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Review Article

Outcome and safety comparison of low-molecular-weight heparin versus unfractionated heparin for bridging anticoagulation in individuals with mechanical heart valves undergoing non-cardiac surgery: A systematic review and meta-analysis

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Abstract

In patients with mechanical heart valves, low-molecular-weight heparin (LMWH) and unfractionated heparin are commonly used as bridging anticoagulation therapies to reduce the risk of thromboembolic events and major adverse cardiac events; however, the efficacy and safety of these therapies remain debatable. The aim of this study was to compare the safety and outcomes of LMWH and unfractionated heparin in patients with mechanical heart valve replacement undergoing non-cardiac surgery. This systematic literature review was conducted from January to June 2023, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines to search for related studies through PubMed, ScienceDirect, and Cochrane Library. Categorical variables were analyzed using a Mantel-Haenszel random-effects model, with relative risk (RR) as the effect size. Higgins I^2 was used to measure the heterogeneity and publication bias was assessed through funnel plots. Out of 814 potential studies, six studies (one randomized control trial and five prospective studies) were included. The analysis revealed no significant differences in thromboembolic event or valvular thrombosis (RR: 0.61; 95%CI: 0.36–1.04; p=0.07; χ^2=1.96; I^2=0%), all-cause mortality (RR: 0.73; 95%CI: 0.40–1.35; p=0.32; χ^2=0.97; I^2=0%), major bleeding (RR: 0.81; 95%CI: 0.53–1.23; p=0.33; χ^2=4.14; I^2=0%), minor bleeding (RR: 1.18; 95%CI: 0.86–1.62; p=0.31; χ^2=4.50; I^2=11%), and thrombocytopenia (RR: 0.56; 95%CI: 0.20–1.59; p=0.27; χ^2=0.85; I^2=0%). The study highlights that LMWH and unfractionated heparin did not differ significantly when used as bridging anticoagulant therapy for non-cardiac surgery in mechanical heart valve patients.

Keywords: Mechanical heart valve, bridging anticoagulation therapy, low-molecular-weight heparin, unfractionated heparin, meta-analysis

Introduction

Long-term anticoagulant use, such as with vitamin K antagonists, is necessary due to the thrombosis risk from prosthetic or mechanical heart valves, which can lead to major adverse

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cardiac events (MACE) [1]. Recipients of long-term anticoagulant therapy require regular monitoring of their international normalized ratio (INR) to ensure both the safety and efficacy of anticoagulant treatment [2]. If INR levels are suboptimal, temporary anticoagulants are used to prevent thromboembolism [3]. In certain situations, anticoagulant therapy may need to be temporarily discontinued to allow for invasive diagnostic or therapeutic procedures, both cardiac and non-cardiac, given the potential for increased bleeding risk [4]. However, discontinuation of anticoagulants can elevate the risk of thrombosis and thromboembolism post-procedure [2]. A carefully planned strategy is essential to minimize the risks of bleeding and thrombosis in patients with mechanical heart valves undergoing invasive or non-invasive surgeries, referred to as anticoagulation bridging therapy [5].

Despite numerous published guidelines addressing thromboembolism risk in patients following mechanical heart valve replacement, the optimal anticoagulation strategy post-surgery remains debated [6,7]. Two primary approaches have been employed: intravenous administration of unfractionated heparin and subcutaneous administration of low-molecular-weight heparin (LMWH) [6,7]. Unfractionated heparin requires hospitalization and monitoring through activated partial thromboplastin time (APTT) values, yet, it increases medical costs for both patients and healthcare systems [8,9]. In contrast, LMWH does not necessitate inpatient care or stringent monitoring [5,8]. Some studies suggest LMWH offers advantages, such as reduced risks of bleeding and thromboembolism, while others report higher bleeding risks compared to unfractionated heparin [10,11]. Additionally, LMWH is contraindicated in patients with significant renal impairment [10,11].

According to the 2021 recommendations by the European Society of Cardiology (ESC) and European Association for Cardiothoracic Surgery (EACTS), unfractionated heparin and LMWH can be used as anticoagulant bridging therapies with comparable efficacy and safety [12]. Similarly, the 2020 guidelines from the American College of Cardiology and the American Heart Association (ACC/AHA) indicate that anticoagulant bridging therapy is appropriate for patients with mechanical heart valve replacement to reduce the risk of thromboembolism associated with temporary discontinuation of anticoagulants [13]. The ACC/AHA guidelines recommend initiating unfractionated heparin or LMWH from 36 to 48 hours before surgery if the INR falls below the therapeutic threshold (2.0 or 2.5) [13]. Unfractionated heparin should be discontinued for four to six hours, and LMWH for 12 hours before the procedure is completed [13].

The use of unfractionated heparin and LMWH has been extensively studied; however, randomized controlled trials comparing the safety and efficacy of bridging anticoagulation therapy in patients with mechanical heart valve replacement, particularly those undergoing non-cardiac surgery, remain limited [11,14]. Furthermore, detailed clinical evidence regarding the specific outcomes of each intervention is still scarce [15]. Therefore, the aim of this study was to compare the safety and outcomes of unfractionated heparin and LMWH in patients with mechanical heart valve replacement undergoing non-cardiac surgery.

Methods

Study design and setting

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were adhered to in the execution of this systematic review and meta-analysis [16]. The research question focused on the comparative safety and outcomes of unfractionated heparin and LMWH regarding thrombocytopenia, all-cause mortality, major bleeding, minor bleeding, thromboembolism, and valve thrombosis.

Search strategy

As of June 11, 2023, a systematic search of three databases (PubMed, ScienceDirect, and Cochrane Library) was conducted to identify experimental studies and randomized clinical trials reporting clinical outcomes such as thrombocytopenia, all-cause mortality, major bleeding, minor bleeding, thromboembolism, and valve thrombosis.

The search terms employed included combinations of: “outcome” AND “non-cardiac surgery” AND “major adverse cardiac event” OR “mortality” AND “bleeding” AND “mechanical

heart valve" AND "heparin" OR "enoxaparin" AND "low-molecular-weight heparin" AND "safety" AND "valve thrombosis" OR "thromboembolism" AND "thrombocytopenia".

Eligibility criteria

The target population consisted of patients who had undergone mechanical heart valve replacement (without restriction to valve location) and were scheduled for non-cardiac surgery. The details of the eligibility criteria are presented in **Table 1**. Studies were excluded if they met the following criteria: (1) significant differences existed in baseline characteristics between groups experiencing MACE and those that did not; (2) follow-up duration was less than 30 days; (3) MACE were not detailed; or (4) study designs were not randomized controlled trials or experimental studies (this includes case reports, review articles, and animal studies).

Table 1. Eligibility criteria of this study following the PICOS framework

PICOS	Inclusion criteria	Exclusion criteria
Population (P)	Patients who had undergone mechanical heart valve replacement (without restriction to valve location) and were scheduled for non-cardiac surgery	Significant differences existed in baseline characteristics between groups experiencing major adverse cardiac events and those that did not
Intervention (I)	Low-molecular-weight heparin	Follow-up duration was less than 30 days
Comparison (C)	Unfractionated heparin	Major adverse cardiac events were not detailed
Outcome (O)	Valve thrombosis, all-cause mortality, major bleeding, minor bleeding, thrombocytopenia	Studies with insufficient data on outcomes
Study design (S)	Randomized controlled trials or experimental studies	Case reports, review articles, animal studies

Screening and data extraction

Data extraction (including author names, country, sample size, mechanical heart valve location, study design, subjects age, follow-up time, LMWH dose, anticoagulant intervention, and outcome) was conducted independently by three researchers (A.B., G.S.N., and R.P.I.M.). We conducted a literature search based on predetermined keywords. After the literature search step, records were screened using tools available on the database website, and duplicates were excluded using Mendeley reference manager software (Elsevier, Amsterdam, Netherlands). Records were then screened manually through meetings and discussions based on title and abstract. If there was a difference of opinion on whether a record should be included, voting was done. Records that did not meet the eligibility criteria in the full-text screening were excluded. All records that pass the full-text screening were included in the study and continued with data analysis. Data were extracted from an identifiable cohort of patients who had previously undergone mechanical heart valve replacement and were receiving non-cardiac surgery to assess the incidence of MACE, minor and major bleeding, thrombocytopenia, thromboembolism, valve thrombosis, and all-cause mortality.

Major bleeding was defined as bleeding at critical postoperative sites (retroperitoneal, intracranial, intraocular, or intraspinal), a hemoglobin decrease of more than 3 g/dL, or the need for transfusion. Minor bleeding was categorized as any bleeding not meeting the criteria for major bleeding. Thrombocytopenia was defined as a platelet count decrease to below 100,000/µL. Thromboembolism was classified as deep vein thrombosis or pulmonary embolism, while valve thrombosis was defined as valvular or cardiac mural thrombus. All-cause mortality was defined as the total number of deaths reported from any cause.

Quality assessment

The quality of the study was assessed using the Risk of Bias (RoB) 2 by the Cochrane Risk of Bias Assessment tool [17]. The RoB 2 is a tool used to analyze a study's bias through several domains based on empirical and theoretical evidence. The overall risk of each study was classified into "high risk of bias," "some concerns," or "low risk of bias" [17].

Statistical analysis

Categorical variables were analyzed as proportions and summarized using a Mantel-Haenszel random-effects model, with relative risk (RR) as the effect size and 95% confidence intervals (95%CI). Heterogeneity was evaluated using Higgins I^2 statistic, where I^2=0% indicates no heterogeneity, and values above 50% suggest high heterogeneity. Publication bias was assessed through funnel plots. Data analysis was performed using Review Manager 5.4.1 software (Nordic Cochrane Center, Cochrane Collaboration, Copenhagen, Denmark). A *p*-value of less than 0.05 was considered statistically significant.

Results

Characteristics of the included studies

A total of 496 potentially relevant studies were initially identified, and following a review of titles and abstracts, 423 studies were excluded (**Figure 1**). Subsequently, 73 studies underwent a more detailed assessment, which was further narrowed down to 12 studies. Finally, six studies were selected for inclusion in the final analysis (**Figure 1**), with the attributes of each study presented in **Table 2**. All of the included studies employed experimental designs. Four studies were conducted in the United States of America (USA) [5,14,18,19], and two were carried out in Europe (Netherlands and Romania) [11,20]. The publication years varied significantly, ranging from 2004 to 2022. The observation period for the studies ranged from 30 to 90 days following non-cardiac surgery. The most commonly used LMWH in these studies was enoxaparin.

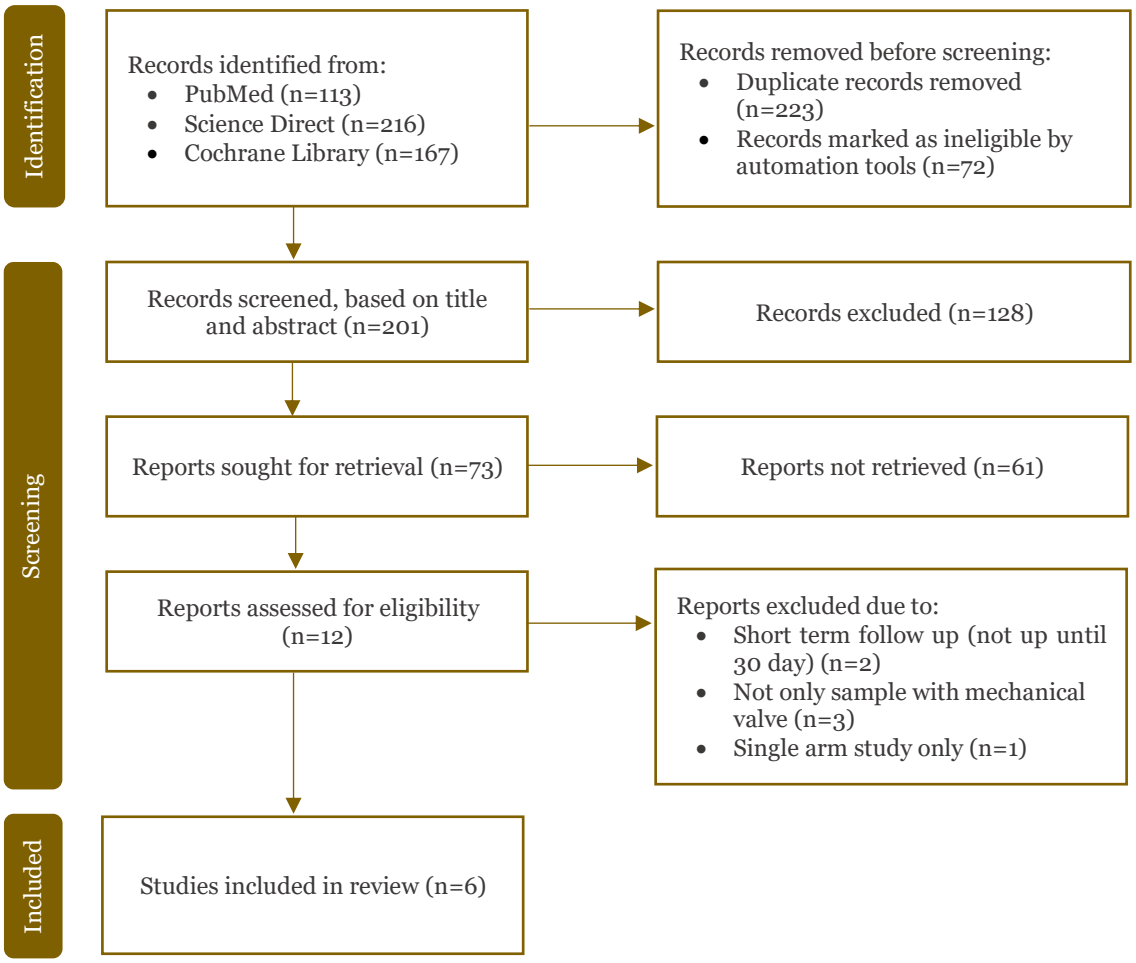

Figure 1. PRISMA flowchart diagram of the study identification process.

Table 2. Characteristics of the included studies

Author	Country	Number of samples	Mechanical heart valve location	Study design	Age (years)	Follow-up time (day)	Low-molecular-weight heparin (LMWH) dose	Anticoagulant intervention	Outcome
Spyropoulos *et al.*, 2006 [19]	USA	901	Aortic 42% and mitral 58%	Multicenter prospective	65.1–68.2	30	1 mg/kg BID, enoxaparin	180 UFH, 721 enoxaparin	Thromboembolism, death, thrombocytopenia, major and minor bleeding
Spyropoulos *et al.*, 2008 [14]	USA	245	Aortic 51%, mitral 37%, both 12%	Multicenter prospective	65–66	30	1 mg/kg BID, enoxaparin	72 UFH, 172 LMWH	Major and minor bleeding, thromboembolism, death, length of stay, thrombocytopenia, valvular thrombus
Spyropoulos *et al.*, 2004 [18]	USA	66	N/A	Prospective single center	63–67	30	1 mg/kg BID, enoxaparin	26 UFH, 40 LMWH	Valvular thrombus, thromboembolism (vein and arterial), death, major and minor bleeding, thrombocytopenia
Daniels *et al.*, 2009 [5]	USA	556	372 aortic, 136 mitral, 48 multiple valve	Prospective study	64–67	90	Ardeparin (130 anti-Xa IU/kg BID), dalteparin 100 anti-Xa IU/kg BID), enoxaparin 1 mg/kg BID	UFH 99, LMWH 243, No UFH 213	Myocardial infarction, major and minor bleeding, death
Hart *et al.*, 2017 [20]	Netherlands	238	174 aortic, 42 mitral, 23 both valves	Prospective study, multicenter	60–70	30	Subcutaneous LMWH BID	UFH 84, LMWH 154	Major bleeding, thrombocytopenia, thromboembolism, death
Iliuta *et al.*, 2022 [11]	Romania	380	Dominant with single mitral and aortic, few mitral + aortic, triple valve, mitral + tricuspid, aortic + tricuspid	Randomized controlled trial	50–70	30	Enoxaparin 85 IU/kg BID → 1 mg/kg BID	192 LMWH, 188 UFH	Mortality, prosthesis thrombosis, length of stay, major and minor bleeding, thrombocytopenia, gluteal ulceration

BID: twice daily; IU: international unit; UFH: unfractionated heparin

Risk of bias

The RoB 2 was employed to evaluate the risk of bias and the quality of the studies included in this analysis; the results of the assessment are summarized in **Figure 2**. One study demonstrated a low risk of bias [11], while the remaining five studies were deemed to have some concerns [5,14,18-20]. This distinction arises from the fact that only one study was a true randomized clinical trial with a detailed methodology, whereas the others used a registry.

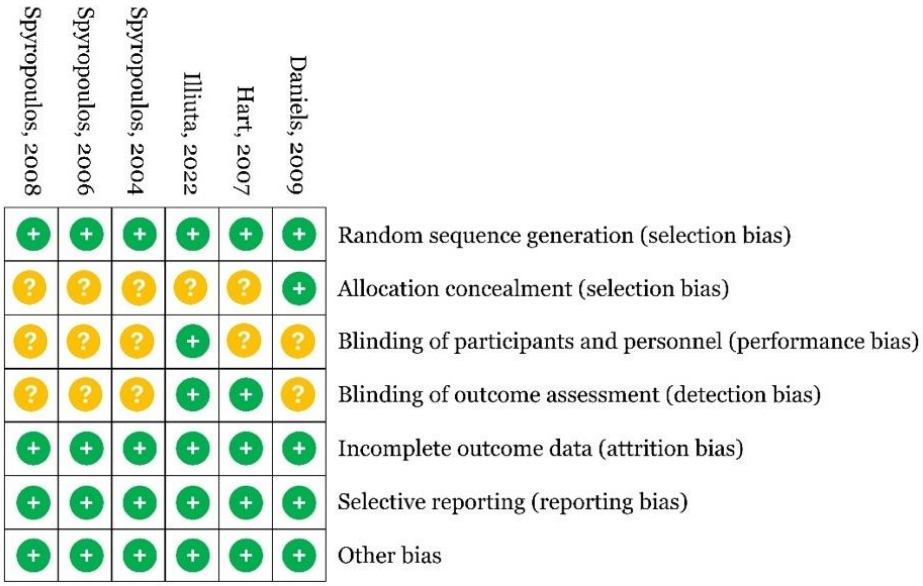

Figure 2. Risk of bias of the included studies.

Association between unfractionated heparin and LMWH on the incidence of thromboembolism and valve thrombosis

Six studies were included to assess the association between type of heparin (unfractionated heparin and LMWH) on the incidence of thromboembolism and valve thrombosis [5,11,14,18-20]. Incidence of thromboembolism and valve thrombosis did not differ significantly among patients with mechanical heart valves undergoing non-cardiac surgery, regardless of whether unfractionated heparin or LMWH was used as the anticoagulant (RR: 0.61; 95%CI: 0.36–1.04; p=0.07; heterogeneity χ^2=1.96; I^2=0%; p-heterogeneity of 0.86; df=5) (**Figure 3**). The publication bias, analyzed using a funnel plot, suggested a low risk of publication bias (**Figure 4A**).

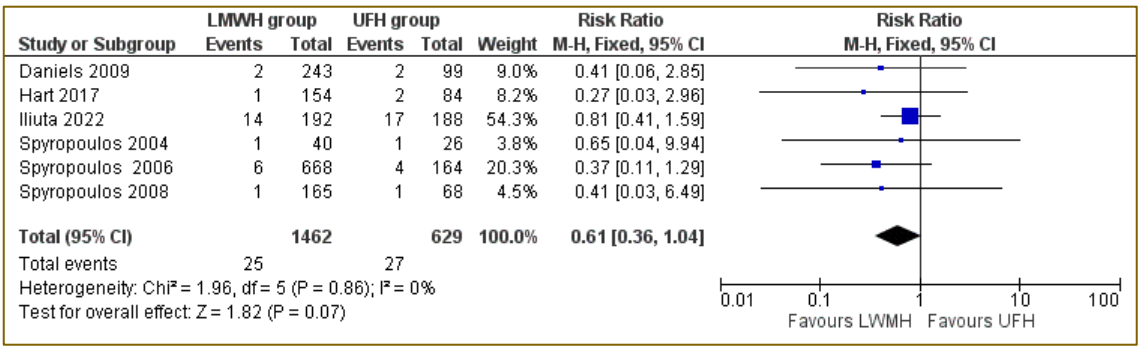

Figure 3. Forest plot of the overall effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on thromboembolism and valve thrombosis.

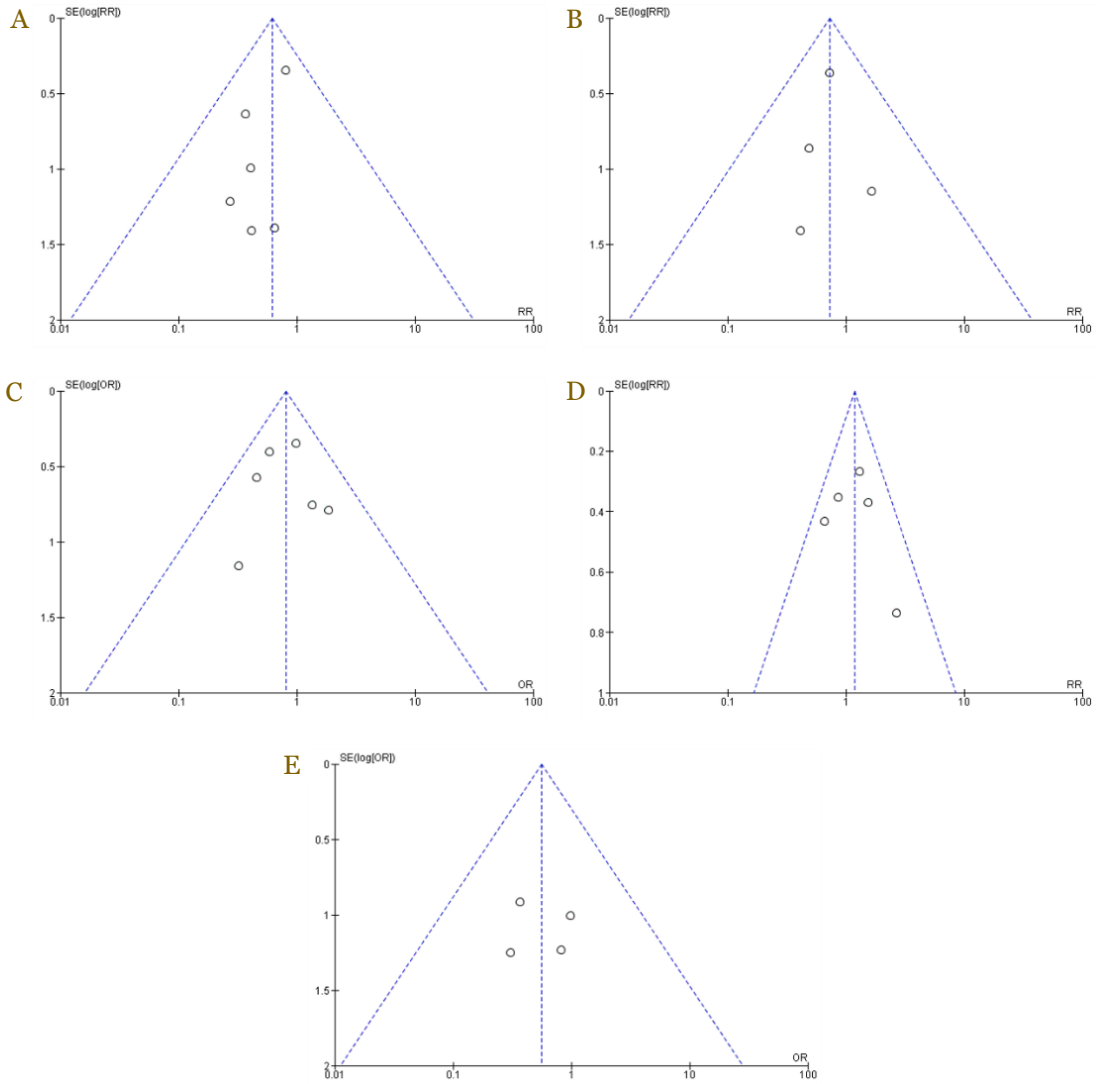

Figure 4. Funnel plot of studies assessing the effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on thromboembolism and valve thrombosis (A), all-cause mortality (B), major bleeding events (C), minor bleeding events (D), and thrombocytopenia (E).

Association between unfractionated heparin and LMWH on the incidence of all-cause mortality events

Four studies were included in the analysis [11,14,19,20]. The incidence of all-cause mortality in patients with mechanical heart valves who underwent non-cardiac surgery while using unfractionated heparin or LMWH as anticoagulants did not differ significantly (RR: 0.73; 95%CI: 0.40–1.35; p=0.32; heterogeneity χ^2=0.87; I^2=0%; p-heterogeneity of 0.83; df=3) (**Figure 5**). The publication bias, analyzed using a funnel plot, suggested a low-risk of publication bias (**Figure 4B**).

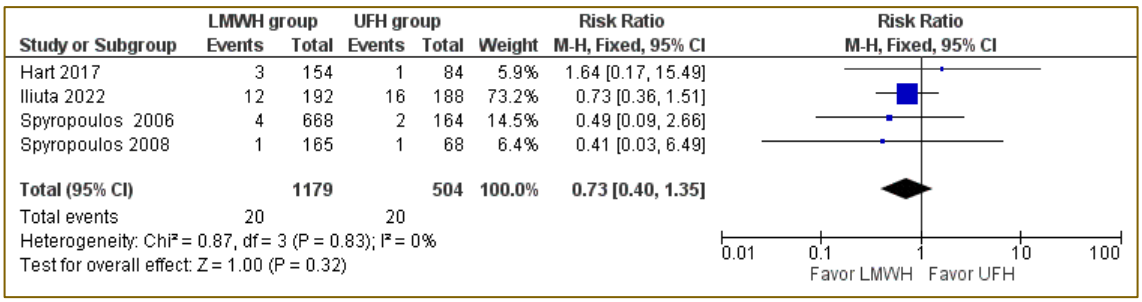

Figure 5. Forest plot of the overall effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on the overall effect of all-cause mortality.

Association between unfractionated heparin and LMWH on the incidence of major bleeding events

Six studies were included in the analysis [5,11,14,18-20]. The frequency of major bleeding did not differ significantly between patients with mechanical heart valves undergoing non-cardiac surgery using unfractionated heparin or LMWH as anticoagulants (RR: 0.81; 95%CI: 0.53–1.23; p=0.33; heterogeneity χ^2=4.14; I^2=0%; p-heterogeneity of 0.53; df=5) (**Figure 6**). The publication bias, analyzed using a funnel plot, indicated a low risk of publication bias (**Figure 4C**).

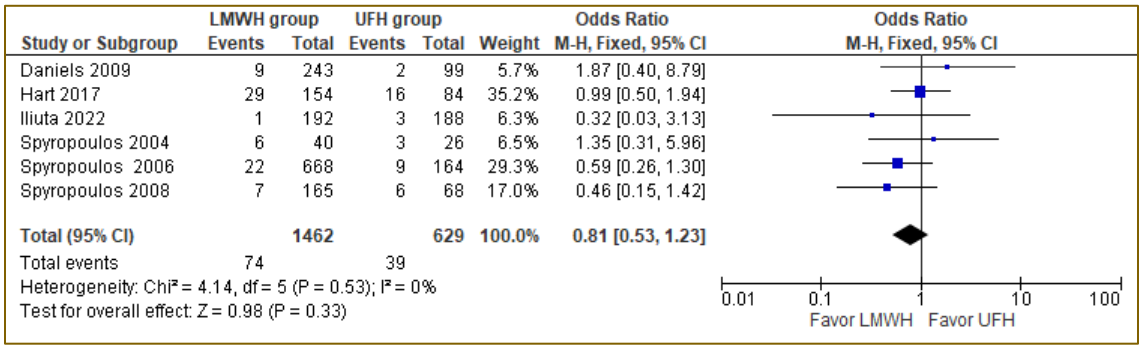

Figure 6. Forest plot of the overall effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on major bleeding events.

Association between unfractionated heparin and LMWH on the incidence of minor bleeding events

Five studies were included in the analysis [5,11,14,18,19]. Patients with mechanical heart valves undergoing non-cardiac surgery while using unfractionated heparin or LMWH as anticoagulants did not exhibit a statistically significant difference in the incidence of minor bleeding (RR: 1.18; 95%CI: 0.86–1.62; p=0.31; heterogeneity χ^2=4.50; I^2=11%; p-heterogeneity of 0.34; df=4) (**Figure 7**). The publication bias, analyzed using a funnel plot, indicated a low-risk of publication bias (**Figure 4D**).

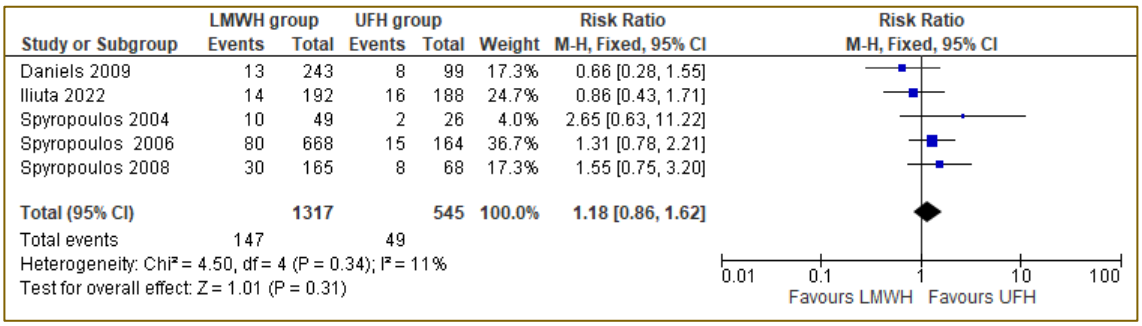

Figure 7. Forest plot of the overall effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on minor bleeding events.

Association between unfractionated heparin and LMWH on the incidence of thrombocytopenia

Four studies were included in the analysis [11,14,18,19]. The incidence of thrombocytopenia did not differ significantly among patients with mechanical heart valves undergoing non-cardiac surgery, regardless of whether unfractionated heparin or LMWH was used as the anticoagulant (RR: 0.56; 95%CI: 0.20–1.59; p=0.27; heterogeneity χ^2=0.85; I^2=0%; p-heterogeneity of 0.27; df=3) (**Figure 8**). The publication bias, analyzed using a funnel plot, showed a low risk of publication bias (**Figure 4E**).

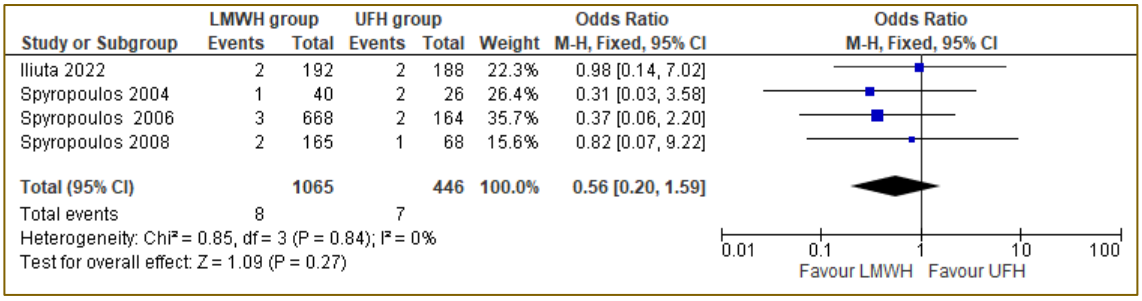

Figure 8. Forest plot of the overall effect of unfractionated heparin and low-molecular-weight heparin (LMWH) on thrombocytopenia.

Discussion

Patients undergoing valve replacement surgery will generally require warfarin which serves as a preventive agent for thromboembolic events [21]. This also applies to patients who already have mechanical heart valves who undergo elective non-cardiac surgery with the same purpose [22]. Since warfarin administration is given as early as 48 hours postoperatively, heparin is often prescribed as a thromboembolic preventive agent as bridging anticoagulants [23].

Our meta-analysis indicated that the incidence of thromboembolism and valve thrombosis in patients with mechanical heart valves undergoing non-cardiac surgery while using unfractionated heparin or LMWH anticoagulants did not differ significantly (RR: 0.61; 95%CI: 0.36–1.04; p=0.07). This finding aligns with a previous meta-analysis, which found that the risk of major bleeding events (OR: 0.66; 95%CI: 0.36–1.19) and thromboembolic events (OR: 0.67; 95%CI: 0.27–1.68) was not significantly different between LMWH and unfractionated heparin/vitamin K antagonist in patients with mechanical heart valves [24]. Another meta-analysis demonstrated a lower risk of thrombosis (RR: 0.67; 95%CI: 0.50–0.88) and venous thromboembolism (RR: 0.68; 95%CI: 0.51–0.90) among patients treated with LMWH [25]. Furthermore, the study found that LMWH reduced the risk of death (OR: 0.54; 95%CI: 0.45–0.65), thrombocytopenia (OR: 0.26; 95%CI: 0.03–2.38), and pulmonary embolism (OR: 0.56; 95%CI: 0.50–0.62) in trauma patients [25].

The risk of thromboembolic events following valve placement is influenced by the type of mechanical prosthesis and its anatomical location [26]. Among all mechanical heart valve types, the bileaflet valve type has the lowest risk of thrombosis, whereas the caged ball valve type is associated with the highest thrombogenic potential [26]. Additionally, valves located in the mitral region are more susceptible to thromboembolism due to the slower blood flow through the mitral orifice [27]. A previous study indicated that regular administration of antiplatelet agents and oral anticoagulants could reduce the embolic incidence rate to as low as one per 100 patient-years [28]. However, other risk factors, including atrial fibrillation, a history of thromboembolism, left ventricular dysfunction, or hypercoagulable conditions, also significantly influence thromboembolic occurrences in patients [28].

In the present study, the use of unfractionated heparin or LMWH anticoagulants did not significantly affect the incidence of major and minor bleeding events in patients with mechanical heart valves undergoing non-cardiac surgery (RR: 0.81; 95%CI: 0.53–1.23; p=0.33 and RR: 1.18; 95%CI: 0.86–1.62; p=0.31, respectively). Patients undergoing non-cardiac surgery are considered to have a reduced risk of bleeding compared to those undergoing cardiac surgery, primarily because the patient does not receive extracorporeal circulation [29]. Nevertheless, the incidence rates of major bleeding reported were notably high, at 19% for LMWH and 19% for unfractionated heparin [20]. Furthermore, a previous meta-analysis involving 25 studies and 35,944 patients demonstrated that patients who underwent elective surgery or invasive procedures while using oral anticoagulants (e.g., heparin) as bridging therapy had a higher risk of bleeding compared to those who did not receive bridging therapy [30].

LMWH preparations are generally preferred over unfractionated heparin due to the ability to adjust dosing based on the patient's renal function and the option to administer a fixed dose according to body weight, which does not require continuous dose adjustments [31]. In

comparison to unfractionated heparin, the occurrence of heparin-induced thrombocytopenia is relatively less common with LMWH [32]. However, unfractionated heparin offers a faster recovery of anticoagulant effects compared to LMWH [32]. A study reported no significant difference in the incidence of major complications among patients with atrial fibrillation undergoing radiofrequency ablation who were administered either LMWH or unfractionated heparin as bridging anticoagulants (2.9% vs 4.1%); the study also noted five thromboembolic events (0.7%) and 24 major bleeding events (3.4%) [33]. Thus, both unfractionated heparin and LMWH effectively reduce the risk of thromboembolic and bleeding complications in patients with mechanical heart valves undergoing non-cardiac surgery without appreciable variations in outcomes [33].

The incidence of all-cause mortality in patients with mechanical heart valves undergoing non-cardiac surgery while using unfractionated heparin or LMWH anticoagulants did not show a significant difference in the present study (RR: 0.73; 95%CI: 0.40–1.35; p=0.32). These findings are consistent with a previous meta-analysis which reviewed six trials involving 1,366 patients, with 852 receiving LMWH and 514 receiving unfractionated heparin, and found no significant difference in all-cause mortality between patients receiving LMWH or unfractionated heparin after non-cardiac or cardiac surgery (RR: 0.52; 95%CI: 0.16–1.66; p=0.271) [34]. A study found that when controlling for baseline characteristics, such as sex, hypertension history, and the presence of cardiac conditions like atrial fibrillation, there was no significant difference in mortality between the groups receiving LMWH or unfractionated heparin therapy [35]. Conversely, a study reported that unfractionated heparin was associated with a higher mortality rate compared to LMWH [11].

In the present study, no statistically significant difference was observed in the incidence of thrombocytopenia among patients with mechanical heart valves undergoing non-cardiac surgery while receiving unfractionated heparin or LMWH anticoagulants (RR: 0.56; 95%CI: 0.20–1.59; p=0.84). These results contrast with a previous meta-analysis which identified LMWH had a lower incidence of thrombocytopenia compared to unfractionated heparin [36]. Similarly, another study reported that patients on LMWH had a significantly lower risk of developing thrombocytopenia compared to those on unfractionated heparin [37]. The different results we found may be due to the different populations included in the meta-analysis. We specifically included patients undergoing non-cardiac surgery who were given heparin (either LMWH or UFH) as bridging anti-coagulant therapy, whereas one previous meta-analysis included patients undergoing all types of surgery [37]and another meta-analysis included only patients undergoing orthopedic surgery [36].

Unfractionated heparin and LMWH exert their anticoagulant effects through antithrombin activation [38]. Upon binding to antithrombin, the pentasaccharides induce conformational changes in the antithrombin molecule, accelerating its interaction with factor Xa and thrombin [38]. Most unfractionated heparin chains contain at least 18 saccharide units, enabling them to form ternary complexes with antithrombin and thrombin [38]. In contrast, the LMWH-antithrombin complex primarily binds to factor Xa, catalyzing its inactivation [31]. Therefore, LMWH exhibits greater activity against factor Xa compared to factor IIa, whereas unfractionated heparin activates both factors [31]. In addition, both unfractionated heparin and LMWH promote the release of tissue factor pathway inhibitors from the damaged endothelium, enhancing their inhibitory effects on factor Xa and factor VIIa, thereby supporting endogenous anticoagulant mechanisms[38,39]. Due to its reduced binding to plasma, endothelial, and macrophage proteins, LMWH has a longer half-life and greater bioavailability than unfractionated heparin, providing a more consistent anticoagulant effect[39,40]. Furthermore, LMWH has less affinity for platelets, von Willebrand factor, and endothelial cells compared to unfractionated heparin [39]. As a result, LMWH has a reduced effect on platelets, lowering the risk of thrombocytopenia, and a milder effect on endothelial cells, reducing the risk of bleeding [39,41]. While monitoring is typically unnecessary for patients treated with LMWH, plasma anti-Xa levels should be assessed in specific populations, such as those with renal impairment or significant deviations in body weight [42-45].

This study has limitations in the form of a small number of clinical trials that compare the outcomes and safety of LMWH and unfractionated heparin as bridging anticoagulants. This

causes the results of this meta-analysis to only reflect the effects and safety of LMWH and unfractionated heparin in a limited population. In addition, most studies on related topics that have been conducted are mostly in Europe and the USA, which means the results obtained still cannot be generalized to the entire population in the world. The results of this meta-analysis included the outcomes and safety in a short period, due to the short follow-up study time included. The existence of these limitations will create a knowledge gap that needs to be closed by conducting further research in larger population size, multicenter, and carried out over a longer period of time.

Conclusion

Patients with mechanical heart valves undergoing non-cardiac surgery, unfractionated heparin and LMWH showed no significant differences in efficacy or outcomes, including risks of thromboembolism, thrombosis, mortality, hemorrhage, or thrombocytopenia. Further randomized trials are needed to confirm these findings.

Ethics approval

Not required.

Acknowledgments

None to declare.

Competing interests

All the authors declare that there are no conflicts of interest.

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Underlying data

Derived data supporting the findings of this study are available from the corresponding author on request.

Declaration of artificial intelligence use

We hereby confirm that no artificial intelligence (AI) tools or methodologies were utilized at any stage of this study, including during data collection, analysis, visualization, or manuscript preparation. All work presented in this study was conducted manually by the authors without the assistance of AI-based tools or systems.

How to cite

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