Direct oral anticoagulation and low molecular weight heparin for thromboprophylaxis in patients having non-cardiac surgery: advantages and disadvantages

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ABSTRACT

To compare the advantages and risks of direct oral anticoagulants against low molecular weight heparin for thromboprophylaxis in individuals having non-cardiac surgery. Randomized controlled trials comparing low molecular weight heparin (prophylactic (low) or greater dose) with direct oral anticoagulants or no active therapy in adults having non-cardiac surgery were chosen. Symptomatic venous thromboembolism, symptomatic pulmonary embolism, and severe hemorrhage were the main outcomes. For network meta-analyses, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) criteria were utilized. When compared to no active treatment, direct oral anticoagulants and low molecular weight heparin reduced venous thromboembolism but probably increased severe hemorrhage to a similar level. Direct oral anticoagulants are more likely than prophylactic low molecular weight heparin to prevent symptomatic venous thromboembolism. .

Key Words: *Cardiac surgery; Anticoagulant; Heparin; Throboprophylaxis*

INTRODUCTION

More than 200 million persons worldwide get significant non-cardiac surgery each year. 1 Surgery raises the risk of deep vein thrombosis and pulmonary embolism, as well as venous thromboembolism. 2 Antithrombotic medications lessen the risk of venous thromboembolism after surgery, but they also raise the risk of bleeding [1]. 345 Recommending a medicine for thromboprophylaxis should be based on the projected net effect based on the risk of venous thromboembolism and hemorrhage. Patients undergoing orthopedic and non-orthopedic surgery have separate recommendations in existing evidence-based guidelines. Elective major orthopedic surgery (e.g., total joint arthroplasty) has been linked to a 5-percentage-point increase in the risk of symptomatic venous thromboembolism (deep vein thrombosis, pulmonary embolism, or both) in the first 35 days after surgery [2].

Given the severity of the risk, researchers conducted numerous randomized controlled studies in this surgical population to compare different active medicines for thromboprophylaxis to each other and to no active treatment. This body of evidence has led guideline panels to either recommend or dismiss pharmacological treatment as a prophylaxis for total joint arthroplasty in patients who do not have a high risk of bleeding [3]. Other types of non-cardiac surgery have a substantially higher risk of venous thromboembolism. There is less evidence from randomized controlled studies on pharmacological treatment for thromboprophylaxis in non-cardiac, non-orthopedics procedures. As a result, current thromboprophylaxis guidelines for non-cardiac, non-orthopedic procedures emphasize the estimated risk of venous thromboembolism based on the individual surgery and circumstances connected to the surgery more typically include less forceful or conditional suggestions for the patient (e.g., malignancy vs. non-malignancy as the reason for surgery) [4].

The optimal choice of thromboprophylaxis medication for orthopedic and other non-cardiac operations is yet unknown. LMWH and direct oral anticoagulants are among the most investigated drugs in orthopedics surgery [5]. Most guidelines have recommended direct oral anticoagulants as an alternative to LMWH since they were first introduced to the market. Direct oral anticoagulants were recently recommended over LMWH for thromboprophylaxis by the American Society of Hematology, based on direct comparative evidence on efficacy and safety, as well as cost effectiveness, equity, acceptance, and feasibility. The data on impacts, on the other hand, was given a moderate level of assurance due to the imprecision of the estimates. Because of the paucity of randomized controlled trials for non-orthopedics procedures, current guidelines do not recommend direct oral anticoagulants as a thromboprophylaxis alternative and LMWH is routinely used by clinicians in practice. In fact, most patients would select an oral prophylactic treatment over a parenteral agent, especially if blood testing for monitoring is not required; when patients choose a parenteral agent over an oral medication, it is usually due to a perceived greater efficacy or faster effect [6]. We conducted a comprehensive review and network meta-analysis of existing randomized controlled trials comparing LMWH, direct oral anticoagulants, and no active treatment for thromboprophylaxis in patients undergoing non-cardiac surgery based on this baseline evidence.

Randomized controlled trials including patients aged 18 years or older who were undergoing major non-cardiac surgery, such as major general surgery, urological and gynecological surgery, orthopedics surgery, and thoracic surgery, using open, laparoscopic, or robotic techniques, were eligible. Only randomized controlled trials were included because they are the most appropriate design for an intervention kind of research issue, and we expected to locate studies that used this design to answer our research question. We had already ruled out studies in vascular surgery, neurology, and trauma surgery (including fracture repair) [7]. Because of the nature of these surgeries (e.g., surgery involving the circulatory system is frequently associated with antithrombotic treatment for other reasons, or with abnormal bleeding), we believe that evaluating thromboprophylaxis in these surgeries requires special efficacy and safety considerations activation and operation of the coagulopathy system (for example, in trauma), or the necessity to examine certain relevant outcomes (e.g., intracranial bleeding).

DISCUSSION

Symptomatic venous thromboembolism happened in 235 patients (0.78 percent) in 25 trials involving 30 230 patients; symptomatic pulmonary embolism occurred in 100 patients (0.25 percent) in 61 studies involving 40 588 patients; symptomatic proximal deep vein thrombosis occurred in 42 patients (0.95 percent) in 13 studies involving 4343 patients; and symptomatic deep vein thrombosis occurred in 173 patients (0.53 percent) When compared to low dose LMWH (odds ratio 0.53, 95 percent confidence interval 0.32 to 0.89) [8], direct oral anticoagulants were associated with a significant (P=0.02) reduction in symptomatic venous thromboembolism, but

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not when compared to high dose LMWH (0.93, 0.51 to 1.71); the evidence was moderately certain. On symptomatic pulmonary embolism, there was no significant difference between the network choices; however, the certainty of the network options was lower. Major bleeding was defined in various ways in each experiment, but it usually included fatal hemorrhage, bleeding in vital organs, bleeding that caused a specified drop in hemoglobin concentration, and bleeding that required reoperation. 345 patients (0.84 percent) suffered serious bleeding in 55 trials including 41 023 people [9]. When compared to no active therapy, all drugs were linked to a significant increase in severe bleeding (P=0.002 for low dose LMWH, from direct comparison; P=0.006 for high dose LMWH; P=0.04 for direct oral anticoagulants; certainty of evidence moderate to high).

We found evidence of moderate-to-high certainty that LMWH and direct oral anticoagulants reduce venous thromboembolic events of any extension associated with symptoms compared to no active treatment in a systematic review and network meta-analysis involving more than 45000 patients undergoing non-cardiac surgery across 68 randomized controlled trials, with point estimates for odds ratios between 0.17 and 0.33 [10]. Direct oral anticoagulants are likely to reduce symptomatic venous thromboembolism more effectively than LMWH at the most common preventive dose (odds ratio 0.53, 95 % confidence interval 0.32 to 0.89). There was no difference in efficacy between LMWH at a conventional preventive dose and LMWH at higher (intermediate) doses, according to the research. On symptomatic pulmonary embolism, we were unable to identify a meaningful relative treatment impact [11]. With point estimates for odds ratios ranging from 2.01 to 3.07, the evidence was moderate to high that all active medicines enhance severe bleeding when compared to no active treatment. When compared to low dose LMWH, LMWH at higher than prophylactic doses probably increase the risk (1.87, 1.06 to 3.31).

The absolute event rates for symptomatic venous thromboembolism outcomes and significant bleeding were low (1% on average) throughout the included studies; the rate of symptomatic pulmonary embolism was very low (0.3%) [12]. As a result of this finding, there were only minor absolute differences between active medications and no active treatment, as well as between various agents. Overall, this finding emphasizes the importance of weighing the benefits of thromboprophylaxis against the risks, taking into account both relative treatment effects and how they translate into absolute rate differences. Our study's strong point is that we were able to acquire higher accuracy estimates of relative treatment effects, despite the fact that we only looked at symptomatic venous thromboembolism occurrences. These occurrences are more important to patients, although they should be less common than venous thromboembolism, which is detected through systematic screening and counted as an outcome independent of symptoms [13]. In addition, we calculated impacts for comparisons that were not directly investigated in previous research (eg, comparisons including direct oral anticoagulants in non-orthopedics surgeries).

Our research has some limitations. The premise of transitivity served as the foundation for our research. In network meta-analyses, transitivity is the assumption that indirect comparisons (AC and BC) accurately predict the unobserved head-to-head comparison (AB). This assumption also means that the studies' distributions of possible effect modifiers are sufficiently close for indirect comparisons to be an acceptable way of comparing two treatment choices. We used a variety of methods to reduce and verify this assumption, as well as explore for potential sources of heterogeneity or effect modifiers. Our subgroup and meta-regression analyses [14], on the other hand, had insufficient power and could only be used for exploratory purposes. We had a modest number of studies in non-orthopedics surgery for the kind of surgical setting as a putative effect modifier, as expected There is only one current research on direct oral anticoagulants in this scenario (only six of 25 for symptomatic venous thromboembolism).

The effect of low dosage LMWH versus no active therapy was found to have a significant (quantitative) interaction (P=0.04), with a bigger and more precise effect in non-orthopedics procedures than orthopedics surgeries . However, the results of two small, single-center, randomized controlled trials in patients undergoing general surgery (mostly cancer resections) that found a high rate of symptomatic venous thromboembolism in the control group (7.4% and 13.8%, respectively) and extreme relative risk reductions of these events with prophylactic LMWH (odds ratios >10), prompted these analyses. Another drawback is that we focused solely on LMWH and direct oral anticoagulants, ignoring additional thromboprophylaxis medication choices such as unfractionated heparin, fondaparinux, vitamin K antagonists, and aspirin. However, we chose to take a pragmatic approach and look at medicines that have been more thoroughly investigated for thromboprophylaxis and may be more appealing alternatives to assess in any future study that our data may inform.

CONCLUSION

We found that both direct oral anticoagulants and LMWH are likely to minimize symptomatic venous thromboembolism in major non-cardiac surgery, with direct oral anticoagulants being more effective than LMWH at the recommended preventive dose. All of the pharmacological therapy alternatives are likely to make you bleed more. Our study offered thorough data on relative treatment effects utilizing a network meta-analysis technique and an emphasis on symptomatic occurrences. Many of our estimates were based on data with a moderate to high level of certainty and can be used to make decisions. We found that pulmonary embolism is uncommon after non-cardiac surgery, and that overall reported rates of symptomatic thrombotic events and significant bleeding events are low (less than 1%), albeit there may be variations across surgical groups and centers. As a result, we emphasize the importance of putting our research findings to good use for a net effect assessment of perioperative thromboprophylaxis that takes these additional parameters into consideration.

REFERENCES

1. Weiser TG, Haynes AB, Molina G, et al. Estimate of the global volume of surgery in 2012: an assessment supporting improved health outcomes. Lancet. 2015;385:11.
2. Kapoor A, Ellis A, Shaffer N, et al. Comparative effectiveness of venous thromboembolism prophylaxis options for the patient undergoing total hip and knee replacement: a network meta-analysis. J Thrombosis Haemost. 2017;15(2):284-294.
3. Mismetti P, Laporte S, Darmon JY, et al. Meta-analysis of low molecular weight heparin in the prevention of venous thromboembolism in general surgery. British J Surgery. 2001;88(7):913-930.
4. Falck-Ytter Y, Francis CW, Johanson NA, et al. Prevention of VTE in orthopedic surgery patients: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2):278-325.
5. Gould MK, Garcia DA, Wren SM, et al. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2):227-277.
6. Kozek-Langenecker S, Fenger-Eriksen C, Thienpont E, et al. European guidelines on perioperative venous thromboembolism prophylaxis: surgery in the elderly. Europ J Anaesthesiol. 2018;35(2):116-122.
7. Mont MA, Jacobs JJ. AAOS clinical practice guideline: preventing venous thromboembolic disease in patients undergoing elective hip and knee arthroplasty. J Am Acad Orthopaedic Surg. 2011;19(12):777-778.
8. Tikkinen KA, Craigie S, Agarwal A, et al. Procedure-specific risks of thrombosis and bleeding in urological cancer surgery: systematic review and meta-analysis. Europ Urology. 2018;73(2):242-251.
9. Lyman GH, Bohlke K, Khorana AA, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update 2014. J Clin Oncol. 2015;33(6):654.
10. Violette PD, Lavallée LT, Kassouf W, et al. Canadian Urological Association guideline: Perioperative thromboprophylaxis and management of anticoagulation. Cana Urolog Asso J. 2019;13(4):105-114.
11. Wong A, Kraus PS, Lau BD, et al. Patient preferences regarding pharmacologic venous thromboembolism prophylaxis. J Hosp Med. 2015;10(2):108-111.
12. Lanéelle D, Le Brun C, Mauger C, et al. Patient characteristics and preferences regarding anticoagulant treatment in venous thromboembolic disease. Front Cardiovas Med. 2021;8.
13. Lim W, Le Gal G, Bates SM, et al. American Society of Hematology 2018 guidelines for management of venous thromboembolism: diagnosis of venous thromboembolism. Blood Advan. 2018;2(22):3226-3256.
14. Wiercioch W, Nieuwlaat R, Akl EA, et al. Methodology for the American Society of Hematology VTE guidelines: current best practice, innovations, and experiences. Blood Advan. 2020;4(10):2351-2365.