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The contracting role of graduated compression stockings in prevention of peri-operative venous thromboembolism

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There can be no doubt that the prevention of venous thromboembolism (VTE) is a healthcare need and priority [1]. The issue remains in sharp focus in surgery with the implementation of VTE risk assessment, and the use of mechanical and pharmacological thromboprophylaxis. These measures have been further enhanced through education, dissemination and have been reinforced through key clinical guidelines [2, 3] and incentivisation [4].

There has been a 15% reduction in hospital-associated (within 90 days of admission) VTE deaths in the UK between 2010 and 2017 [5], with concurrent falls in pulmonary embolism-related mortality amongst European countries [6]. This is likely to be more impressive when considering that improved awareness and imaging are likely to have increased the diagnosis of VTE, resulting in a further reduction in case fatality rate. The factors responsible for this reduction are likely to be multifactorial. The can be attributed to a long list of varied and important factors, including (but not limited to) prehabilitation, systematic VTE risk assessment (including computer-aided [7]), enhanced recovery with early mobilisation, patient hydration, advanced minimally invasive surgical techniques resulting in a reduction in the systemic inflammatory response (both magnitude and duration), and of course thromboprophylaxis.

Given the number of relevant factors at play, it is challenging to know which are dominant and this also applies when considering mechanical and pharmacological thromboprophylaxis. Much of the evidence underpinning peri-operative thromboprophylaxis, is dated and may not reflect modern surgical practice. Furthermore, these studies were for the most part using mechanical thromboprophylaxis alone or pharmacological thromboprophylaxis alone, with little

evidence relating to the use of both mechanical and pharmacological strategies [8]. Many were funded by stocking manufacturers [9]. It was for these and a number of other reasons that doubt was cast over the evidence that formed the basis of recommendations for mechanical thromboprophylaxis, particularly the use of graduated compression stockings (GCS) [9, 10]. What should be considered is whether, in individuals receiving pharmacological thromboprophylaxis, does GCS *further* reduce the VTE risk.

The first CLOTS trial randomised 2518 patients admitted to hospital following an acute stroke to receive either routine care including thigh-length GCS, or routine care with the avoidance of GCS [11]. Not only was there no significant reduction in symptomatic or asymptomatic deep vein thrombosis (DVT), complications of skin breaks, ulcers, blisters and skin necrosis were significantly more common in the GCS arm of the trial [12]. A subsequent RCT was performed amongst individuals in critical care who were receiving pharmacological thromboprophylaxis to receive either additional intermittent pneumatic compression (n=991) or no additional intermittent pneumatic compression (n=1012) [12]. In this trial, the addition of intermittent pneumatic compression did not result in a lower incidence of proximal lower-limb DVT than pharmacological thromboprophylaxis alone [12]. These studies generated further uncertainty around the role of mechanical thromboprophylaxis in medical inpatient and critical care settings, respectively.

What does this mean for the surgical patient? In 2007, an RCT of individuals undergoing hip surgery was published [13]. This compared post-operative VTE or

sudden death between those randomised to the combination of fondaparinux and compression stockings (n=395, 19 DVT events) or fondaparinux alone (n=400, 22 DVT events), and concluded “the addition of graduated compression stockings to fondaparinux appears to offer no additional benefit over the use of fondaparinux alone” [13].

This trial set the scene for a large UK National Institute for Health Research (NIHR)-funded Graduated compression stockings as an Adjunct to Pharmacoprophylaxis in Surgery (GAPS) Trial. GAPS aimed to elucidate the role of GCS in individuals undergoing elective surgery who were risk assessed as being at moderate or high risk for VTE and who were receiving prophylactic dose low molecular weight heparin (LMWH) [14]. The primary outcome, imaging-confirmed lower limb DVT with or without symptoms, or pulmonary embolism with symptoms within 90 days of surgery occurred in 16 of 937 (1.7%) patients in the LMWH alone group compared with 13 of 921 (1.4%) in the LMWH and GCS group. LMWH alone was confirmed to be statistically non-inferior (non-inferiority margin of 3.5% risk difference) to the combination of LMWH and GCS in this surgical patient group [15, 16]. Considering this

subgroup of elective surgical patients, removing the cost of purchasing and of the nursing time required to apply GCS, it has been conservatively estimated that more than £60 million per annum could be liberated from NHS budgets in England alone on a recurring basis [14]. This estimate did not consider the costs of treating the complications related to GCS such as those that were reported by the CLOTS investigators [11]. There is an appetite for implementation of the results of the GAPS trial into widespread clinical practice [17].

The RCT by Cohen et al [13] and GAPS [15, 16] support the diminishing role of GCS in the prevention of peri-operative VTE. GAPS, however, did not include the full spectrum of peri-operative patients, for example those having non-elective surgery, those in whom extended pharmacological thromboprophylaxis is indicated beyond the inpatient stay (including orthopaedic and abdomino-pelvic surgery), and individuals assessed as being at low risk for VTE and hence will not be prescribed pharmacological thromboprophylaxis. For the latter two surgical populations, systematic reviews have been completed to explore the role of GCS. In both cases, the evidence has been reported to be lacking [18, 19]. The recently funded NIHR-

funded Prevention of vEnous Thromboembolism in low-risk Surgical patients (PETS) RCT aims to cluster randomise 21,472 participants undergoing day case and short stay elective surgical procedures who have been risk assessed as being low risk for VTE to receive GCS or no thromboprophylaxis [20].

The American Public Health Association has stated that the "disconnect between evidence and execution as it relates to DVT prevention amounts to a public health crisis" [21]. It can be argued that the same consideration should be given to implementation and evidence-based practices in allowing limited healthcare resources to be allocated in a way that is maximally impactful to positive patient outcomes.

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Declaration of interests

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