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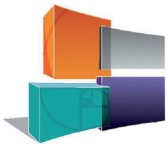

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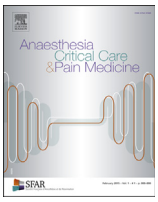

Editorial

Vena Cava filters in severely-injured patients: One size does not fit all

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Venous thromboembolism (VTE) is common following trauma. In the absence of chemoprophylaxis, proximal deep vein thrombosis (DVT) in the limbs and subsequent pulmonary embolism (PE) may occur as frequently as 18% and 11%, respectively [1]. Symptomatic PE following trauma is reported to occur in more than 30% of cases, within the first 96 hours of injury [2]. A concerning observation is that fatal PE accounts for about 12% of all trauma-related deaths, with half of these considered preventable [3].

Early anticoagulant prophylaxis remains the gold standard in minimising the risk of subsequent VTE post trauma. The challenge is many clinicians perceive the risk of bleeding to be greater than that of the risk of VTE [4]. This concern for bleeding has resulted in delays or even omission of VTE prophylaxis in a significant proportion of trauma patients placing, them at increased risk of both VTE and mortality [5–7].

Mechanical thromboprophylaxis, including inferior vena caval (IVC) filters or intermittent pneumatic compression devices have the advantage of not inducing bleeding, and are used to reduce VTE for critically injured patients [8,9]. Intermittent pneumatic compression devices recently failed, in a large randomised controlled trial (RCT), to demonstrate additional risk reduction of either DVT or PE, when combined with chemoprophylaxis [10]. Mechanical VTE prophylaxis often remains the only option available for patients who have active bleeding or are considered at high-risk of bleeding. Retrievable IVC filters are now widely employed in many trauma centres as the primary prophylactic strategy to prevent PE, when chemoprophylaxis is considered contraindicated [9,11]. This is arguably the most contentious application of IVC filters, as there is no high-quality data to support its efficacy/safety in this setting. Furthermore, IVC filters are (a) expensive, (b) invasive with potential serious complications, and (c) often not retrieved [12]. Therefore, it is paramount that high quality evidence is available to inform about clinicians about the efficacy of using prophylactic IVC filters as a primary means of PE prevention in major trauma patients.

The da Vinci multicentre RCT was conducted to address this perplexing issue, by assessing if placement of a retrievable IVC filter in trauma patients with a contraindication to standard DVT chemoprophylaxis within 72 hours of admission reduced mortality or incidence of symptomatic PE [13,14]. Two hundred and forty major trauma patients (Injury Severity Score (ISS) $>$ 15) and a contraindication to anticoagulant prophylaxis within 72 hours of admission to one of the three major trauma centres in Australia, were included in the study. This landmark trial showed that early prophylactic placement of an IVC filter in these patients did not reduce the primary composite outcome of 90-day mortality or symptomatic PE ($P = 0.98$). As an a priori subgroup analysis of those patients who survived for more than 7 days after major trauma and remained untreated with anticoagulant prophylaxis ($n = 80$), early IVC filter placement significantly reduced symptomatic PE (0% in the filter group vs. 14.7% in the control group, including one fatal PE confirmed by post-mortem examination; $P = 0.01$). Importantly IVC filters did not increase the incidence of lower limb DVT compared to those patients without an IVC filter (11.4% vs. 10.1% respectively; $P = 0.84$). IVC filter thrombus was detected in six patients (4.9%) at the time of filter removal. It is interesting to note that the number of patients with thrombus entrapped in the IVC filters (in the filter group) was identical to the number of patients with symptomatic PE in the control group. It is tempting to speculate that filters were achieving precisely the desired effect: preventing embolisation of lower limb thrombi to the pulmonary circulation.

Because the da Vinci trial is not a mega-patient RCT, we certainly cannot exclude a modest mortality benefit of IVC filter placement beyond seven days of admission. This trial remains the best evidence in addressing the contentious issue of using IVC filters as a primary means to prevent VTE in major trauma patients who have a contraindication to anticoagulant prophylaxis. As with all RCTs there are strengths and obvious limitations to be acknowledged with any study (Table 1). This trial has at least two important clinical implications for clinicians and researchers involved in trauma care. First, this trial has clearly identified patients who will likely benefit from using an IVC filter prophylactically, as an alternative when anticoagulant prophylaxis is contraindicated. Furthermore, this trial has convincingly demonstrated that there is no urgency to place an IVC filter,

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Table 1
The strengths and limitations of the da Vinci trial.

Strengths	Limitations
Using enrichment techniques to increase the chance of confirming the benefits of an inferior vena cava filter	Underpowered to exclude a small to moderate difference in mortality
Practical enrichment: excluding patients who had severe injury that was considered non-survivable to improve the rate of completion of the study follow up of the enrolled patients until day-90	
Prognostic enrichment: recruiting patients with an Injury Severity Score (ISS) > 15 and a high Trauma Embolic Scoring System (TESS) who were at highest-risk of developing venous thromboembolism	
Diagnostic enrichment: using a proactive approach and objective criteria to perform CT pulmonary angiography to diagnose symptomatic segmental pulmonary embolism (and at the same time avoiding diagnosing sub-segmental pulmonary embolism and exposing young trauma patients to unnecessary radiation) and post-mortem examination if deemed necessary by the coroners	
Minimal cross-over (or contamination) between the two treatment groups	Survivorship bias may affect the validity of the positive secondary outcome on risk of symptomatic pulmonary embolism for those who survived longer than 7 days after injury but could not receive anticoagulant within the first 7 days. Patients who survived beyond 7 days after injury could be less sick with a lower risk of venous thromboembolism
Adequate allocation concealment, independent data management and statistical analyses	Blinding was not used (for safety reasons). The presence of filters may have influenced decisions to initiate anticoagulation, introducing potential bias by having more patients with a higher bleeding risk in the control group (even though ISS and TESS were similar between the two treatment groups)
Minimal lost to follow-up until day-90	Filters were inserted and removed promptly, and anticoagulation were initiated as soon as possible; all these processes may not be possible in a standard clinical environment outside a clinical trial setting

unless the contraindication to anticoagulant chemoprophylaxis will likely be prolonged beyond 7 days following injury. Patients falling into this subgroup were principally neurotrauma patients with multiple cerebral contusions, who often require repeated surgical interventions within the first 7 days of injury. This is certainly a much smaller subgroup of major trauma patients than clinicians might previously have perceived as requiring an IVC filter for primary VTE prophylaxis [9,11] The use of IVC filters in a more select subgroup of major trauma patients will reduce unnecessary potential complications, the associated trauma care financial burden and medical litigation [15].

Secondly, this trial firmly reinforces the importance of early initiation of anticoagulant prophylaxis for major trauma patients. Ideally we should ultimately be able to reliably identify patients who are more prone to develop thrombosis rather than bleeding after major trauma. It may be with the assistance of point of care testing or formal coagulation parameter studies that this holy grail of thrombosis prediction is achieved [16]. If this strategy is realised and anticoagulant prophylaxis can be safely initiated as soon as possible for many trauma patients, we will anticipate further reduction in prophylactic IVC filter usage in major trauma. Unavoidably, there will always be major trauma patients, in particular those with severe multiple cerebral or spinal contusions, who will require an IVC filter as a temporising measure until anticoagulant prophylaxis can be safely established without interruptions. The newly developed, absorbable IVC filters, which are absorbed over a 32-week period, have demonstrated an ability to prevent PE for at least 5 weeks after placement in a swine model [17]. For that small group of trauma patients with contraindications to early anticoagulant chemoprophylaxis (within 7 days of their injury), absorbable filters may well represent the IVC filter's new dawn.

Disclosure of interest

Dr KM Ho served on the global DVT advisory board of Medtronic in 2015-2016 and has been an advisor to Cardinal Health since 2017 on issues related use of pneumatic compression devices.

Dr Holley and Lipman declare that they have no competing interest.

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