SYSTEMATIC REVIEW

The Efficacy of Bone Wax in Total Joint Arthroplasty: A Systematic Review and Meta-Analysis

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Abstract

Objectives: This meta-analysis was conducted to study the hemostatic efficacy of bone wax in total joint arthroplasty (TJA) defined in this manuscript as total knee arthroplasty and total hip arthroplasty.

Methods: PubMed, Embase, Google Scholar (page 1-20), and Scopus were searched updated to November 2023. Only comparative studies were included. The clinical outcomes evaluated were the transfusion rate, total blood loss, and the loss of hemoglobin on day 1, 3, and 5 post-operatively.

Results: Only 3 studies met the inclusion criteria and were included in this meta-analysis. Bone wax was associated with a reduced transfusion rate ($p=0.01$), reduced total blood loss ($p=0.001$), and a decrease in hemoglobin loss on day 1 ($p<0.00001$), day 3 ($p<0.0001$), and day 5 ($p<0.00001$) after the surgery.

Conclusion: Bone wax reduced the rate of transfusion, total blood loss, and hemoglobin loss after the surgery. This may induce a reduction the cost of correcting post-operative anemia as well as decrease hospital stay and improving functional outcomes in patients undergoing TJA. Better-conducted randomized controlled studies and cost-effectivity studies could strengthen these findings.

Level of evidence: III

Keywords: Bone wax, Hemostasis, Post-operative anemia, Total hip arthroplasty, Total knee arthroplasty

Introduction

The average life expectancy of people is continuing to raise with the medical advancements.[1] According to research, there will be a 135% increase in the number of people over the age of 65 between the years 2000 and 2050.[2] Four chronic musculoskeletal disorders have been highlighted by the World Health Organization as conditions that will rise in frequency as the population ages. Rheumatoid arthritis (RA) and osteoarthritis (OA), which both afflict millions of people globally are two of these disorders.[3] Total Hip Arthroplasty (THA) and Total Knee Arthroplasty (TKA) are the surgical management of choice to relieve joint deterioration, reduce pain, and improve quality of life when conservative care of RA and OA has failed and the overall quality of life for an individual continues to diminish.[4–7] Around 3.5 million primary total knee arthroplasty (TKA) procedures and nearly 600,000 primary total hip arthroplasty (THA) procedures are anticipated to be performed annually in the US by 2030.[1]

One of the complications of both TKA and THA is perioperative blood loss (PBL). The mean value of PBL in THA ranges from 450 to 2800 ml[8,9] and 1450 to 1790 ml in TKA.[10] Resulting complications such as postoperative anemia was associated to infections, poor recovery, wound complications, and venous thromboembolism.[11,12] When managed with transfusions, this can also increase the risk of hemolytic reactions, coagulopathy, and infection transmission.[13]

Many strategies exist to reduce PBL such as local hemostatic agents,[14] tranexamic acid,[15] neuraxial anesthesia,[16] and many others. Bone wax, a widely used local hemostatic agent due to its malleability, cohesiveness, practicality, and cost effectiveness, works by occluding the cut vessels and haversian canals.[17,18] Despite numerous publications about the efficacy of bone wax in the field of surgery, there is no meta-analysis about its effectiveness in Total Joint Arthroplasty (TJA). Therefore, this meta-analysis

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is designed to evaluate the efficacy of this local hemostatic agent in both TKA and THA.

Materials and Methods

Search strategy

The PRISMA guidelines were followed in this study. Google Scholar (page 1-20), Embase, PubMed, and Scopus were searched updated till November 2023 to find relevant studies to evaluate the efficacy of bone wax in TJA. The PICO in this study was "In patients undergoing TJA, how does bone wax compared with no hemostatic agent affect blood loss and rate of transfusions". In the search, the Boolean operators were used ("Wax" AND ("joint" OR "hip" OR "knee") AND ("replacement" OR "arthroplasty")). In addition, literature was identified by going through reference lists from included studies and Internet searches. One author extracted the data, and another author confirmed the choice of the articles. The PRISMA flowchart summarized the process [Figure 1].

Studies were included if they met the following criteria such as (1) comparative studies: randomized controlled trails, retrospective comparative studies, prospective clinical trials; (2) patients operated with a TKA or THA; (3) bone wax was used as a hemostatic agent compared to nothing in another group. Exclusion criteria were: (1) non-comparative studies ; (2) non-relevant outcomes.

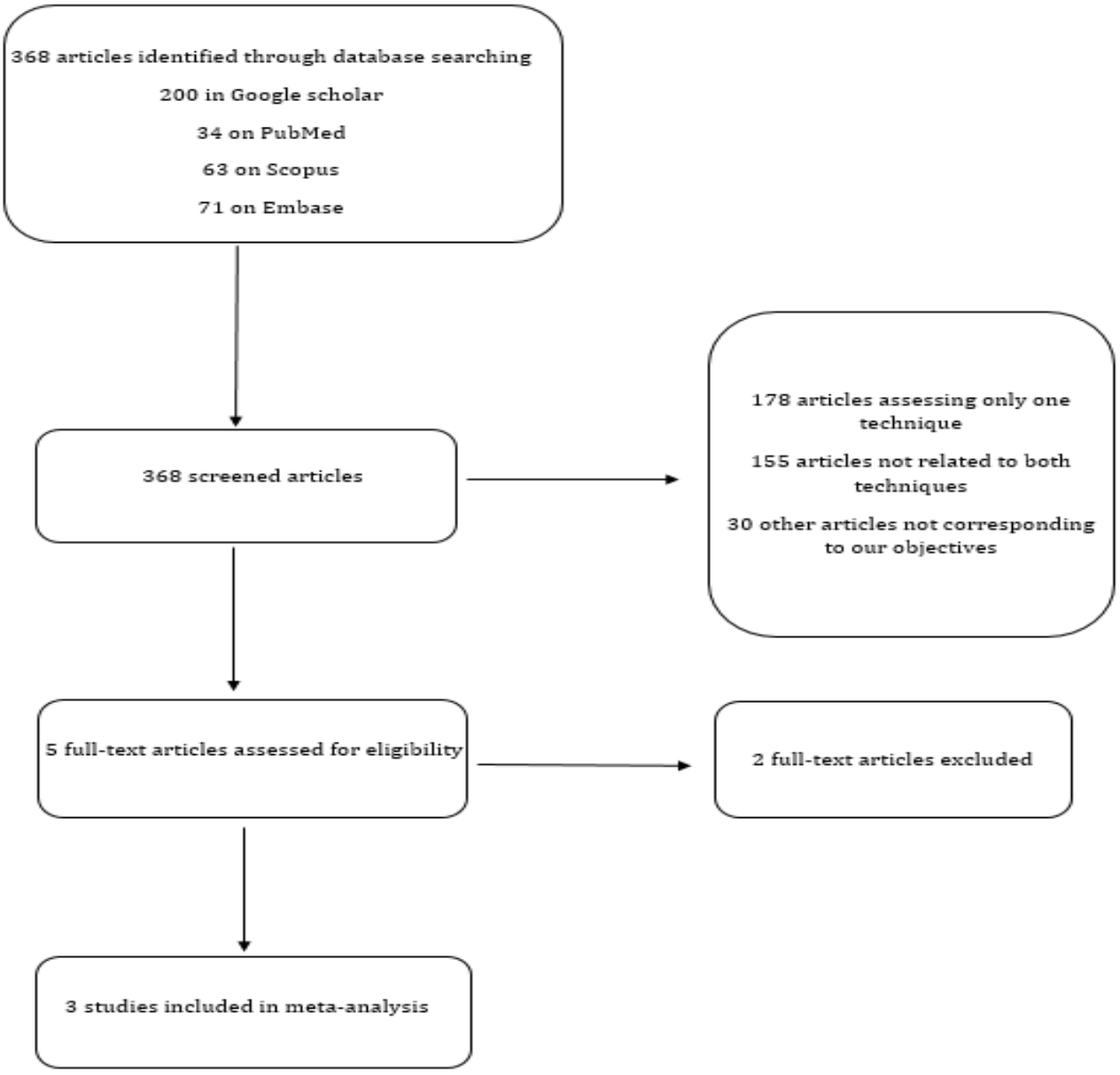

Figure 1. PRISMA flowchart for article selection process

Data extraction

Two impartial reviewers determined the studies' eligibility. Extraction of the examined data was made from the included studies and it consisted of two parts. The initial section comprised the fundamental details, which included the names of the authors, the title, the year of publication, the journal, the volume, the issue, the pages, the study design, the sample size, the size of each management group, and the various forms of bias that were suspected in each study. The bias in at least one domain were considered to have a high risk of bias. Trials with a low risk of bias in all domains were considered to have a low risk of bias. In case where neither of these conditions were satisfied, the trials were considered to show an unclear bias risk. The ROBINS-I tool was used in a similar manner by two authors independently to assess the risk of bias of included studies. [19] Articles were excluded if they had a critical risk of bias. In addition, to assess for publication bias, we inspected the symmetry of the funnel plot for each outcome.

second part consisted of the clinical outcomes which were the rate of transfusions, total blood loss, hemoglobin (Hb) drop 1, 3, and 5 days post-operatively. Any arising difference between the investigators was resolved by discussion.

Risk of bias assessment

The Cochrane risk-of-bias tool was used by two authors to independently assess the risk of bias for randomized controlled trials. [Figure 2 (A&B)]. Trials with a high risk of

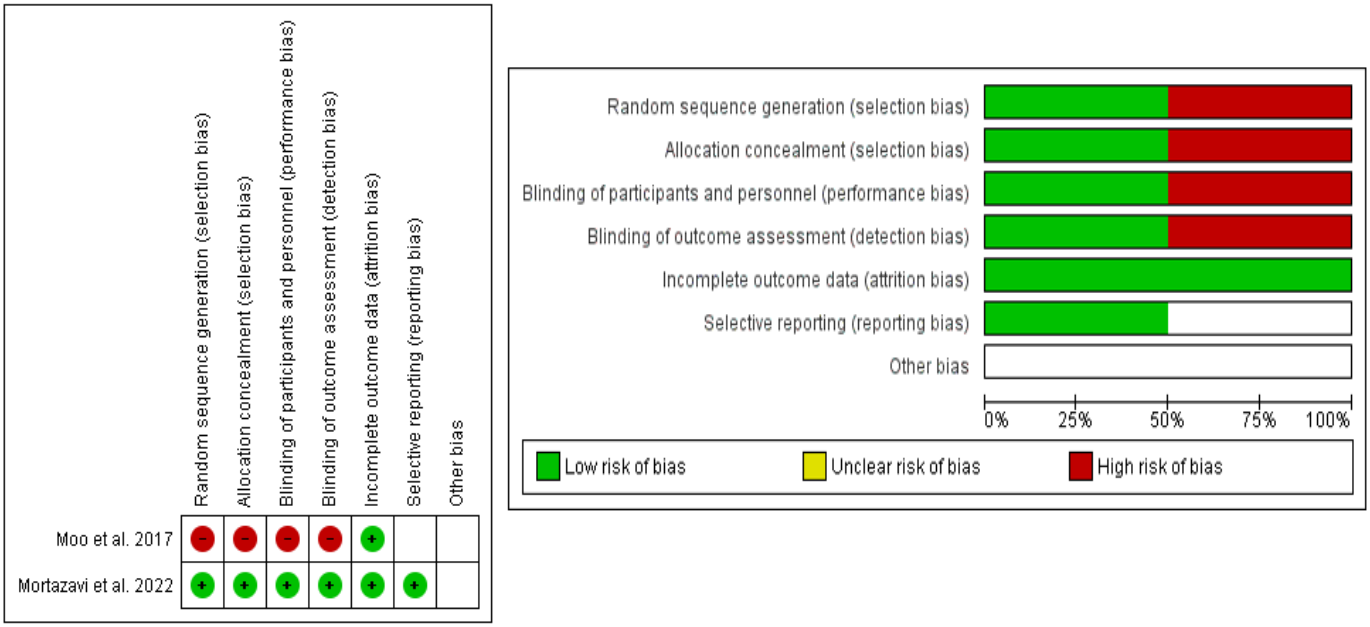

Figure 2. Risk of bias item for each included study. (B) Risk of bias item presented as percentages across all included studies

Statistical analysis

Review Manager 5.4 (The Cochrane Collaboration, 2020) was used to perform all statistical analysis. For dichotomous data, the odds ratio (OR) with 95% confidence intervals (CI) were utilized. For continuous data, the mean differences (MD) and standardized mean differences (SMD) with 95% CI were used. Heterogeneity was evaluated by Q tests and I^2 statistics. If considerable heterogeneity was present, as indicated by a $p \leq 0.05$ or $I^2 > 50\%$, a random-effects model was used. Otherwise, a fixed-effect model was chosen ($p > 0.05$ or $I^2 < 50\%$). The threshold for statistical significance was set at $p \leq 0.05$. A meta-analysis was performed when there were at least three studies included in the analysis and a pooled estimation was performed when the analyzed studies were less than three. Statistical significance threshold was chosen at p=0.05.

Results

Characteristics of the included studies

Three studies [20–22] were included in the meta-analysis with 2 randomized controlled trials and 1 retrospective comparative study. It involved 227 subjects in the bone wax group and 229 subjects in the conventional hemostasis group.

The main characteristics of the included studies are summarized in [Table 1]. In four out of the five analyzed outcomes, the heterogeneity was not significant making the studies fairly homogenous. Only in one of the outcomes, the heterogeneity significant (I^2>50%).

Table 1. Main characteristics of the included studies

	Study Design	Participants		Country	Mean age (SD)		Measured Outcomes	Follow-up time
		With bone wax	Without bone wax		With bone wax	Without bone wax		
Moo et al. 2017	Randomized controlled trial	50 14 males, 36 females	50 10 males, 40 females	Singapore	65 (8)	67 (7)	Hemoglobin loss, transfusions, blood loss,	3 months
Mortazavi et al. 2022	Randomized controlled trial	75 32 males, 43 females	77 43 males, 34 females	Iran	46.9 (16.2)	48.5 (14.7)	Blood loss, Transfusions	11.5 months
Shin et al. 2020	Retrospective comparison	102 12 males, 90 females	102 9 males, 93 females	South Korea	72.13 (6.55)	72.78 (7.27)	Hemoglobin loss, blood loss, post-operative drainage, Transfusion rate, volume of transfusion	NA

Bias results

The risk of bias assessment is presented in [figure 2 (A &B)]. Selection and detection bias were reported to be high in the majority of the studies whereas there were low performance and attrition bias. One trial was deemed as having a high risk of bias [20] and the other was deemed as having a low risk of bias. [21] The retrospective study was assessed and shown to have a moderate risk [Table 2]. Furthermore, the funnel plot was symmetrical for each of the analyzed outcomes making the publication bias minimal [Figure 3 A-E].

Table 2. Bias assessment of the included retrospective study

Studies	Confounding bias	Selection bias	Classification bias	Bias due to deviation from interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of reported results	Results
Shin et al. 2020	Low risk	Low risk	Low risk	Low risk	Low risk	Moderate risk	Low risk	Moderate risk

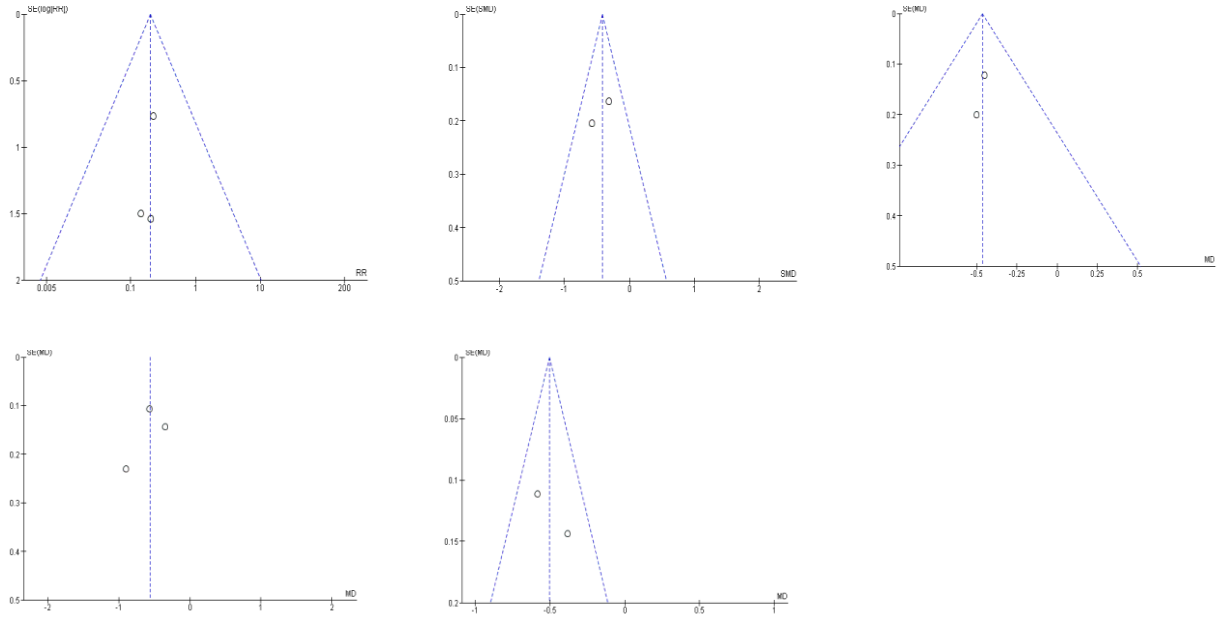

Figure 3 (A). Funnel plot to assess for publication bias in the rate of transfusions. (B) Funnel plot to assess for publication bias in total blood loss. (C) Funnel plot to assess for publication bias in Hb drop day 1 post-operatively. (B) Funnel plot to assess for publication bias in Hb drop day 3 post-operatively. (B) Funnel plot to assess for publication bias in Hb drop day 5 post-operatively

Transfusions

Three studies on 456 subjects had data on post-operative transfusion rate [20–22]. Bone wax was shown to significantly reduces the rate of transfusions post-operatively (RR = 0.20; 95% CI=0.06–0.68, p=0.01, I^2=0% [Chart 1]).

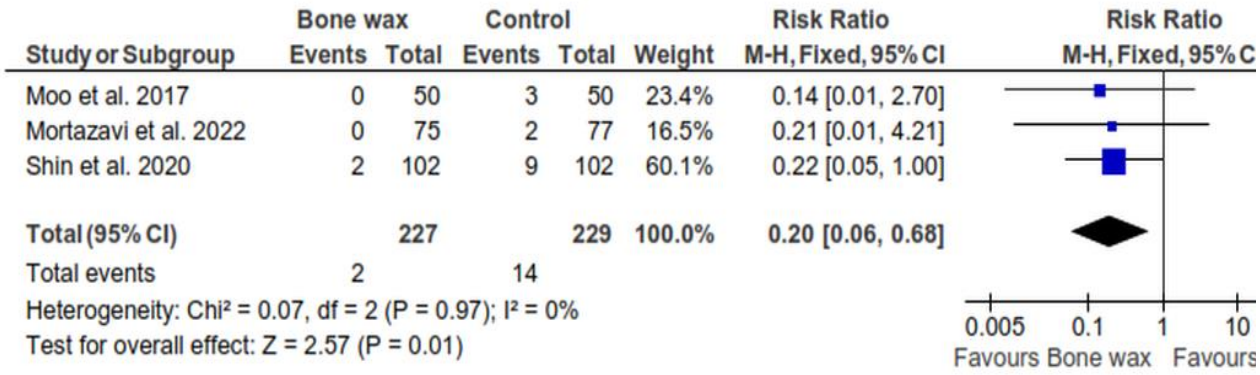

Chart 1. Forest plot showing the rate of Transfusions in TJA with and without bone wax

Total blood loss

Two studies on 252 subjects had data on total blood loss. [20,21] Bone wax was shown to significantly reduces total blood loss (Mean difference= -0.41; 95% CI= -0.66– -0.16, p=0.001, I^2=0% [Chart 2]).

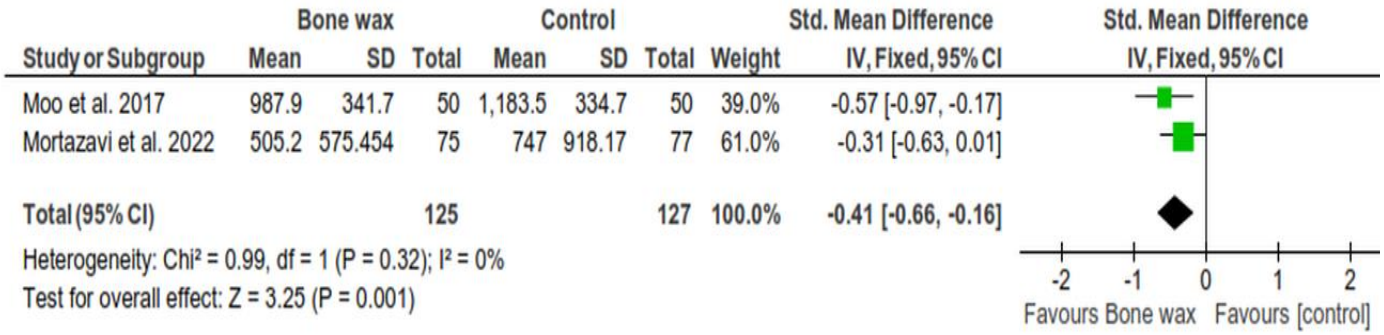

Chart 2. Forest plot showing the total blood loss in TJA with and without bone wax

Hemoglobin drop

Two studies on 304 subjects had data on hemoglobin drop, day 1 post-operatively [20,22]. Bone wax shown to significantly reduce hemoglobin drop 1 day after the surgery (Mean difference= -0.46; 95% CI =-0.67– -0.26, , p<0.00001, I^2=0% [Chart 3A]) In contrast, three studies on 456 subjects had data on hemoglobin drop day 3 post-operatively. [20–22] Bone wax was shown to significantly reduce hemoglobin drop 3 days after the surgery (Mean difference, -0.56; 95% CI -0.81– -0.31, p<0.0001, I^2=53% [Chart 3B]). Finally, two studies on 356 subjects had data on hemoglobin drop day 5 post-operatively [21,22]. Bone wax was shown to significantly reduce hemoglobin drop 5 days after the surgery (Mean difference= -0.50; 95% CI -0.68– -0.33, p<0.00001, I^2=17% [Chart 3C]).

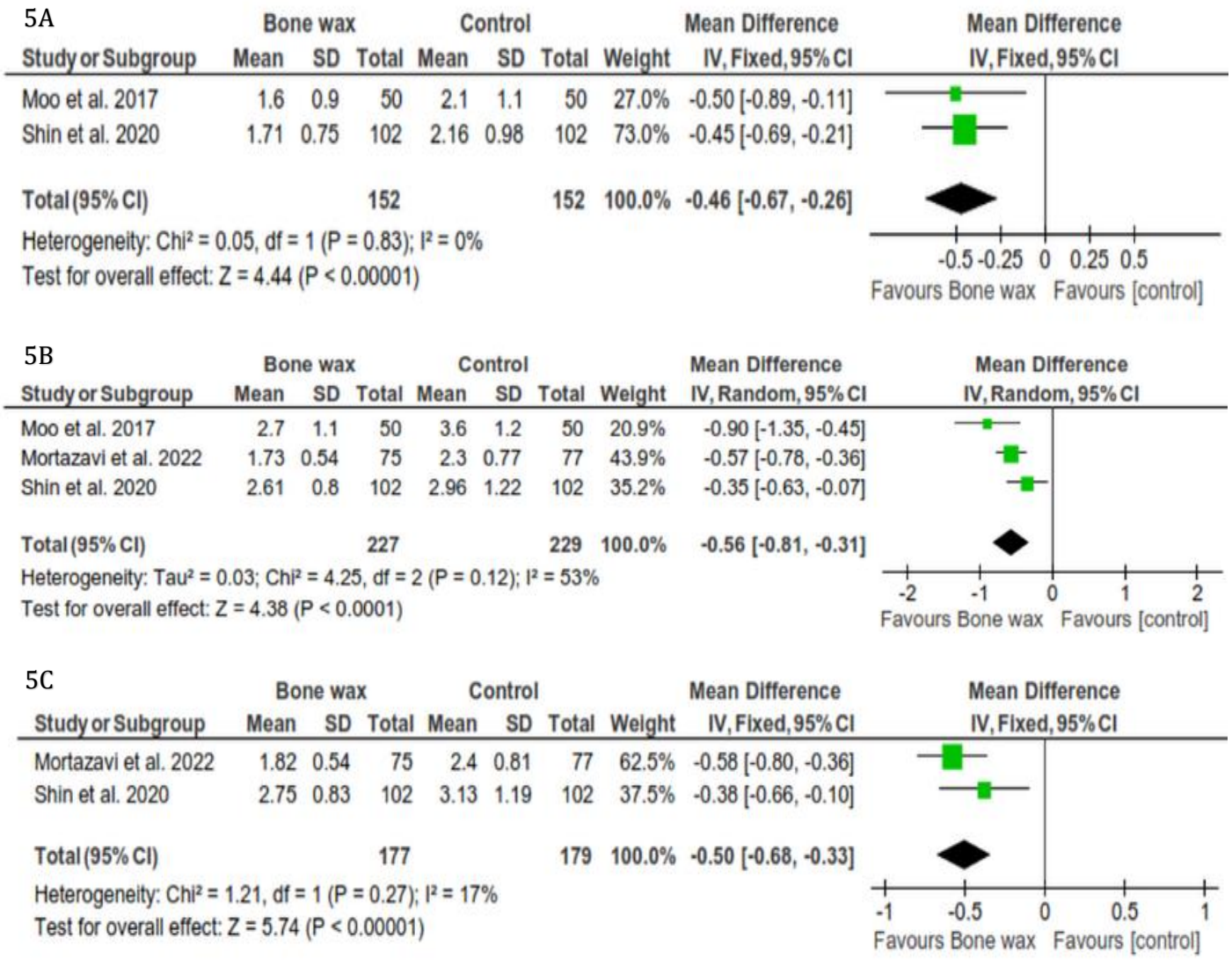

Chart 3. (A): Forest plot showing the Hb drop day 1 post-operatively in TJA with and without bone wax. (B): Forest plot showing the Hb drop day 3 post-operatively in TJA with and without bone wax. (C): Forest plot showing the Hb drop day 5 post-operatively in TJA with and without bone wax

Discussion

Total joint arthroplasties are expected to increase over time due to the aging population and obesity. A commonly faced adverse events in such procedures is PBL and post-operative anemia. The efficacy of bone wax has been studied in TJA. However, this is the first meta-analysis or randomized controlled trials assessing the efficacy of bone wax in both TKA and THA. The outcomes of this meta-analysis can be divided into three section: Transfusions, PBL, and hemoglobin drop. Bone wax was favored and showed a higher statistically significant benefit when compared to its non-usage in all of these outcomes.

Blood exudation occurs from the exposed bone not covered by the prostheses and after osteophytes removal.[23] This bleeding cannot be controlled by ligature or electrocautery and the latter may even cause thermal damage in the tissues.[24,25] Thus, the importance of local hemostatic agents. However, there are methods other than the bone wax used to reduce blood loss such as the usage of bone plug placed in the intramedullary canal, or fibrin sealant, thrombin-based sealant, or hydrogen peroxide wash.[26,27] Both thrombin and fibrin based sealants do not work on patients with an inherent or acquired coagulopathy as they require a functional clotting cascade to work.[28] However, this is not seen with bone wax as its effectiveness in blood loss reduction is due to its ability to immediately plug and seal bone marrow sinusoids and ultimately preventing blood oozing.[20]

Moreover, fibrin based local agents need an additional person in the operating room for them to draw blood from the patient in order to produce fibrin-rich cryoprecipitate.[20] Adding to that, a meta-analysis by Wang et al.[29] showing that this local hemostatic agent did not reduce total blood loss in TKA. When it comes to thrombin-based sealants, although

they have been shown to reduce total blood loss in TKA,[30] their expensiveness and potential complications such as blood-borne infectious disease transmission, immunologically induced coagulopathy, thromboembolic events, and Immunoglobulin E-mediated anaphylaxis.[31] As for the bone wax, being a foreign agent should raise concerns of infection as its application can permeate into the systemic circulation which can potentially lead to thromboembolisms.[20] However, no complications related to bone wax application were seen in the included studies.[20–22] Moreover, care must be taken when using bone wax such as using a thin layer and removing the excess of this local hemostatic agent.[20]

The lost hemoglobin can take around 56 days to be restored back to its initial value. To do so, the patient should be in an ideal condition and on a standard diet which is not seen after TJA.[21] The blood loss resulting from TJA increases the cost for the patient. This cost can range from €13 to €128. Nevertheless, this could be prevented using a bone wax costing around 3 to 4$. To add to that, bone wax usage can help reduce hospital stay and potentially help patients have a same-day discharge after TJA by reducing PBL as some centers are requiring an intraoperative blood loss lower than 500 ml or an hemoglobin level or more than 9.7 g/dl to send the patients home the same day after the operation.[32,33]

The anemia occurring after TJA can also affect functional outcomes. A study by Conlon et al. showed that there was an improvement of 8.57 and 2.9 in Short Form-36 and Functional assessment of Cancer Therapy-Anemia for an each restoration of 1 g/dl of hemoglobin.[34] Other studies showed a positive correlation between post-operative hemoglobin and the 6 minute walking test[35] as well as a better recovery of muscle strength in the hip with a post-operative:pre-operative hemoglobin ratio of more than 0.85 on day 10 after the surgery.[36]

Strengths and limitations

This study had some limitations such as the low number of included comparative studies, the different inclusion and exclusion criteria for patients across the included studies, and the limited comprehensive analysis due to the data used for analysis being pooled and the absence of individual patients' data. On the other hand, this study has several strengths. In fact, it is the first meta-analysis assessing the efficacy of bone wax in TJA. Moreover, only comparative studies were included reducing the risk of operative and matching bias, and therefore making the study less heterogenous.

Conclusion

This is the first meta-analysis assessing the hemostatic efficacy of bone wax in TJA. It showed that bone wax reduced the rate of transfusion, PBL and Hb drop 1, 3, and 5 days post-operatively. It is also superior to other local hemostatic agents by having a lower rate of complications and reduced cost. Moreover, Bone wax can reduce the cost of correcting post-operative anemia as well as decreasing hospital stay and improving functional outcomes in patients undergoing TJA. However, more randomized controlled studies and cost-effectivity studies are needed to confirm the benefits of this local hemostatic agent.

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