Editorial Commentary

Intermittent pneumatic compression plus pharmacological thromboprophylaxis to prevent deep vein thrombosis

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Provenance: This is an invited article commissioned by the Section Editor Xue-Zhong Xing [National Cancer Center (NCC)/Cancer Hospital, Chinese Academy of Medical Sciences (CAMS) and Peking Union Medical College (PUMC), Beijing, China].

Comment on: Arabi YM, Al-Hameed F, Burns KEA, *et al.* Adjunctive Intermittent Pneumatic Compression for Venous Thromboprophylaxis. N Engl J Med 2019;380:1305-15.

Submitted May 01, 2019. Accepted for publication May 08, 2019.
doi: 10.21037/jtd.2019.05.38
View this article at: http://dx.doi.org/10.21037/jtd.2019.05.38

Venous thromboembolism (VTE) is a disease that comprises pulmonary embolism (PE) and deep vein thrombosis (DVT), being a preventable cause of mortality and morbidity (1). Pharmacologic thromboprophylaxis with low molecular weight heparin (LMWH) or unfractionated heparin (UFH), in trials, have shown a reduction of the incidence of DVT nearly 50% (2). Due to evaluation of bleeding, many physicians perceive that the harm of thromboprophylaxis is higher than VTE risk, and for that reason thromboprophylaxis is underused (3,4). Intermittent pneumatic compression devices (IPCD) sporadically apply external pressure on vasculature and calf muscles. IPCD are recommended in patients in whom pharmacologic thromboprophylaxis is contraindicated (5,6).

In 2013, Ho *et al.* published a stratified meta-analysis that assessed the effect if IPCD on VTE risk, excluding trials that used IPCD less than 24 hours or trials that compared different types of IPCD (7). In addition, this stratified meta-analysis had the hypothesis that IPCD was as affective as pharmacological thromboprophylaxis, and additional IPCD to pharmacological thromboprophylaxis could improve its effectiveness reducing VTE. This work included more than 16,000 patients from 70 trials. IPCD prophylaxis *vs.* no IPC was more effective in reducing DVT [7.3% *vs.* 16.7%; 95% confidence interval (CI): 7.9–10.9%; relative risk (RR): 0.43; 95% CI: 0.36–0.52; P<0.01] and PE (1.2% *vs.* 2.8%; 95% CI: 0.9–2.3%; RR: 0.48; 95% CI: 0.33–0.69; P<0.01). IPC was as effective as pharmacological thromboprophylaxis but with lower risk of bleeding (RR: 0.41; 95% CI: 0.25–0.65; P<0.01). Moreover, IPCD plus pharmacological thromboprophylaxis *vs.* IPCD alone reduced the risk of DVT (RR: 0.54; 95% CI: 0.32–0.91; P=0.02). Results of this study contrast with another meta-analysis published in 2016 by Park *et al.* (8). This meta-analysis of randomized controlled trials (RCT) compared overall incidence of DVT using pharmacological (UFH or LMWH) and IPCD, in critical ill patients. This work included more than 8,000 patients from 12 RCT, and the incidence of DVT was lower in patients with UFH [odds ratio (OR), 0.45; 95% credible interval (CrI), 0.22–0.83] or LMWH (OR, 0.38; 95% CrI, 0.18–0.72) *vs.* control group. However, there were no differences between IPCD *vs.* control group (OR, 0.50; 95% CrI, 0.20–1.23). On the other hand, the risk of major bleeding was similar between all treatment groups and also in patients with a high risk of bleeding.

The addition of IPCD to pharmacologic thromboprophylaxis to reduce the risk of VTE is uncertain, due to indirect evidences and controversial results (7,8). In addition, IPCD are easy to use and non-invasive, but imply more cost and may be associated with reduced mobility, skin injury and

discomfort. For that reason, PREVENT (The Pneumatic Compression for Preventing Venous Thromboembolism trial) trial was designed (9,10). This was an investigator-initiated, international, pragmatic, randomized, multicenter controlled trial that evaluated, in critical ill patients, whether IPCD in patients that received pharmacologic thromboprophylaxis (UHF or LMWH) had lower incidence of proximal lower-limb DVT than pharmacologic thromboprophylaxis alone. Ultrasonography of proximal venous of both lower limbs was preformed within 48 hours after randomization and then twice weekly (and on clinical suspicion of DVT) until ICU discharge, death, attainment of full mobility, or trial day 28, whichever occurred first. The primary outcome was incident DVT, although DVT detected on the first 3 days of the trial were considered as prevalent and were not included in the primary outcome analysis. After evaluation of 16,053 patients, 2,003 patients were randomized (991 to IPCD and 1,012 to control group). In the arm of IPCD, median time per day of IPCD was 22 hours (inter quartile range, 21–23 hours). In this trial IPCD had no effect on the incidence of proximal DVT in critically ill patients who were receiving pharmacologic thromboprophylaxis, with an incident proximal DVT of 3.9% in IPCD arm *vs.* 4.2% in control group (RR: 0.93; 95% CI: 0.60–1.44; P=0.74). This trial had several limitations. The main limitation was that the incidence of the DVT in the control group was lower than expected. Second, along the manuscript authors affirm that in 98% of patients at least one ultrasonography was done, but the key point will be to know in how many patients ultrasonography was not done despite having required. And another point to comment is about that devices IPC applied were different, although in almost 80% knee-length sleeves was used.

For the moment the indication of intermittent pneumatic compression will be relegated to those situations in which pharmacological prophylaxis is contraindicated

Acknowledgments

None.

Footnote

Conflicts of Interest: Dr. Jara-Palomares reports speaker bureau from Bayer Hispania, Actelion, Rovi, PFIZER, Menarini, and from Leo-Pharma, outside the submitted work; Research funding Leo-Pharma. Dr. Elias-Hernandez reports Honoraria for lectures: MSD; Honoraria for advisory boards activities: Bayer Heathcare, Sanofi; Fees from Bayer Healthcare, GSK, Actelion. Dr. Otero-Candelera: Honoraria for lectures Actelion, Leo-Pharma, Bayer Healthcare, MSD, Sanofi Honoraria for advisory board activities Actelion, Bayer Heathcare, MSD, Sanofi Research funding Bayer Heathcare, Leo-Pharma; Fees: Actelion, Bayer Heathcare, MSD, Leo Pharma. The other authors have no conflicts of interest to declare.

References

1. Office of the Surgeon General (US); National Heart, Lung, and Blood Institute (US). The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism. Rockville (MD): Office of the Surgeon General (US); 2008. Available online: https://www.ncbi.nlm.nih.gov/books/NBK44178/. Accessed May 20, 2019.
2. Alhazzani W, Lim W, Jaeschke RZ, et al. Heparin thromboprophylaxis in medical-surgical critically ill patients: a systematic review and meta-analysis of randomized trials. Crit Care Med 2013;41:2088-98.
3. Ginzburg E, Dujardin F. Physicians' perceptions of the definition of major bleeding in major orthopedic surgery: results of an international survey. J Thromb Thrombolysis 2011;31:188-95.
4. Eikelboom JW, Quinlan DJ, O'Donnell M. Major bleeding, mortality, and efficacy of fondaparinux in venous thromboembolism prevention trials. Circulation 2009;120:2006-11.
5. Qaseem A, Chou R, Humphrey LL, et al. Venous thromboembolism prophylaxis in hospitalized patients: a clinical practice guideline from the American College of Physicians. Ann Intern Med 2011;155:625-32.
6. Kahn SR, Lim W, Dunn AS, et al. Prevention of VTE in nonsurgical patients: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2012;141:e195S-e226S.
7. Ho KM, Tan JA. Stratified meta-analysis of intermittent pneumatic compression of the lower limbs to prevent venous thromboembolism in hospitalized patients. Circulation 2013;128:1003-20.
8. Park J, Lee JM, Lee JS, et al. Pharmacological and Mechanical Thromboprophylaxis in Critically Ill Patients: a Network Meta-Analysis of 12 Trials. J Korean Med Sci

2016;31:1828-37.
9. Arabi Y, Al-Hameed F, Burns KEA, et al. Statistical analysis plan for the Pneumatic CompREssion for PreVENting Venous Thromboembolism (PREVENT) trial: a study protocol for a randomized controlled trial. Trials 2018;19:182.
10. Arabi YM, Al-Hameed F, Burns KEA, et al. Adjunctive Intermittent Pneumatic Compression for Venous Thromboprophylaxis. N Engl J Med 2019;380:1305-15.

Cite this article as: Jara-Palomares L, Marin-Romero S, Asensio-Cruz MI, Elias-Hernandez T, Otero-Candelera R. Intermittent pneumatic compression plus pharmacological thromboprophylaxis to prevent deep vein thrombosis. J Thorac Dis 2019;11(5):1731-1733. doi: 10.21037/jtd.2019.05.38

