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Aspirin—A New Concept of Anticoagulation After Joint Arthroplasty Postprint

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Abstract

Venous thromboembolism is a serious complication following joint replacement surgery, and effective postoperative anticoagulation represents its primary preventive and therapeutic measure. Low molecular weight heparin, factor Xa inhibitors, and other anticoagulant agents are currently the first-line medications for venous thromboembolism prophylaxis. Although their efficacy is well-established with relatively low bleeding risk, they are associated with limitations including high cost and inconvenience in administration and storage. In recent years, some guidelines and studies have proposed that aspirin, an antiplatelet agent, may also be utilized for venous thromboembolism prevention after joint replacement surgery. Aspirin demonstrates comparable prophylactic efficacy to anticoagulants, a favorable safety profile, and advantages such as low cost, no requirement for monitoring, and convenient oral administration; furthermore, low-dose aspirin alone can provide adequate preventive effects. Additional research suggests that aspirin carries a lower perioperative bleeding risk compared to anticoagulant drugs. In summary, aspirin represents a new option for postoperative anticoagulation following joint replacement surgery, offering established efficacy and good safety for venous thromboembolism prevention.

Full Text

Aspirin: A New Perspective on Anticoagulation After Joint Arthroplasty

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Abstract

Venous thromboembolism (VTE) is a serious complication following joint arthroplasty, and effective postoperative anticoagulation represents the primary preventive and therapeutic measure. While anticoagulants such as low-molecular-weight heparin and factor Xa inhibitors are currently the preferred drugs for VTE prophylaxis, they remain associated with issues including high costs and inconvenient administration and storage despite their proven efficacy and low bleeding risk. In recent years, several guidelines and studies have suggested that aspirin, an antiplatelet agent, may also be used for VTE prevention after joint arthroplasty. Aspirin demonstrates comparable prophylactic efficacy to anticoagulants with favorable safety profiles, offering advantages such as low cost, no requirement for monitoring, and convenient oral administration. Moreover, low-dose aspirin appears sufficient for preventive purposes. Some studies further indicate that aspirin carries lower perioperative bleeding risk compared to anticoagulants. In summary, aspirin represents a promising new option for VTE prophylaxis after joint arthroplasty, with confirmed efficacy and good safety.

Keywords: Aspirin; Venous Thromboembolism; Prevention; Arthroplasty

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Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a relatively common yet serious complication following joint arthroplasty. PE constitutes a major cause of unexpected in-hospital mortality after orthopedic surgery. Active and effective pharmacological anticoagulation constitutes an important measure for VTE prevention and treatment after joint arthroplasty [1]. While anticoagulants such as low-molecular-weight heparin and factor Xa inhibitors demonstrate proven efficacy with low bleeding risk and are widely recommended for postoperative VTE prophylaxis, they suffer from drawbacks including high cost and inconvenient administration. Aspirin inhibits platelet aggregation and prevents arterial thrombosis, and is currently widely used for preventing and treating cardiovascular and cerebrovascular diseases. Recent studies suggest aspirin may also prevent venous thrombosis [2,3,4], offering advantages of low cost and convenient use compared to anticoagulants. However, the efficacy and safety of aspirin for VTE prophylaxis after joint arthroplasty remain controversial [2,5]. This review summarizes the current research status in this area.

I. Aspirin' s Antithrombotic Mechanism and Clinical Application

First introduced as an over-the-counter analgesic in 1899, aspirin' s effects on coagulation were first reported by Rudolf Singer in 1945. In 1970, John Vane elucidated aspirin's inhibitory effects on prostaglandins, and subsequent research further revealed its mechanism: aspirin irreversibly acetylates serine residues of cyclooxygenase (COX), thereby blocking the binding of the COX catalytic site to its substrate and causing permanent COX inactivation, which inhibits prostaglandin production.

Platelet aggregation plays a crucial role in thrombosis. Thromboxane A2 (TXA2), a potent platelet aggregation stimulator and vasoconstrictor produced by platelets, significantly promotes thrombus development. COX-1 serves as the key catalytic enzyme in TXA2 synthesis in platelets. By irreversibly inhibiting platelet COX-1 activity, aspirin reduces TXA2 synthesis, suppresses platelet aggregation, and thereby inhibits thrombus formation. Since platelets lack nuclei and cannot synthesize new COX-1, aspirin' s inhibition of platelet TXA2 synthesis is permanent. With a platelet lifespan of approximately 7-10 days and a daily turnover rate of about 10%, coagulation function only returns to normal after 5-6 days of discontinuation when more than 50% of platelets have been renewed. This sustained and stable antiplatelet aggregation effect is crucial for preventing arterial thrombosis, and both domestic and international guidelines recommend routine aspirin use for primary and secondary prevention of cardiovascular and cerebrovascular diseases.

In recent years, aspirin' s role in preventing venous thrombosis such as DVT and PE has gradually attracted attention. Its mechanisms for venous thrombosis prevention may involve inhibition of critical coagulation steps or structures including platelet function, prothrombin activation, and fibrin formation [3]. Some histological studies suggest that platelet activation and aggregation also occur during venous thrombogenesis. Platelet -granules and other intracellular substances released during this process significantly promote venous thrombus formation, and the cell membranes provided by platelet aggregation are important for activating and functioning of coagulation substances such as thromboplastin, fibrinogen, and vWF. This represents the platelet-dependent mechanism for aspirin' s venous thrombosis prevention [3,6]. Additionally, aspirin may inhibit venous thrombosis through platelet-independent pathways. Research indicates aspirin can reduce tissue factor expression, increase tissue factor pathway inhibitor (TFPI) secretion, and acetylate prothrombin and platelet membrane components, thereby reducing thrombin activation and activity and inhibiting venous thrombosis. This inhibitory effect is particularly significant in thrombosis caused by intimal injury [3,7-9]. In later stages of thrombosis, aspirin acetylates lysine residues of fibrinogen, reducing fibrinogen polymerization capacity, altering fibrin clot structure, increasing solubility, decreasing thrombus stability, and promoting venous thrombus degradation [10-12]. These basic research findings on aspirin' s mechanisms for venous thrombosis prevention provide a theoretical foundation for its clinical application.

II. VTE Pathogenesis and Prevention

VTE represents a relatively common serious complication after major orthopedic joint surgery, encompassing DVT and PE. DVT primarily manifests as lower limb swelling and muscle pain, significantly impairing postoperative joint function recovery and patient satisfaction. PE is a life-threatening complication and currently constitutes an important cause of unexpected in-hospital death after major orthopedic surgery.

The classic Virchow' s triad is considered the primary mechanism underlying VTE development. Virchow' s triad posits that hypercoagulability, blood stasis, and vascular endothelial injury represent the three major risk factors for VTE. After orthopedic joint arthroplasty, reduced lower limb activity and diminished muscle pump function lead to stasis of lower extremity blood flow; surgical bleeding, intraoperative fluid loss, and inadequate postoperative fluid replacement cause hemoconcentration; advanced patient age and postoperative inflammatory responses can produce hypercoagulable states; and surgical manipulation such as traction and compression can cause lower extremity vascular intimal injury. These three factors contribute to the high incidence of VTE after orthopedic joint arthroplasty.

Since the widespread implementation of the 2009 Chinese Guidelines for Prevention of Venous Thromboembolism in Major Orthopedic Surgery, the incidence of DVT after total joint arthroplasty (TJA) in China has significantly decreased, fully demonstrating that active and effective preventive measures constitute the most important strategy for managing postoperative DVT [1]. The 2016 Chinese Guidelines for Prevention of Venous Thromboembolism in Major Orthopedic Surgery (hereinafter referred to as the 2016 Guidelines) recommend that all patients undergoing major orthopedic surgery should receive pharmacological thromboprophylaxis after adequate assessment of thrombotic and bleeding risks [1]. Currently used anticoagulants in China mainly include unfractionated heparin, low-molecular-weight heparin, factor Xa inhibitors, vitamin K antagonists, and antiplatelet drugs. Among these, low-molecular-weight heparin, fondaparinux, apixaban, and rivaroxaban are specifically recommended in the 2016 Guidelines for thromboprophylaxis after joint arthroplasty [1].

Although unfractionated heparin and vitamin K antagonists can effectively reduce perioperative VTE risk after joint arthroplasty, they have gradually fallen out of favor due to narrow therapeutic windows, high individualization requirements, relatively high bleeding risk, and need for routine coagulation monitoring. Low-molecular-weight heparin (LMWH) demonstrates proven efficacy for postoperative VTE prophylaxis with relatively low bleeding risk, but it requires subcutaneous injection and carries a risk of heparin-induced thrombocytopenia (HIT). Factor Xa inhibitors are new oral anticoagulants (NOACs) that offer convenient administration and low bleeding risk. Most studies confirm their efficacy for VTE prophylaxis, and they feature wide therapeutic windows without requiring monitoring, representing a new direction in VTE pharmacological prevention. However, NOACs are expensive, substantially increasing patients' economic burden [13].

III. Aspirin for VTE Prevention After TJA

As a representative antiplatelet agent, aspirin demonstrates proven efficacy and safety for preventing arterial thrombotic diseases and is widely used for primary and secondary prevention of cardiovascular and cerebrovascular diseases. In venous thrombotic disease, an earlier meta-analysis reported that antiplatelet

therapy (with aspirin as the representative) significantly reduced perioperative DVT and PE incidence in 8,000 high-risk postoperative patients from plastic and general surgery [4]. Both the WARFASA and ASPIRE prospective double-blind randomized controlled trials concluded that aspirin significantly reduces recurrent venous thrombosis incidence [3]. However, controversy remains regarding whether aspirin can serve as routine prophylaxis after joint arthroplasty.

The earliest report of aspirin for VTE prevention after joint arthroplasty came from Salzman et al. in 1971, who suggested aspirin could prevent venous thrombosis after total hip arthroplasty (THA) with efficacy and bleeding risk similar to warfarin [14]. However, due to limited research evidence for aspirin' s VTE prevention and the rapid development of effective, low-risk anticoagulants such as LMWH, aspirin never gained widespread application for TJA VTE prophylaxis. In recent years, with widespread implementation of postoperative thromboprophylaxis, problems associated with anticoagulants like LMWH—including economic burden, inconvenient administration, and bleeding risk—have become increasingly apparent. As an economical, convenient, and safe classic antithrombotic drug, aspirin has once again attracted widespread scholarly attention regarding its potential for VTE prevention after joint arthroplasty.

3.1 Efficacy of Aspirin for VTE Prevention After TJA The 9th edition of the ACCP (American College of Chest Physicians) guidelines for thrombosis treatment and prevention (2012) and the AAOS (American Academy of Orthopaedic Surgeons) guidelines both recommend aspirin, along with LMWH and rivaroxaban, for VTE prophylaxis after THA or total knee arthroplasty (TKA), with evidence grade IB [15-16]. Numerous recent studies also support aspirin' s utility for VTE prevention after joint arthroplasty.

Although multiple guidelines including ACCP and AAOS recommend aspirin for venous thrombosis prevention, anticoagulants such as LMWH and factor Xa inhibitors remain the most commonly used drugs for VTE prophylaxis after TJA. Some current studies suggest aspirin is also effective for post-TJA VTE prevention. The PEP study published in *Lancet* in 2000 concluded that aspirin effectively reduces PE and DVT incidence in high-risk VTE patients. This study enrolled 13,356 patients with femoral neck and proximal femur fractures and 4,088 patients undergoing elective joint arthroplasty, randomly assigning them to receive either 160 mg aspirin or placebo. In hip fracture patients, VTE incidence was 1.6% (105/6,679) in the aspirin group versus 2.5% (165/6,677) in the placebo group, representing approximately a one-third reduction with aspirin (P=0.0003). For fatal pulmonary embolism, aspirin significantly reduced PE incidence compared to placebo (0.3% vs. 0.6%, P=0.002). In elective arthroplasty patients, VTE incidence was 1.1% (23/2,047) in the aspirin group versus 1.4% (28/2,041) in the placebo group, though this difference was not statistically significant (P=0.4) [17].

David R. Anderson et al. investigated the efficacy of sequential anticoagulant-to-aspirin therapy for VTE prevention after joint arthroplasty. Anderson' s 2010

study found that LMWH followed by aspirin for extended VTE prophylaxis after THA showed no significant difference in efficacy compared with continued LMWH use (aspirin vs. LMWH: 0.3% vs. 1.3%, non-inferiority test: P<0.001, superiority test: P=0.22) [18]. Another study compared rivaroxaban followed by aspirin versus continued rivaroxaban for post-arthroplasty VTE prophylaxis, finding no statistically significant difference in preventive efficacy (aspirin vs. rivaroxaban: 0.64% vs. 0.70%, non-inferiority test: P<0.001, superiority test: P=0.84) [19].

Chu J et al. retrospectively analyzed VTE incidence in 231,780 TKA patients and 110,621 THA patients receiving three different prophylactic regimens: aspirin alone, anticoagulants alone, or aspirin combined with anticoagulants. Results showed that VTE incidence with aspirin alone was similar to that with anticoagulants, with no significant association between aspirin use and VTE risk (TKA patients OR: 0.34 [0.24-0.48]; THA patients OR: 0.82 [0.45-1.51]) [20]. In 2014, Raphael et al. followed 2,800 TJA patients receiving aspirin prophylaxis and 26,123 patients receiving warfarin for six months, finding lower VTE incidence in the aspirin group (DVT: 0.29% vs. 0.99%, P<0.001; PE: 0.14% vs. 1.07%, P<0.001). The authors concluded that aspirin combined with intermittent pneumatic compression devices provides effective VTE prophylaxis with reduced complications [21]. A 2017 meta-analysis including 110,643 patients concluded that aspirin could be used for VTE prevention from various causes while reducing bleeding-related complications, with efficacy similar to rivaroxaban and LMWH [22].

A 2014 prospective randomized controlled study compared the efficacy of aspirin, rivaroxaban, and LMWH for VTE prevention after TKA, concluding that rivaroxaban was superior to aspirin (3 [2.94%] vs. 18 [16.36%], P=0.017), while aspirin showed similar efficacy to LMWH (14 [12.50%] vs. 18 [16.36%], P=0.831) [23]. Yi et al. reported a prospective randomized controlled study showing no significant difference in DVT incidence between aspirin and LMWH followed by rivaroxaban for thromboprophylaxis after TKA (aspirin vs. anticoagulants: 16.7% vs. 18.3%, P=0.5), with no symptomatic VTE detected during follow-up [24]. Retrospective studies by Perez Agaba et al. and Guy Cafri et al. both concluded that aspirin can be used for VTE prevention after joint arthroplasty, with VTE incidence similar to anticoagulants during 2-3 month follow-up periods [25,26].

However, in actual clinical practice, the proportion of patients receiving aspirin alone for VTE prophylaxis after joint arthroplasty remains small. Chu J et al. reported that among 231,780 TKA patients, only 7.5% received aspirin alone for VTE prophylaxis, while among 110,621 THA patients, the proportion was 8.0%. In contrast, patients receiving anticoagulants alone or anticoagulants plus aspirin accounted for 92.5% and 92.0% of TKA and THA patients, respectively. Although this study affirmed the efficacy of aspirin alone for post-arthroplasty VTE prevention, anticoagulants remain the first-choice drugs, with aspirin alone not being a routine option [20]. In clinical practice, aspirin is pri-

marily used for preventing and treating arterial thrombotic diseases. For venous thrombosis, it was previously believed that its antithrombotic mechanism did not align with the pathogenesis of post-TJA venous thrombosis, suggesting potentially weaker preventive effects compared to anticoagulants. In the ACCP-9 guidelines, although aspirin was recommended for post-arthroplasty VTE prevention, LMWH remained the recommended primary prophylactic drug after major orthopedic surgery, with aspirin only as an alternative for patients unable to receive daily subcutaneous injections, and requiring careful risk-benefit assessment regarding potential reduced efficacy [15].

3.2 Safety of Aspirin for VTE Prevention After TJA Drugs used for VTE prevention after joint arthroplasty should effectively prevent venous thrombosis while offering low bleeding risk, cost-effectiveness, and convenient management. Aspirin was previously considered a potential risk factor for perioperative bleeding, with its antiplatelet effects thought to increase perioperative blood loss, transfusion rates, and postoperative drainage, leading to recommendations against its perioperative use [27]. Recent literature has also reported that new oral anticoagulants such as rivaroxaban and dabigatran may increase perioperative bleeding risk and prolong hospital stay [5,23,26].

The PEP study followed 13,356 femoral neck and proximal femur fracture patients for 35 days postoperatively, finding that patients receiving 160 mg aspirin for VTE prophylaxis experienced greater perioperative hemoglobin decline (2.3 g/L vs. 2.0 g/L, $P<0.0001$), higher overall transfusion rates (2.9% vs. 2.4%, $P=0.04$), and greater mean red blood cell transfusion volumes (367 ml vs. 315 ml, $P<0.0001$) compared to placebo. Although aspirin increased perioperative bleeding risk in this study, the follow-up period was limited to the early postoperative period, and no fatal bleeding events occurred [17].

With rapid advances in surgical techniques and hemostatic methods, aspirin' s impact on perioperative bleeding complications has gradually diminished. Most scholars now believe that continued perioperative aspirin use does not increase overt or hidden blood loss. David R. Anderson' s prospective studies published in 2013 and 2018 both reported that anticoagulant therapy followed by 81 mg aspirin for perioperative VTE prevention did not increase perioperative blood loss compared with continued anticoagulant use [18-19]. Patel et al., after analyzing multiple relevant studies, concluded that continued perioperative aspirin use does not increase blood loss when bleeding and thrombotic risks are adequately assessed. For patients with cardiovascular or cerebrovascular diseases such as coronary artery disease or cerebral infarction undergoing major orthopedic surgery, continued perioperative aspirin can reduce the risk of perioperative acute cardiovascular and cerebrovascular events [28]. Studies by Meier et al. and Schwab et al. both concluded that with reasonable and effective perioperative blood management measures for joint arthroplasty, continued perioperative aspirin monotherapy does not increase surgical and postoperative blood loss and can avoid increased thrombotic risk from aspirin withdrawal syndrome [29,30].

Radzak et al.' s retrospective analysis of 377 TKA patients found that patients receiving enoxaparin for thromboprophylaxis experienced significantly greater perioperative hemoglobin decline and higher transfusion rates compared to the aspirin group, while VTE prevention efficacy was similar between enoxaparin and aspirin [31]. Yi et al. reported a prospective controlled study showing that aspirin for VTE prevention after joint arthroplasty resulted in less blood loss than LMWH followed by rivaroxaban (aspirin vs. anticoagulants: 33.4±3.7 g/L vs. 38.1±3.8 g/L, P<0.001), with fewer postoperative subcutaneous ecchymoses [24].

The high risk of VTE after joint arthroplasty can persist for months, and once VTE occurs, patients face high risks of mortality or other sequelae. In comparison, although aspirin may increase perioperative bleeding risk, the benefits of VTE prevention and its consequences outweigh these concerns, making postoperative aspirin prophylaxis advantageous for patients.

Some studies suggest aspirin may reduce postoperative wound complications and avoid rare complications such as heparin-induced thrombocytopenia. Although Zou et al.' s prospective study concluded that rivaroxaban was superior to aspirin for VTE prevention, it found that rivaroxaban (10 mg/day) increased perioperative hidden blood loss compared to aspirin (100 mg/day) during 4-week follow-up (1.71 L vs. 1.30 L, P=0.004). Additionally, rivaroxaban increased perioperative wound complication risk (5 [4.9%] vs. 2 [1.82%], P=0.014) and postoperative subcutaneous ecchymoses (74 [72.55%] vs. 54 [49.09%], P=0.039) [23]. Bloch et al. compared perioperative wound exudate in 1,728 TJA patients and found that dabigatran significantly increased wound leakage compared to LMWH followed by aspirin (20% vs. 5%, P<0.001) [5]. Kulshrestha et al. concluded that aspirin reduced wound-related complication risk after TJA compared to LMWH (2/194 [1%] vs. 56/706 [7.9%], P=0.0005) [32].

Heparin-induced thrombocytopenia (HIT) is a rare complication of perioperative heparin-based thromboprophylaxis. Although its incidence is low (approximately 0.1-1% with LMWH and 3-5% with unfractionated heparin), the resulting coagulation dysfunction can substantially increase perioperative thrombotic and bleeding risks [33,34].

Gastrointestinal reactions are the most common adverse effects of aspirin. The PEP study found that patients receiving 160 mg aspirin for VTE prophylaxis had higher gastrointestinal bleeding risk than placebo [17]. Previous studies have suggested aspirin' s gastrointestinal toxicity is dose-dependent, with lower doses significantly reducing gastrointestinal adverse effects [35]. Feldstein et al. reported that gastrointestinal side effects occurred in 3.2% of patients receiving 325 mg aspirin versus 0.8% of those receiving 81 mg aspirin for unilateral knee arthroplasty VTE prophylaxis, a statistically significant difference [36]. Retrospective studies have also reported similar gastrointestinal adverse reactions with new oral anticoagulants and LMWH. Nielen et al. reported a retrospective study showing that LMWH carried higher gastrointestinal bleeding risk than aspirin in TJA patients (THA HR: 2.0 [0.2–17.2]; TKA HR: 20.9

[1.9–232.3]; Aspirin: Reference), and new oral anticoagulants also showed higher risk than aspirin in total hip replacement patients (HR: 9.4 [1.1–82.0]; Aspirin: Reference) [13].

3.3 Socioeconomic Value of Aspirin for VTE Prevention Aspirin is a basic medication for multiple diseases, offering low cost, reliable safety, and minimal side effects. For anticoagulation therapy, aspirin provides significant price advantages over LMWH and new oral anticoagulants such as rivaroxaban and dabigatran. Pharmacoeconomic studies by Schousboe et al. and Mostafavi et al. demonstrated that aspirin for VTE prophylaxis after TJA significantly reduces medical expenses compared to LMWH or warfarin, with proven efficacy [37-38]. Aspirin' s relatively low bleeding risk for post-arthroplasty VTE prophylaxis eliminates the need for routine hematological monitoring, avoiding repeated blood draws and reducing medical costs. As an oral medication, aspirin offers greater convenience than subcutaneous injections of LMWH, improving patient compliance.

3.4 Dosage and Duration Studies for Aspirin VTE Prophylaxis The AAOS VTE prevention guidelines recommend aspirin at 325 mg twice daily starting on the day of surgery and continuing for 6 weeks. However, due to limited research on the optimal dosage and duration for VTE prevention after joint arthroplasty, the recommendation grade for aspirin dosage and duration is level C [16]. Previous studies have generally followed the AAOS guideline recommendations. In Raphael' s study, patients received aspirin 325 mg twice daily for 6 weeks postoperatively [21]; in Radzak' s study, the same dose was administered for 30 days postoperatively [31]. Guy Cafri's study included 30,499 patients, of whom 5,124 received aspirin for post-arthroplasty anticoagulation, with most receiving 325 mg daily; only 473 patients received 81 mg daily or 162 mg daily [26].

Regarding timing, most studies initiated oral aspirin prophylaxis on the day of surgery, while some used aspirin as supplementary or continuation therapy after anticoagulants. A 2015 retrospective analysis of 9,035 post-arthroplasty patients who received LMWH during hospitalization followed by oral aspirin for 6 weeks post-discharge reported symptomatic VTE incidence of 2.55%, PE incidence of 1.28%, and fatal PE incidence of 0.03% during 6-week follow-up [39]. David R. Anderson' s two prospective studies used aspirin as continuation therapy after anticoagulants, either after 5 days of rivaroxaban or after 10 days of LMWH. Both studies found no significant efficacy difference between switching to aspirin and continuing the original anticoagulant, but switching to aspirin reduced medical expenses and avoided traumatic subcutaneous injections, improving patient compliance [18-19]. No studies have compared the efficacy of aspirin alone versus anticoagulants followed by aspirin for post-arthroplasty VTE prophylaxis.

Regarding dosage, increasing evidence suggests low-dose aspirin provides effec-

tive thromboprophylaxis, similar to high-dose aspirin, and may even offer better thrombosis inhibition. An in vitro coagulation experiment showed decreased thrombin generation at 75 mg/day aspirin but not at 500 mg/day [40]. Similarly, a double-blind randomized controlled trial found 75 mg/day and 300 mg/day aspirin had similar effects in reducing thrombin generation after microvascular injury [9]. Regarding fibrin, Antovic' s study found that 320 mg/day aspirin had weaker inhibitory effects on fibrin than 37.5 mg/day [12], while other research suggests higher aspirin doses may reduce anticoagulant activity by acetylating antithrombin III [41]. Clinical studies on cardiovascular and cerebrovascular disease prevention suggest low-dose aspirin (75-100 mg) provides sufficient preventive effects [42]. Feldstein et al. compared 81 mg versus 325 mg aspirin for unilateral TJA VTE prophylaxis, both for 4 weeks, finding no difference in PE or DVT incidence but significantly higher gastrointestinal toxicity (nausea, vomiting, etc.) with 325 mg [36]. Parvizi et al.' s prospective study found similar VTE incidence with 81 mg twice daily versus 325 mg twice daily aspirin for 4 weeks (0.1% vs. 0.3%, P=0.345) [43]. Therefore, low-dose aspirin provides effective VTE prevention after joint arthroplasty while reducing gastrointestinal adverse effects and other risks.

IV. Limitations of Current Research

Although international guidelines including ACCP-9 and AAOS recommend aspirin for VTE prevention after joint arthroplasty, and numerous studies support its efficacy, most research still has significant limitations, and controversy remains regarding whether aspirin should be routine for post-arthroplasty VTE prophylaxis.

First, most current studies are retrospective case-control studies, lacking more comprehensive, rigorous multicenter prospective randomized controlled trials. Retrospective studies are prone to selection bias, and although some studies used strict inclusion and exclusion criteria to increase randomization, enrolled cases still showed substantial differences in age, sex, comorbidities, VTE prophylaxis regimens, and duration, which may affect outcomes. Second, although no guidelines explicitly propose risk stratification and corresponding anticoagulant selection principles for post-arthroplasty patients, high-risk TJA patients, such as those with prior VTE history, typically receive anticoagulants as first-line prophylaxis, with aspirin reserved for routine prevention. This introduces selection bias. Furthermore, questions remain regarding aspirin' s mechanisms for venous thrombosis prevention. Historically, arterial thrombosis was thought to depend heavily on platelet adhesion and aggregation, while the slower venous system was considered less platelet-dependent, leading to the belief that antiplatelet drugs were primarily effective for arterial thrombosis prevention with limited efficacy for venous thrombosis. Although current studies support aspirin' s efficacy and safety for postoperative venous thrombosis prevention, further basic research is needed to elucidate its mechanisms in venous thrombosis prevention.

Conclusion

Based on guideline recommendations and current research, aspirin may be considered a routine option for VTE prophylaxis after joint arthroplasty, offering comparable efficacy to LMWH and factor Xa inhibitors with low bleeding risk, good safety, and advantages of low cost, convenient administration, and no monitoring requirements. Regarding dosage, low-dose aspirin provides effective prevention while reducing gastrointestinal adverse effects. However, large-scale prospective randomized clinical trials and further mechanistic studies on aspirin for VTE prevention after orthopedic joint arthroplasty are needed to provide more robust evidence for clinical practice.

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Note: Figure translations are in progress. See original paper for figures.

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