

G67: Does the type of venous thromboprophylaxis affect the incidence of Surgical Site Infection (SSI)/Periprosthetic Joint Infection (PJI) in patients undergoing major orthopedic surgery?

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Response/Recommendations:

Yes. The type of venous thromboprophylaxis appears to affect the incidence of Surgical Site Infection (SSI)/Periprosthetic Joint Infection (PJI). Warfarin is associated with the highest risk of infection, while aspirin shows the lowest risk.

Level of Evidence: Limited

Delegate Votes:

Rationale:

Venous thromboprophylaxis is crucial in postoperative management after total joint and lower limb fractures surgery [1]. The risk of symptomatic venous thromboembolic (VTE) complications after major lower limb surgery ranges from 1 to 4% [2][3]. Wound complications and periprosthetic joint infection (PJI) are one of the devastating complications and a main cause of morbidity after total joint arthroplasty and trauma surgery [4][5]. Studies have showed that there is a relation between the use of anticoagulation in orthopedic surgery and the occurrence of infection related complications. The association with postoperative wound complications and administration of anticoagulation is also well known (REF). Prolonged wound discharge is a concerning issue as it is one of the major risk factor for surgical site infection and PJI (REF). Postoperative hematoma formation and other bleeding complications that may occur after anticoagulation therapy are also risk factors for infections [6][7].

To answer the above question, we conducted a comprehensive search of PubMed and Scopus databases using the MeSH terms that were developed by librarians. Our initial search yielded 3,266 potential articles. After screening by two independent reviewers, 3,024 studies were excluded and 45 randomized controlled trials (RCTs) were added in our final meta-analysis. We also decided to provide evidence from non-RCT trials as the outcome PJI may require large sampled studies for long follow up periods and due to small number of reported events of PJI in RCTs. We decided to answer two questions: Q1: Does the incidence of SSI/PJI differs in patients receiving venous thromboprophylaxis versus no prophylaxis? And Q2: Does the incidence of SSI/PJI differs with different agents of venous thromboprophylaxis?

Our meta-analysis results showed that eight studies [8][9][10][11][12][13][14][15] reported the outcome of infection with no statistically significant difference between patients who received

thromboprophylaxis (18/954) and the control group (11/972) (RR: 1.25 CI: 0.66, 2.37). eleven studies[8][16][17]

[14][15][21][41][42][22][23]reported the outcome of hematoma formation with no statistically significant difference between patients who received thromboprophylaxis treatment (14/904) and the control group (10/916). Three studies[8][9][10] reported the outcome wound discharge with no statistically significant difference between venous thromboprophylaxis group (24/407) and the placebo group (10/417) (RR 2.53 CI: 1.28, 5.00). One study [15]reported the outcome of PJI with no cases of PJI during the period of follow up. We also compared the risk of infection, hematoma formation, wound drainage, and PJI between different agents of venous thromboprophylaxis.

Our metaanalysis showed no difference in outcomes between patients who received venous thromboprophylaxis and placebo groups as regard risk of SSI/PJI, wound hematoma, wound drainage. Also, there was no difference between different thromboprophylaxis agents as regard risk of SSI/PJI, wound hematoma, wound drainage. However, we have downgraded the evidence of our meta-analysis ~~two~~ level due to imprecision as all studies had small sample size. Also, there was few data available about the risk of PJI in the included RCTs with weak reporting of the PJI outcome.

The retrospective studies on the other hand demonstrated significant associations between administration of VTE prophylaxis and subsequent SSI/PJI. Pai et al. reported a higher 90-day readmission risk in patients who received pharmacological VTE prophylaxis with LMWH for three days and postoperative low dose aspirin compared to the control group. They reported a 90 day risk of PJI of 0.4% (8/1957) in patients who received pharmacological prophylaxis compared to 0.1% (8/5554) in the control group[43]. Parvizi et al. reported that the rate of PJI was higher in patients received anticoagulation therapy with LMWH, and warfarin, specially when the International Normalized Ratio (INR) level was more than 1.5 [44]. Sachs et al. 2003 in their cohort reported double infection related complication rate in patients who received warfarin treatment after total joint arthroplasty[45]. Recent studies showed increased rate of infection with the use of aggressive protocols of VTE prophylaxis such as warfarin, LMWH, fondaparinux, and factor X inhibitors. These studies recommended the use of less aggressive modalities as low dose aspirin and sequential pneumatic devices as they observed non-increased risk of thrombosis with their use [46][47]. Data from most retrospective reports showed that the risk of PJI is higher with the use of warfarin and least with the use of aspirin [48][49][50][51]. Anil et. al. reported that aspirin may have the lowest risk of PJI among all VTE prophylaxis agents and being reported to as effective as other agents in preventing VTE related complications[50]. Najafi et al recommended the use of low dose aspirin as it has a protective effect against staphylococcal infection and has a synergistic action with antibiotics compared to the high dose aspirin[52]. The limitations of these reports are that they provide a conflicting relation between the type of venous thromboprophylaxis agent and the risk of PJI, lack of clear definitions of infection and being non randomized retrospective studies making its results affected by many confounders.

Conclusion:

Based on the available data, majority of which emanates from retrospective cohort studies, there is some evidence that the type of VTE prophylaxis given to patients undergoing orthopedic procedures does influence the subsequent risk of SSI/PJI. Because of low rate of SSI/PJI, the few available randomized studies were not powered to be able to examine the possible correlation between the type of VTE prophylaxis and subsequent infections in orthopedic patients. However, data from most retrospective cohorts showed that warfarin is associated with the highest risk of SSI/PJI and to varying extents enoxaparin, fondaparinux and rivaroxaban. Studies are in favor of low dose aspirin as the VTE prophylaxis of choice for orthopedic patients, as aspirin is least associated with the infection related complications. Large sized randomized studies are needed to determine the exact association between the type of VTE prophylaxis and SSI/PJI risk and to investigate the applicability of both the aggressive and less aggressive regimens on high risk patients who are at increased risk for either SSI/PJI or venous thromboembolic events.

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