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Commentary

Prediction of venous thromboembolism in patients with lower-limb immobilization

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Lower-limb injuries requiring immobilization by brace or casting are highly prevalent worldwide and are associated with an increased risk of deep venous thrombosis (DVT) and pulmonary embolism (PE) [1]. The use of thromboprophylaxis in this setting is highly debated and current practices as well as clinical guidelines differ significantly ranging from no indication to thromboprophylaxis for most patients [2-4]. Such heterogeneity may derive from the limited evidence available and the uncertain benefits of thromboprophylaxis in reducing clinically relevant outcomes.

The incidence of thrombotic complications in patients with lower-limb immobilization has varied broadly across studies depending on design, quality, and whether outcomes included asymptomatic DVT or only symptomatic events [5]. In patients who do not receive prophylaxis, the incidence of DVT varied up to 10-fold, from 4·3 to 40%, with lower rates of proximal DVT (0·9 to 6·4%), and relatively rare cases of PE. The corresponding figures in patients receiving low molecular weight heparin prophylaxis (LMWH) ranged between 0 and 37% for any DVT, and from 0 to 4% for proximal DVT.

LMWH is associated with lower incidence of DVT, but no clear difference for PE [5]. The absolute reduction observed with LMWH differs according to the outcome considered: the number of patients to be treated with LMWH to prevent one event is 12 for any DVT, 50 for proximal DVT, 83 for symptomatic venous thromboembolism (VTE), and 250 for PE.

Given the large variability in thrombotic risk and benefits expected from LMWH, development of risk-stratification models may help tailoring the use of thromboprophylaxis by identifying high-risk patients who could benefit from prophylaxis as well as low-risk patients in whom prophylaxis could be withheld to limit overexposure and reduce the associated risk of bleeding. A model with high sensitivity would reduce the chances of missing VTE, but may increase patient burden related to overtreatment due to lower specificity.

Several stratification tools were proposed, although none gained wide acceptance, which may be related to lack of proper validation and complexity of calculation [6-8].

In an attempt to overcome these limitations, Nemeth and colleagues developed and validated the TRIP(cast) score using 14 readily available variables related to trauma severity, degree of immobilization, and patients' characteristics [9]. The authors developed a mobile phone application that may simplify calculation and uptake of the score in clinical practice. At the cut-off proposed by the authors, sensitivity was 76·1% implying that about 24% of patients who develop VTE may be missed by the score resulting in significant under-treatment. Specificity was 51% meaning that 49% of patients who will not develop VTE would be erroneously classified as high risk and receive unnecessary anticoagulation. The TRIP(cast) score showed a negative predictive value of 99·2%, which suggests that the model may be suitable to safely identify patients who may be withheld from treatment. According to the TRIP (cast) score, 50·7% of patients were at low risk and symptomatic VTE occurred in only 0·8% of them. In those at high risk who represented 49% of the total, symptomatic VTE incidence was 2·5%. Of note, LMWH did not reduce VTE in this latter group compared with no treatment. Although longer duration or higher doses of prophylaxis may achieve greater reductions of VTE, the efficacy and safety of this approach is unclear. While the incidence of bleeding associated with standard thromboprophylaxis is low in a relatively young population with lower-limb immobilization, risk may increase with higher intensity of treatment, especially in older and unselected patients, outweighing benefits.

In other clinical settings, the addition of biomarkers improved the performance of prediction models. In patients hospitalized for acute medical illnesses, for instance, circulating markers such as D-dimer showed promise for VTE prediction [10]. Similarly, biomarkers have proven useful to predict the risk of thromboembolic complications in ambulatory patients with cancer. However, the use of biomarkers adds complexity to the calculation of the score and comes with higher costs.

While awaiting validation of available scores, the decision to use thromboprophylaxis in patients with lower-limb immobilization needs to be carefully evaluated case-by-case and consider patient

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preferences, effects on quality of life, and costs. The relatively low incidence of symptomatic VTE and the questionable efficacy of LMWH suggest that withholding thromboprophylaxis and clinical monitoring may be the preferable approach for most patients. Before the TRIP(cast) score can be implemented in clinical practice, it will require evaluation in randomized studies which assign patients with lower-limb immobilization classified as at high risk according to the score to receive or not thromboprophylaxis.

Declaration of Competing interest

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