienced in both hepatobiliary/pancreatic and laparoscopic surgery. [2] In addition to the known benefits of laparoscopic surgeries such as reduced postoperative pain, hospital stay and morbidity, laparoscopic liver resections have shown early improvement in serum transaminase levels. [3] Intraoperative haemorrhage is one of the greatest challenges that we face in both laparoscopic and conventional liver surgery. Furthermore, unmanageable blood loss is one of the principal reasons for conversion to open approach during laparoscopic liver surgery. [4-6] Intraoperative bleeding and the need for blood transfusion negatively affect post-operative morbidity and mortality rates, as well as long-term outcomes. [7]

The amount of blood loss differs during each phase of liver surgery, with most of bleeding encountered during the parenchymal transection phase. Various techniques have been developed to reduce the risk of intraoperative blood loss during liver resection. [8] Pringle's manoeuvre reduces haemorrhage by limiting the blood flow through the inflow vascular pedicle. [9] The risk of postoperative hepatic failure depends upon the duration of the vessel occlusion time, besides that, Pringle's manoeuvre does not control blood loss from the hepatic veins. [10,11] In 2002, Weber et al. introduced a new technique for pre-coagulation of the liver parenchyma using RF energy creating ischemic zone before transection of the liver parenchyma. [12] This technique has been used for laparoscopic surgery as parenchymal resection is then performed in a relatively bloodless field.

As the number of laparoscopic hepatic resections has increased in recent years, several devices have been used to assist laparoscopic procedures, haemostasis, and in particular parenchymal transection. [13] Herein we discuss and review the emergence of RF devices in laparoscopic liver resection, focusing on technical aspects and complication rates of the different available devices described in the literature.

Materials and Methods

A comprehensive systematic literature review was performed following registration in PROSPERO an international database of prospectively registered systematic reviews (registration number CRD42016049331). We searched all the published articles on PUBMED, Cochrane, Crossref, and Scopus databases on 31st January 2017, for original articles describing the application of RF for parenchymal transection during laparoscopic liver resection. The systematic search covered the period 1990 (the year of the first laparoscopic liver resection reported in the literature) to 31st January 2017. The search was carried out by using the medical subject headings (MeSH) term: 'laparoscopic liver resection, 'radiofrequency-assisted', and 'laparoscopic radiofrequency device'. The initial search yielded a total of 185 manuscripts. After careful evaluation, 143 articles were excluded. The remaining 42 papers, of which four review articles were sought as an additional source of original works otherwise overlooked, were considered and full-text was obtained.

Inclusion Criteria: Original studies available in English and published between 1990-2017 (January) were included. Only studies which systematically and quantitatively assessed the role of equipment based on radiofrequency were analysed. Publication type as comparative studies, retrospective and prospective studies, case reports and case series were included. Papers on hand-assisted techniques were also included when matching inclusion criteria. Articles describing RF-assisted open and laparoscopic procedures were included when data from laparoscopic approaches could be extrapolated from the article. We have excluded kinds of literature as editorials, reviews, letters, articles on animal studies, prototypes or on thoracoscopic approach. Two other articles were also excluded because they reported a case of liver resection in children.

Data Extraction: Using a standardized quality assessment tool and pre-specified inclusion and exclusion criteria, authors (IR & KJ) independently analysed all papers with studies and in the case of any lack of consensus, the analysis was made by the final reviewer (MP) to solve the matter. This systematic review was performed using the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines and registered in PROSPERO an international database of prospectively registered systematic reviews. (**Fig.1**) Eventually, a total of 18 articles matched the previously described inclusion criteria. However, data from 3 papers (Pai et al. 2008; Vavra et al. 2014 and Vavra et al. 2015) [14-16] were part of other studies (Jiao et al. 2008, and Vavra et al. 2012) [17,18] already included in the analysis and therefore not considered as additional numbers to this review. Vavra et al. 2012 was selected because more information regarding outcomes was reported. [18] (**Table.1**)

Data Analysis: The quality of all the included articles were assessed by QUADAS-2 (quality assessment for studies of diagnostic accuracy) and pre-specified inclusion and exclusion criteria. QUADAS-2 is an evidence-based bias assessment tool to assess the quality of diagnostic accuracy studies in a systematic review. We have reviewed each study comprehensively, and data were extracted for the outcomes such as blood loss, transfusion requirement, operative time, morbidity and mortality and recurrence rates.

Results

A total of 15 peer-reviewed studies were included in this analysis. 10 studies were from single-centre, whilst 5 were multi-institutional studies. Furthermore, five of these studies were conducted mainly or partly in the United Kingdom whereas rest 10 studies were conducted in the United States, Italy, France, Greece, Belgium, Czech Republic, India and, Malaysia.

All the available data from these 15 studies were analysed with a total of 176 cases of liver resection performed for various indications as benign, primary, secondary malignant liver tumours thus, cirrhosis was not a common feature of patients. The techniques used in these studies were pure laparoscopic in 12, whilst the hand-assisted technique has been used in three studies (Miyazawa et al. 2006, Clancy et al. 2005, and Vavra et al. 2012). [18-20] A total of five different types of devices have been used, including monopolar and bipolar devices. Monopolar consisted of different Cool-tip RF ablation systems, which were used in 7 studies [11,19,21-25], and the StarBurst XL RF ablation device, employed in only 1 study together with a bipolar device (Habib 4X Laparoscopic) [26]. Three bipolar devices were used; [27-29] the Habib 4X Laparoscopic (also named Habib Sealer) was used in 5 studies [17,18], whilst the InCircle B-RFA and Inline RF coagulation were used in one study each [20,30]. (**Table. 2**)

Total number of resections completed laparoscopically was 165, with 11 cases converted to open approach. The surgery types covered in these studies included anatomic and non-anatomical hepatic resections, bisegmentectomy, and hemihepatectomy as shown in Table 3. Major resections (3 or more segments) were performed only in a minority of cases (3.6% of all resections).

The indications for laparoscopic liver resection were 25 (14.2%) benign lesions (including 9 haemangioma; 5 adenoma; 4 focal nodular hyperplasia; 2 biliary cystadenoma; 2 chronic inflammation; 1 hamartoma; and 2 not specified) and 151 (85.8%) malignant lesions (62 colorectal liver metastases, 56 hepatocellular carcinoma; 5 cholangiocarcinoma; 1 gallbladder cancer; 4 breast metastases; 1 gastrointestinal stromal tumour metastasis; 1 neuroendocrine tumour metastasis; 1 sarcoma metastasis; 1 lung metastasis; 1 anal cancer metastasis; 1 lymphoma; and 17 not specified). (data not shown in the tables) Although majority of cases were done for malignant lesions, description of macroscopic vascular invasion was mentioned only in Hompes et al 2007 [11] where in one case there was hepatic vein involvement. This is the only series where they have performed major hepatectomies (1 left and 2 right hepatectomies) and they had 2 cases with macroscopic invasion, one of the diaphragm and one of the hepatic vein. However, more than 60% of the cases performed in the rest of the series were mainly tumorectomies or segmentectomies for benign and malignant cases (more than 60%).

The outcomes analysed in the 15 studies included intraoperative blood loss, the need for blood transfusion, and the rate of conversion to open approach, use of vascular control, transection time and total operative time. No data regarding change in liver enzyme levels were reported in any study.

Of the 15 studies analysed, data for intraoperative blood loss was reported in only 13 studies [11,17-19,21-23,25-30] (**Table. 4**), whilst in two studies (Clancy et al. 2005 and Curro et al. 2008) [20,24] this data was not available. Nine studies have reported minimal blood loss, ranging from less than 50 ml to 200 ml. [17-19,21,23,25,27-29] Alemi et al. 2011 [30] reported the highest blood loss among all the studies using bipolar devices. The median estimated blood loss was of 300 ml (20–3000 ml). Operations performed were anatomic segmental resections in 11 patients and multi-segmental resection or hemihepatectomy in six patients.

One study (Akyildiz et al. 2011) [26] describing results from the use of two different devices, monopolar and bipolar, has compared reported intraoperative haemorrhage. The mean intraoperative blood loss was greater in the monopolar group (224 cc ± 79 cc) than in the bipolar (89 cc ± 77 cc), however, this difference was not statistically significant. Only one prospective, non-randomized study (Hompes et al. 2007) [11] has compared results of laparoscopic liver resections with and without the aid of a monopolar device and described a median blood loss of 200 ml, but with a range of 5 ml to 3000 ml. In seven cases intraoperative bleeding was experienced. The operations performed with RF-assistance included 8 segmental hepatectomies, 9 left lateral lobectomies, 1 left lateral hemihepatectomies and 3 right hemihepatectomies for benign and malignant diseases.

The requirement of blood transfusions was reported in 13 studies with 12 reporting no blood transfusion due to minimal blood loss [17-23,25-29]. The two patients who required higher blood transfusion has been reported by Alemi et al. 2011 in their series because of the intraoperative blood loss ranging up to 3000 ml [30]. Two studies did not detail the need for blood transfusion [11,24].

The Vascular control was required in three studies. (**Table. 4**) Gadiyaram et al. 2012 [28] described a laparoscopic resection of a giant liver haemangioma involving segment V and VI. They identified and occluded the feeding artery of the lesion, arising from the right anterior branch of the right hepatic artery and then completed the resection with parenchymal coagulation with Habib 4x probe. For major resections (i.e. right or left laparoscopic hemihepatectomy), as we described in our previous paper on all RF-assisted liver resection performed at our Institution (open and laparoscopic), when performing the parenchymal resection with RF, a standard hilar dissection is seldom performed, with vascular clamping being very rarely required. [31] In Hompes et al. 2007 [11] the Pringle manoeuvre (inflow occlusion) was applied to 4 patients, with a median duration of 15 min

(7–45 min). In Alemi et al. 2011 [30], Pringle's manoeuvre was used in selected operations, depending on the magnitude of resection. Radiofrequency was sufficient to seal small blood vessels and bile ducts (up to 3 or 4mm). In patients who underwent a right or left hemihepatectomy, the inflow vessels were controlled selectively prior to parenchymal transection, without a Pringle's manoeuvre, and divided between endoclips or with Endo GIA stapler, as described by Hompes at al 2007 [11] and by Zacharoulis et al 2013 [29]. Some authors reduced the power of the RF generator to seal large vessels like hepatic veins, as described by Vavra et al 2012 [18], since decreasing the power paradoxically achieved a wider coagulation effect. [31] However, for non-anatomical resections, RF was generally sufficient to achieve satisfactory haemostasis.

The rate of conversion was analysed in the available data from 14 studies. The rate of conversion to open was outlined in five studies while in 9 studies no conversion to laparotomy was required [18-21,23,24,27-29]. (**Table. 4**) Adhesions were the cause of conversion in Jiao et al. 2008 [17]; Bachellier et al. 2007 [22] converted to open due to the presence of adhesions in 2 cases and the finding of an extra lesion posteriorly located in 1 case. In three patients conversion was necessary due to unmanageable bleeding. Conversion from a laparoscopic procedure to an open hepatic resection was necessary for Hompes et al. 2007 [11] in 2 patients because of uncontrollable intraoperative bleeding from the right hepatic vein (at right hemihepatectomy) with a blood loss of 3000 ml, and from the middle hepatic vein (at segmental hepatectomy S4a) with 2600 ml of bleeding. Akyildiz et al. 2011 [26] reported one conversion for a patient in the bipolar group because of intraoperative bleeding from the liver bed. Finally, Curro et al. 2009 [25] did not specify the reason for conversion in one patient. (**Table. 5**)

We evaluated total operative time (OT) in only 11 studies as this was not reported in 4 studies [20,23-25]. (**Table. 4**) An average time of less than 130 minutes was reported in 6 studies [11,17-19,27,29]. Two studies had a total operative time of less the 4 hours [22,28]. Akyildiz et al. 2011 [26] had reported similar OT with monopolar and bipolar devices (242 min ± 75 and 224 min ±79, respectively). The one case reported by Weber et al 2003 [21] lasted 300 min and a monopolar device was applied for the resection of a large haemangioma. Lastly, the higher OT was reported by Alemi et al. 2011 [30], with a median duration of 434 min (131-830). Operative time did not always correlate with the type of surgery (data not shown).

Further analysis showed that mean transection time was measured in only 7 studies [17,18,21-23,25,26]. Time reported notably varied between series. (**Table. 4**) Nevertheless, a relationship with the type of surgery was not clearly identifiable (data not shown). The bipolar RF-assisted resections were faster than operations when a monopolar device was applied, where longer transection time reached 167 minutes in Bachellier et al 2007 [22] and 240 minutes in Weber et al. 2003 [21].

Data concerning hospital stay, morbidity and, mortality rates were accessible in most of the study. Postoperative bleeding was not reported in any of the studies. The outcomes such as recurrence rate, resection margins and, tumour dissemination were not available for review.

We have studied the length of hospital stay (LOHS) for twelve studies as three studies did not report the length of hospital stay (LOHS) [20,24,26]. The reported LOHS in studies was rather variable. (**Table. 6**) The shorter LOHS was reached by Vavra et al. 2012 [18], who performed 15 cases (7 metastasectomies, 5 segmentectomies, and 3 bisegmentectomies) with a median LOHS of 2.1 days (range 4-7). Gadiyaram et al. 2012 [28] reported for their case a LOHS of 3 days, as well as Zacharoulis et al. 2013 [29] (median 3 days). In 7 studies LOHS ranged between 5 and 7 days [11,17,21-23,27,30], though two of them (Alemi et al. 2011 and Hompes et al. 2007) reported a LOHS as high as 35 and 41, respectively [11,30]. Curro et al. 2009 [25] had a LOHS ranging between 2 and 13 days (for Segment II resection, which was eventually converted to the open approach). Miyazawa et al. 2006 [19] who performed two laparoscopic-assisted tumour resections (in Segment II and in Segment V-VI) experienced a LOHS of 13 and 11 days, respectively. Once more, no evident relation between the type of surgery and length of hospital stay could be noticed in these studies (**Table. 6**).

All studies reported complications, such as bile leak, abscess, necrosis of the resection bed and hepatic failure. (**Table. 6**) Alemi et al. 2011 [30] reported a biloma in one patient. In Hompes et al. 2007 [11] one patient had a biliary leakage with intra-abdominal abscess formation. No necrosis of the resection bed was reported in any of the study (data not shown). Hepatic insufficiency presented in five patients. Two studies (Jiao et al. 2008 and Bachellier et al. 2007) reported one case each of transient liver failure with postoperative ascites in two patients who underwent resection of hepatocellular carcinoma (HCC) in a background of cirrhosis. The patients were successfully treated with supportive care. [17,22] Alemi et al. 2011 reported 2 postoperative liver failure, one was due to portal vein thrombosis and led to patient's death. [30] Ascites were found postoperatively in two cases (Curro et al. 2008 and Alemi et al. 2011) (data not shown in the table). [24,30] General complications such as ileus [30], pulmonary embolism [30], pulmonary infection [11], exacerbation of asthma [17], and wound infection [18] were reported in five studies. (**Table. 7**) Finally, one pneumothorax during surgery for accidental puncture of pleura with RF probe occurred in Bachellier et al. 2007 [22].

The only mortality was reported by Alemi et al. 2011 [30] as postoperative death, which occurred from liver failure as a result of portal vein thrombosis 1 week after resection.

Discussion

Liver resection is the only potentially curative treatment in patients with hepatic tumours. [14] However, hepatic resection remains a major procedure with marked morbidity and mortality, with intraoperative bleeding and postoperative bile leak still being the main problems faced by the surgeon. [13]

Laparoscopic liver resection was introduced to clinical practice several years ago. Since then, it has been proven as a feasible method of treatment for different liver neoplasms. [3] The main advantages of laparoscopic surgery, such as magnified visibility (2.5 times), shortened hospital stay, decreased postoperative pain, reduced peritoneal adhesions, improved cosmetic results, shorter recovery and faster return to normal activity, all apply well to hepatic surgery. [3] However, intraoperative bleeding has remained a cause of concern and the main reason of conversion during laparoscopic liver surgery. [7] Intraoperative haemorrhage is also an important factor for operative morbidity and mortality, especially for cirrhotic patients. [32]

Several advances in laparoscopic instruments and operative technique have been made, and intraoperative blood loss is now lower compared with open hepatectomy. [33] Amongst them, RF has increasingly been used to minimize blood loss during hepatic parenchymal transection and to facilitate tissue-sparing liver resection. [14,34] In spite of these advantages, some authors have reported potential severe complication after RF-assisted liver resection. [5,10,13]

In this review we have compared pooled data from all included studies with the largest single study of laparoscopic hepatectomy using serial applications of the EndoGIA stapler (Covidien), Harmonic scalpel and Enseal device done by Cannon et al. 2011. [35] Nine studies including 66 patients have reported minimal blood loss [17-19,21,23,25,27-29], ranging from less than 50 ml to 100 ml, with the maximum reported median blood loss of 200 ml (Jiao et al. 2008)[17] while Cannon et al 2011 [35] reported median blood loss of 150 ml (minimal – 1,500ml). The blood transfusion was needed in only 2 cases of Alemi et al. 2011[30] compare to 21 times in Cannon et al. 2011[35]. The Vascular control was required in three studies i.e. [11,28,30] while it was required in all resections in this study of Cannon et al. 2011[35]. In pooled data of 176 patients we found two cases of bile leak [11,30] and five of hepatic insufficiency [17,22,24,30]. The purpose of this review was to assess the current scientific literature on laparoscopic RF-assisted liver resection in order to analyse its related complications and assess its safety in laparoscopic liver surgery.

On the one hand, the main limitation is that no randomised controlled trials (RCTs) are available for the laparoscopic approach and that even the bigger series have actually included small numbers of cases. On the other hand, the evidence that laparoscopic liver surgery is a safe and effective approach to the surgical management of liver disease (The Louisville Statement, 2008) together with the conclusions on open RF-assisted liver resections (NICE interventional procedure guidance, 2005) allows to consider RF-assisted liver resection as one method that may be used in laparoscopic liver surgery. [1,2] Reducing blood loss and the need for blood transfusions is a key outcome measure. In the studies we have considered for this review, haemorrhage was minimal, with major blood loss limited to two studies (Hompes et al. 2007 and Alemi et al. 2011) with a minimum requirement of blood transfusions. [11,30] (**Table. 4**) While Hompes et al. 2007 [11] found that the type of surgical procedure was a determinant for the amount of intraoperative blood loss, and that significant bleeding occurred from large hepatic vessels at major resections, definitive conclusion cannot be made because of inhomogeneity of data in the literature. However, major resection was not a common risk factor for intraoperative blood loss amongst other studies.

The type of device may be a factor influencing blood loss during hepatic resection. Monopolar and bipolar devices have been widely employed in the literature. (**Table. 2**) Although there was a probable difference in operative time between the two types of devices (**Table. 4**), with bipolar RF-assisted resection been faster in the coagulation of the liver parenchyma, a difference in the incidence of intraoperative bleeding was not detectable. The two studies that reported the larger blood loss (Hompes et al. 2007 and Alemi et al. 2011) have used a monopolar (Single cool-tip electrode) and a bipolar (InCircle Bipolar RF Ablation) device, respectively. [11,30] Different techniques for vascular control have been described as a way to generally minimize blood loss and increase the effectiveness of RF by preventing heat loss owing to the heat-sink effect. [13,36] However, on the basis of the type of vascular control used, bleeding can still occur from the backflow from the hepatic veins (during Pringle's manoeuvre) and the ischaemic-reperfusion injury to the liver parenchyma can be very dangerous especially in patients with underlying liver disease. [3,10] Vascular control was not necessary in most of the series considered in this review, showing an additional potential advantage of the use of RF for liver resection. (**Table. 4**)

Precoagulation is an important tool to overcome unexpected and uncontrolled bleeding during laparoscopic liver resection, especially in cirrhotic patients. [37] Apart from RF, microwave energy can also be applied in liver surgery. [38-40] Microwave causes polarized water molecules to oscillate, causing friction and coagulative necrosis. Recently, few reports have demonstrated the safety and efficacy of microwave coagulation in laparoscopic surgery, mainly for HCC in cirrhotic patients undergoing minor hepatic resection. [41-45] The effect of microwave is not influenced by the heat-sink effect and can achieve a larger coagulation volume in a shorter time. [46] When comparing ablation performed with RF and microwave, recurrence rates are similar, although microwave may be more effective on larger lesions. [47] There are still concerns about the difficulty in predicting and controlling the effect of microwave energy, about some technological limitations, and larger series are need to confirm microwave safety and feasibility as precoagulation device in open and laparoscopic liver resection, although preliminary results are encouraging. [37,48]

Precoagulation devices are indeed useful in laparoscopic liver resection, but costs represent an issue. Currently, the choice of the parenchymal transection technique depends on surgeon's preference and his familiarity with the instruments available. [37] From one hand, crush-clamp technique is the most cost-effective technique in open liver surgery. [10] However, crush-clamp technique requires Pringle manoeuvre, and once the blood vessels and bile ducts are exposed, they have to be divided by suture, bipolar electrocautery, vessel sealing devices, or vascular clips, and these instruments have also a cost. In laparoscopic surgery, crush-clamp technique is not generally used due to technical difficulties and concerns about possibility of uncontrolled bleeding. One of the issues about costs with many devises is that 2 different instruments are required to perform the resection, one for the parenchymal transection and one to achieve haemostasis. RF combines the two, and laparoscopically only scissors are needed to divide the parenchyma, with rarely any need for clips or staplers. Moreover, both RF and microwave have the advantage to allow ablation of lesions when not resectable or in case of multiple lesions where resection can be combined with ablation. These advantages may overcome the cost related to the instruments in RF assisted laparoscopic liver surgery.

Bleeding is also generally reported as the commonest cause for conversion during laparoscopic liver resection. [7] However, with the use of RF, we found that adhesions were the main reason of conversion to open (**Table. 5**), with most of the procedures being securely conducted on laparoscopy. Bile leak is another major concern in liver surgery.

However, it was seldom encountered in the studies reviewed here, confirming the sealing effect of RF on bile ducts during coagulation of the liver parenchyma. [12]

It has been reported that the coagulation necrosis caused by RF along the plane of transection poses a risk for postoperative infection. [13] However, the incidence of postoperative abscess and necrosis of the resection margins was practically zero in all the series.

Liver failure is the most severe complication after liver surgery and it is the most common cause of postoperative death, particularly in patients with preoperative abnormal liver function. [7] It has been reported that RF-assisted liver resection may cause a sharp increase in transaminase levels after surgery. [13] No data regarding postoperative liver enzymes were reported. Liver-related complications included transient liver failure in 2 cases, ascites in another 2 cases, and only one death related to liver failure as a result of portal vein thrombosis, where the type of resection was not reported. (**Table. 6**) In this context, it is difficult to establish whether liver failure may be related to RF or to other causes. Besides, significant intraoperative bleeding and an extensive use of vessel occlusion techniques may also lead to postoperative hepatic failure. [10] Nevertheless, the advantages of RF-assisted resection in reducing blood loss and the need of vascular control can contribute to a reduction in the risk of postoperative liver failure.

Laparoscopic liver resection is considered a safe and effective procedure for treatment of benign and malignant liver lesions, with similar oncological outcomes for malignant lesions compared to open approach. In the literature, more than 9.000 cases of laparoscopic liver resection have been reported, according to the largest review available published by Ciria et al in 2016. [49] Our review has shown that majority of RF assisted laparoscopic liver resections were performed for malignant lesions (85.8%) and were mainly minor liver resections (i.e. tumourectomy, segmentectomy and bisegmentectomy), and this is similar with the results from Ciria et al [49]. Although it won't be correct to compare our results with their review, blood loss and blood transfusion appeared to be lower in the laparoscopic resections performed with the RF (blood transfusion between 5 and 15% of cases vs. less than 2% in our review). However, RF has been used only in a small minority of cases worldwide. Although RF allows resection without the need for vascular clamping, with minimal blood loss, and it is relatively simple since there is rarely need for clips, stiches or staplers, and parenchymal dissection can be performed with laparoscopic scissors, RF cannot be applied close to the hilum or vena cava, and a necrotic resection margin of 1cm is left on the remnant liver with relatively increased risk of bile leak and abscess formation. [10] However, if applied meticulously and with an excellent knowledge of liver anatomy along with an accurate intraoperative ultrasound, RF can be particularly useful to perform laparoscopic non-anatomical, parenchymal preserving liver resections, with adequate oncological margin on the remaining liver. [41] Moreover, RF can be particularly advantageous in single-incision laparoscopic minor liver resections, where technical difficulties in handling the instruments and in controlling bleeding are major limitations to its wider application in liver surgery. [50]

Conclusion

The present review showed that laparoscopic RF-assisted resection is safe and feasible for different liver diseases resulting in minimal blood loss and few complications. However, RCTs and big series are needed to better understand the potential advantages of the use of RF in laparoscopic hepatic resection in terms of blood loss and morbidity compared with other available methods in laparoscopic liver surgery.

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Professor Habib Nagy is the inventor of the Habib™ 4X

Legends for illustrations

Figure 1: Flow chart of the search strategy and study selection used in this systematic review.

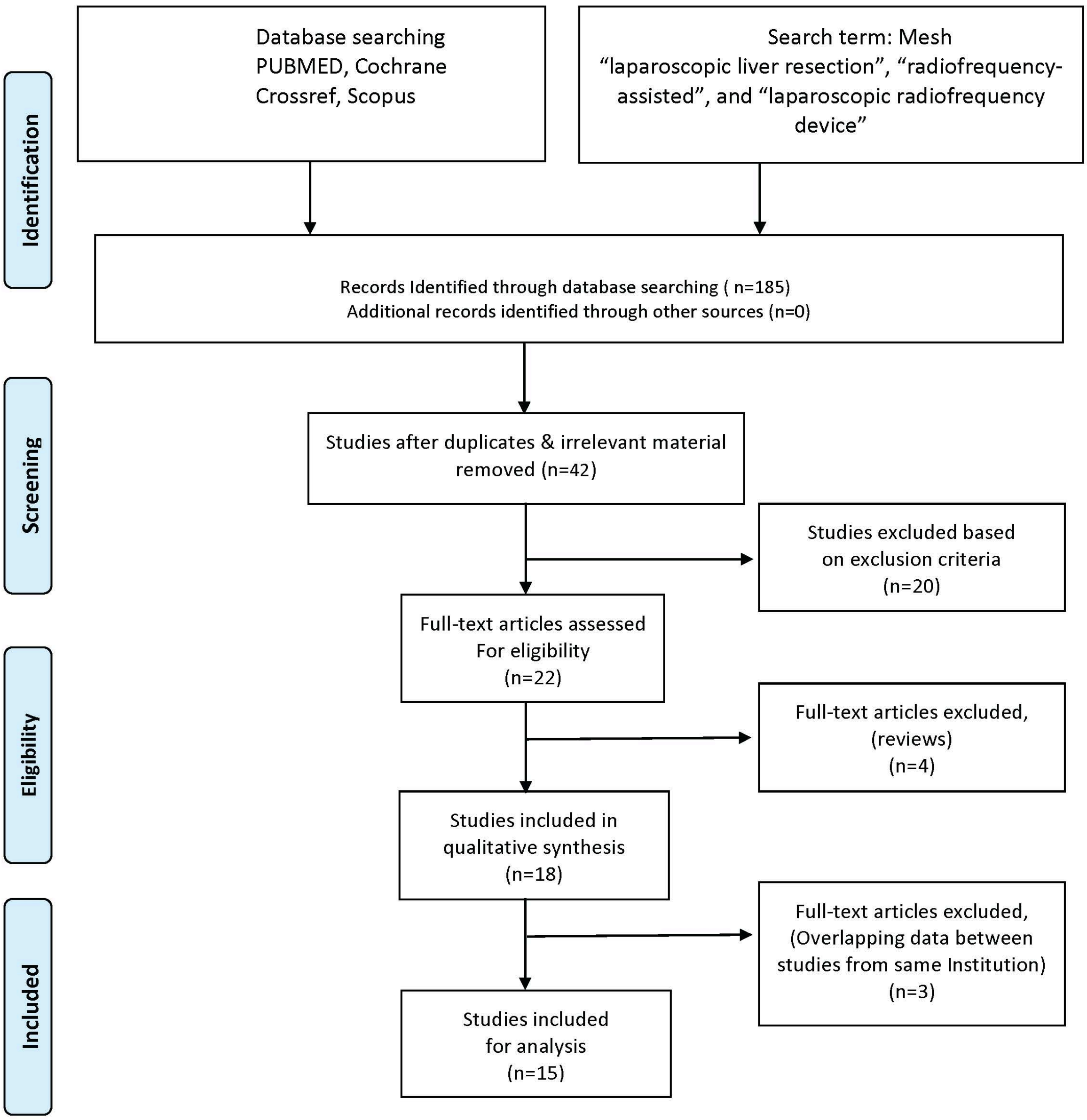

Fig1- **Search strategy and study selection used in this systematic review as per PRISMA protocol**

TABLES

Table 1: Criteria for the inclusion of laparoscopic liver resection studies.

Study design	Defined study population as Prospective, retrospective, case series and case reports
Study group	RF- based Laparoscopic liver resection
Study size	Any
Length of follow-up	Any
Source	Peer-reviewed journals
Language	English
Outcome measure	Patient safety, perioperative outcomes

Table 2: Showing characteristics of included studies

Article	Year	Device (Company)	# of Patients	Presence of Cirrhosis	Hand-assisted
Alemi et at [30]	2011	InCircle™ Bipolar RF system (RFA Medical Inc.)	17	N/A	NO
Weber et al [21]	2003	Cool-Tip Monopolar probe	1	NO	NO
Bachellier et al [22]	2007	Cool-Tip Monopolar probe	18	5/18	NO
Hompes et al [11]	2007	Cool-tip Monopolar electrode	20	1/20	NO
Navarra et al [23]	2008	Cool-Tip Monopolar probe	10	8/10	NO
Miyazawa et al [19]	2006	Cool-tip Monopolar RF system (Radionics, Inc.)	2	2/2	YES
Curro et al [24]	2008	Cool-Tip Monopolar probe	11	11/11	NO
Curro et al [25]	2009	Cool-Tip Monopolar probe	14	8/14	NO
Clancy et al [20]	2005	InLine RF coagulation (ILRFC) Bipolar device (Resect Medical)	2	2/2	YES
Acharya et al [27]	2012	Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics)	1	NO	NO
Gadiyaram et al [28]	2012	Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics)	1	NO	NO
Zacharoulis et al [29]	2013	Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics)	5	2/5	NO
Vavra et al [18]	2012	Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics)	15	N/A	YES
Jiao et al [17]	2008	Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics)	28	9/28	NO
Akyildiz et al [26]	2011	Starburst® XL Monopolar RF catheter (AngioDynamics) (19/31) Laparoscopic Habib 4X®Bipolar RF coagulator (Angiodynamics) (12/31)	31	N/A	N/A

RFA: radiofrequency; N/A: not available

Table 3: Types of liver resection

Article	Year	# of Patients*	# of Tumorectomy	# of Segmentectomy	# of bisegmentectomy	# 3 or more segments resected
Alemi et at [30]	2011	**17**	-	11	6 (multi-segment and hemihepatectomy)	
Weber et al [21]	2003	**1**		*Not mentioned*		
Bachellier et al [22]	2007	**15**	11	2	2	-
Hompes et al [11]	2007	**18**	-	6	9 (left lateral)	3 (1 left and 2 right hemihepatectomies)
Navarra et al [23]	2008	**10**	-	10	-	-
Miyazawa et al [19]	2006	**2**	1 (wedge)	1	-	-
Curro et al [24]	2008	**11**	*Not specified (procedures performed for tumours in left lateral or anterior segments)*			
Curro et al [25]	2009	**13**	-	13	-	-
Clancy et al [20]	2005	**2**	-	-	2 (left lateral)	-
Acharya et al [27]	2012	**1**	-	-	1 (left lateral)	-
Gadiyaram et al [28]	2012	**1**	1 (wedge)	-	-	-
Zacharoulis et al [29]	2013	**5**	-	-	5 (left lateral)	-
Vavra et al [18]	2012	**15**	7	5	3	-
Jiao et al [17]	2008	**24**	12	3	9	-
Akyildiz et al [26]	2011	**30**	19 (wedge and segmental)		12	-

**** Including only cases completed laparoscopically***

Table 4: Showing various operative details included in studies

	Blood loss	# of Transfusions	Vascular control	Conversion	Transection time	Total operative time
Alemi et at [30]	300 ml (20–3000)	2	YES	N/A	N/A	434 min (131-830)
Weber et al [21]	75 ml	0	NO	NO	240 min	300 min
Bachellier et al [22]	121 ml ± 68	0	NO	3	167 min ± 45	213 min ± 59
Hompes et al [11]	200 ml (5-3000)	N/A	YES	2	N/A	120min (50-310)
Navarra et al [23]	32.5 ml ± 17.2	0	NO	NO	51.8 min ± 9.2 (40-60 min)	N/A
Miyazawa et al [19]	50 ml & 65 ml	0	NO	NO	N/A	130 and 115 min
Curro et al [24]	N/A	N/A	NO	NO	N/A	N/A
Curro et al [25]	10-100 ml	0	NO	1	30-120 min	N/A
Clancy et al [20]	N/A	0	NO	NO	N/A	N/A
Acharya et al [27]	<50 ml	0	NO	NO	N/A	90 min
Gadiyaram et al [28]	50 cc	0	YES	NO	N/A	220 min
Zacharoulis et al [29]	minimal	0	NO	NO	N/A	75 min (60-90)
Vavra et al [18]	74 ml (25-115)	0	NO	NO	33 min (21-75)	92 min (45-130)
Jiao et al [17]	48 ml ± 54 (10-200)	0	NO	4	60 min ± 23	94 min ± 37
Akyildiz et al [26]	Bipolar: 89 cc ± 77 Monopolar: 224 cc ± 79	0	NO	1	Bipolar: 22.5 min ± 7.2 Monopolar: 33.6 min ± 15.9	Bipolar: 242 min ± 75 Monopolar: 224 min ±79

N/A: not available

Table 5: Showing causes of conversion in included studies

Article	Type of surgery	Conversion	Causes
Jiao et al 2008 [17]	Tumorectomy Resection	4	Adhesions
Bachellier et al 2007 [22]	Tumorectomy Resection	3	2 adhesions 1 extra lesion (posteriorly)
Hompes et al 2007 [11]	Hemihepatectomy Resection S4ga	2	Bleeding (3000 and 2006 ml)
Akyildiz et al 2011 [26]	Resection	1	Bleeding
Curro et al 2009 [25]	Resection	1	Not specified

Table 6: Showing complications and outcomes in various included studies

	Hospital Stay	Bile leak	Abscess	Liver failure	Other Complications	Mortality
Alemi et at [30]	7 days (3-35)	1	NO	2	YES	1
Weber et al [21]	6 days	NO	NO	NO	NO	NO
Bachellier et al [22]	6 days ± 1.5	NO	NO	1	YES	NO
Hompes et al [11]	7 days (5-41)	1	1	NO	YES	NO
Navarra et al [23]	5.7 day ± 2.6 (<10)	NO	NO	NO	NO	NO
Miyazawa et al [19]	13 and 11 days	NO	NO	NO	NO	NO
Curro et al [24]	N/A	NO	NO	1	NO	NO
Curro et al [25]	2-13 days	NO	NO	NO	NO	NO
Clancy et al [20]	N/A	NO	NO	NO	NO	NO
Acharya et al [27]	5 days	NO	NO	NO	NO	NO
Gadiyaram et al [28]	3 days	NO	NO	NO	NO	NO
Zacharoulis et al [29]	3 days (2-5)	NO	NO	NO	NO	NO
Vavra et al [18]	2.1 days (4-7)	NO	NO	NO	YES	NO
Jiao et al [17]	5.6 days ± 2	NO	NO	1	YES	NO
Akyildiz et al [26]	N/A	NO	NO	NO	NO	NO

N/A: not available

Table 7: Showing occurrence of other complications in included studies

Article	Complications
Alemi et at 2011 [30]	1 ileus, 2 pulmonary embolism
Jiao et al 2008 [17]	1 exacerbation of asthma
Bachellier et al 2007 [22]	1 pneumothorax
Hompes et al 2007 [11]	1 pulmonary infection
Vavra et al 2012 [18]	1 wound infection

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