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INTERNATIONAL JOURNAL OF SURGERY

OPEN

Comment on 'The role of aspirin versus low-molecular-weight heparin for venous thromboembolism prophylaxis after total knee arthroplasty: a meta-analysis of randomized controlled trials'

Xiaochen Zhang, MS[a], Yu Ren, MM[b], Hua Luo, MM[c,*]

Dear Editor,

We were intrigued by a recent meta-analysis comparing aspirin and low-molecular-weight heparin (LMWH) for venous thromboembolism (VTE) prophylaxis after total knee arthroplasty by Meng *et al*.[1]. Six randomized controlled trials, comprising 6772 patients were analyzed. A notable discovery of this meta-analysis was the efficacy of LMWH in VTE prevention. The substantial decrease in thromboembolic risk linked to LMWH, compared to aspirin, is highly significant. We sincerely appreciate the authors' efforts in data collection and analysis. However, we believe that the following concerns require further clarification.

Firstly, in the results, the authors stated that a total of 6772 patients were included in the study. However, during the actual meta-analysis, it was noted that 11 patients from the study by Westrich *et al*.[2], who did not undergo an ultrasound examination were excluded. Therefore, a more precise representation of the total number of included patients would be 6761.

Secondly, in Westrich *et al*.'s study[2], patients took oral enoxaparin 30 mg bid in hospital, then switched to 40 mg qd upon discharge for 3 weeks. The aspirin group received oral aspirin 325 mg bid. Hence, the description in Table 1 is incorrect.

Thirdly, the authors mistakenly included data from the Zhou *et al*.[3] twice in Figure 4B. There was one case of gastrointestinal bleeding attributed to aspirin (Zhou-2023.2), while in the other instance, it was zero (Zhou-2023.1). As shown in Zhou *et al*.'s study[3], one case of gastrointestinal bleeding occurred in both the aspirin and rivaroxaban groups, while none occurred in the LMWH group. Therefore, we suggest excluding the data from Zhou-2023.1.

Fourth, it's clear that the author combined the results of double-zero studies from Figures 4B and 5B. However, this merger could introduce serious issues. Since these studies lacked valid data, their inclusion may distort overall effect estimates and confidence intervals. This could hamper result interpretation, hinder understanding, and affect heterogeneity tests, lowering result credibility and scientific value. It's advisable to exclude double-zero studies to maintain the accuracy and reliability of the meta-analysis results.

Fifth, we are concerned about the accuracy of the data collected by the author. Despite the mention of the use of four independent researchers to extract and cross-validate data, some obvious data errors persist. For instance, in Fuente *et al*.'s study[4], the aspirin group comprised 188 participants, while the LMWH group had 214 participants. However, in the meta-analysis (as shown in Figures 3–5 by Meng *et al*.[1]), the sample sizes for these two groups differed from those stated in the original study. The error in Figure 3 from Meng *et al*. has been outlined with a red box in Figure 1. This discrepancy raises concerns about the article's reliability. Upon recalculating the data, although the final conclusions remained consistent, the results of RR and 95% CI are varied. We pooled these results again and revealed that compared to the LMWH, aspirin is significantly associated with an increased overall VTE incidence (RR 1.47; 95% CI: 1.17–1.85, $I^2 = 0\%$). Nevertheless, no significant differences were found between the two groups regarding bleeding complications rate (RR 0.89; 95% CI: 0.70–1.13, $I^2 = 0\%$), gastrointestinal bleeding (RR 3.0; 95% CI: 0.13–72.20), deep vein thrombosis (RR 1.23; 95% CI: 0.85–1.77, $I^2 = 0\%$), and pulmonary embolism (RR 1.05; 95% CI: 0.16–7.13, $I^2 = 0\%$).

Sixth, the author mentions adherence to PRISMA and AMSTAR guidelines but overlooks heterogeneity tests and publication bias detection in the meta-analysis. This oversight may obscure the true extent of heterogeneity and publication bias, thereby compromising the reliability of result interpretation. It could mislead the understanding of overall effect estimates, impacting policy formulation and clinical decision-making and ultimately weakening the study's scientific credibility and

[a]Department of Psychiatry, Taizhou Second People's Hospital, [b]Department of Pharmacy, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University and [c]Department of Orthopedic, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, Taizhou, Zhejiang, People's Republic of China

Xiaochen Zhang and Yu Ren have contributed equally to this work and share first authorship.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

*Corresponding author. Address: Department of Orthopedic, Taizhou Hospital of Zhejiang Province affiliated to Wenzhou Medical University, No. 150 Ximen Road, Taizhou 317000, Zhejiang, People's Republic of China. Tel.: +86 187 321 96 660. E-mail: 18732196660@163.com (H. Luo).

International Journal of Surgery (2024) 110:5907–5909

Received 7 May 2024; Accepted 9 May 2024

Published online 22 May 2024

http://dx.doi.org/10.1097/JS9.0000000000001672

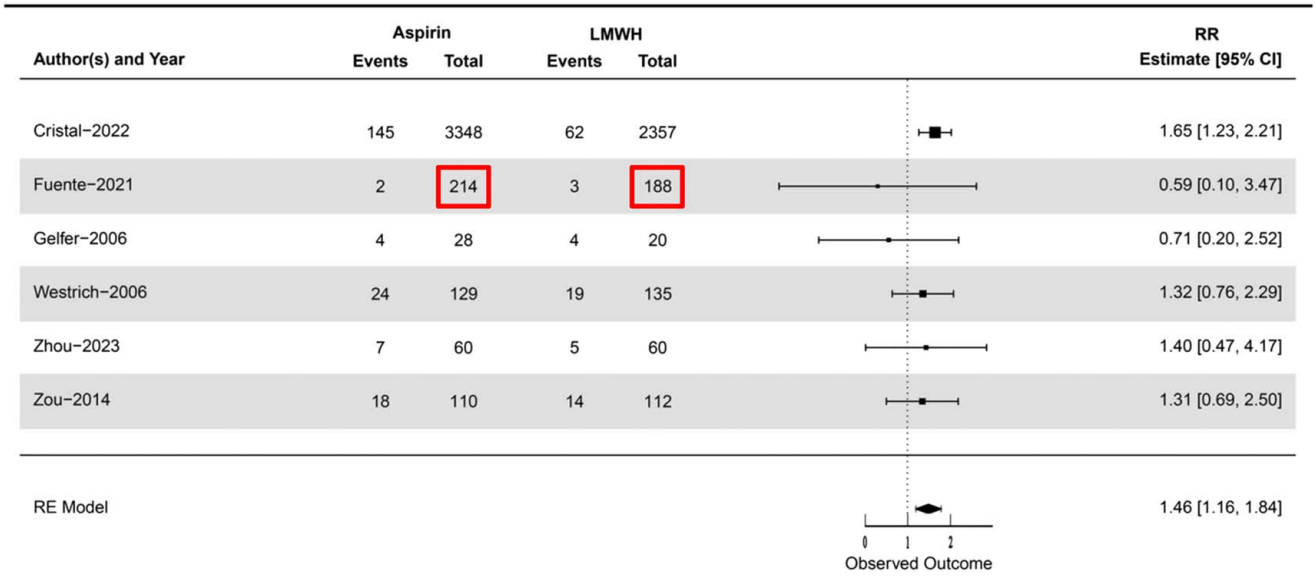

Figure 1. The pooled effect of venous thromboembolism rate from the study conducted by Meng *et al*.[1]. We indicated the data with errors using a red box.

transparency. Although our repeated meta-analysis studies found no heterogeneity in the results ($I^2 = 0\%$), the author should have addressed this in the study. Additionally, sensitivity analysis, absent from this meta-analysis, would have aided in assessing result reliability. For instance, excluding Sidhu *et al*.'s study[5] altered conclusions regarding overall VTE rate (RR 1.23; 95% CI: 0.85–1.77, $I^2 = 0\%$), indicating potential bias due to their focus on all joint arthroplasty. Since randomization occurred among patients undergoing all joint replacements, selecting only knee arthroplasty patients could introduce result bias.

We trust that our insights will aid readers in understanding the article's findings and inspire future scientific endeavors. Continuous enhancement is crucial, and we advocate for researchers to undertake a refreshed meta-analysis.

Ethical approval

Not applicable.

Consent

Not applicable.

Sources of funding

This study was supported by Enze Medical Center (Group) Scientific Research (No. 24EZB07) and Zhejiang Medicine and Health Scientific Research Project (No. 2024KY531).

Author contribution

H.L.: proposed the design, collected, analyzed and interpret the data, and wrote the study; X.Z. and Y.R.: collected, analyzed and interpreted the data, and designed the figure.

Conflicts of interest disclosure

There are no conflicts of interest.

Research registration unique identifying number (UIN)

Not applicable.

Guarantor

Hua Luo.

Data availability statement

All the data are available in the article.

Provenance and peer review

Commentary, internally reviewed.

Acknowledgements

Not applicable.

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