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REVIEW

Assessment of thromboembolic risk and preventive strategies in major orthopaedic surgery

Evaluación del riesgo tromboembólico y estrategias preventivas en cirugía ortopédica mayor

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ABSTRACT

Introduction: venous thromboembolic disease (VTD), comprising deep vein thrombosis (DVT) and pulmonary embolism (PE), was one of the main causes of preventable mortality in hospitalized patients. Its incidence increased significantly in those who underwent hip (THA) and knee (TKA) arthroplasty, which led to the development of effective prevention strategies.
Development: risk factors associated with both the patient and the surgical procedure were identified. The Caprini scale was used to stratify them, including in orthopedic patients. In terms of pharmacological prophylaxis, anticoagulants such as low molecular weight heparins (LMWH), direct oral anticoagulants (DOAC) and aspirin (ASA) were compared. Different studies showed that ASA was similarly effective to LMWH in low-risk patients, with advantages such as lower cost and better tolerance. However, DOACs offered a slight superiority in efficacy, although with a higher risk of bleeding. Current recommendations favored a combination of pharmacological and mechanical measures such as early ambulation and the use of compression stockings.
Conclusion: the prevention of VTE in major orthopedic surgery required an individualized and evidence-based approach. Aspirin emerged as a valid alternative in certain cases, without completely replacing other anticoagulants in high-risk patients. Further research was considered essential, especially in local contexts such as Argentina, to adapt strategies according to the needs of the health system.

Keywords: ETV; Arthroplasty; Aspirin; Heparin; Prophylaxis.

RESUMEN

Introducción: la enfermedad tromboembólica venosa (ETV), compuesta por la trombosis venosa profunda (TVP) y la tromboembolia pulmonar (TEP), constituyó una de las principales causas de mortalidad prevenible en pacientes hospitalizados. Su incidencia aumentó significativamente en quienes fueron sometidos a artroplastias de cadera (ATC) y rodilla (ATR), lo que motivó el desarrollo de estrategias eficaces de prevención.
Desarrollo: se identificaron factores de riesgo asociados tanto al paciente como al procedimiento quirúrgico. Para estratificarlos, se utilizó la escala de Caprini, incluso en pacientes traumatológicos. En cuanto a la profilaxis farmacológica, se compararon anticoagulantes como las heparinas de bajo peso molecular (HBPM), anticoagulantes orales directos (ACOD) y la aspirina (AAS). Distintos estudios demostraron que la AAS presentó eficacia similar a las HBPM en pacientes de bajo riesgo, con ventajas como menor costo y mejor tolerancia. Sin embargo, los ACOD ofrecieron una leve superioridad en eficacia, aunque con mayor riesgo hemorrágico.

Las recomendaciones actuales favorecieron una combinación de medidas farmacológicas y mecánicas como la deambulación precoz y el uso de medias de compresión.
Conclusión: la prevención de la ETV en cirugía ortopédica mayor requirió un enfoque individualizado y basado en evidencia. La aspirina emergió como una alternativa válida en ciertos casos, sin reemplazar completamente a otros anticoagulantes en pacientes de alto riesgo. Se consideró esencial seguir investigando, especialmente en contextos locales como Argentina, para adaptar las estrategias según las necesidades del sistema sanitario.

Palabras clave: ETV; Artroplastia; Aspirina; Heparina; Profilaxis.

INTRODUCTION

Venous thromboembolic disease (VTE) is one of the leading causes of preventable morbidity and mortality in hospitals and the third leading cause of death after acute myocardial infarction and stroke. The term VTE encompasses two closely related clinical entities: deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE), both of which have significant clinical implications, especially in patients undergoing major orthopedic surgery such as hip (THA) and knee (TKA) arthroplasty. Despite the global impact of this condition, information on its incidence and management in countries such as Argentina is scarce, reinforcing the need for further research and the promotion of effective prevention strategies.[1,2]

Total hip or knee arthroplasty is a surgical procedure frequently indicated in patients with advanced osteoarthritis, given its ability to improve quality of life significantly. However, this type of surgery is associated with a high risk of VTE, especially in the absence of prophylactic measures, reaching rates of up to 50 % when sensitive diagnostic techniques such as venography are used. This high incidence has led to the development and refinement of both pharmacological and mechanical prophylaxis protocols.[3,4]

Several studies have identified risk factors for VTE, including pre-existing patient conditions (such as obesity, diabetes, advanced age, or a history of thrombosis) and characteristics of the surgical procedure (duration, type of anesthesia, blood loss). Tools such as the Caprini scale have proven useful even in trauma populations to stratify this risk.[5,6]

Regarding pharmacological prophylaxis, there has been extensive debate about the comparative efficacy of different agents, such as low molecular weight heparins (LMWH), direct oral anticoagulants, and aspirin (ASA). Recent studies and meta-analyses have shown that ASA, in addition to being effective, has a favorable safety profile and lower cost, positioning it as a viable option, especially in low-risk patients. However, in patients with a higher risk of thrombosis, using LMWH or direct-acting oral anticoagulants is still recommended. The choice of drug should be individualized, always considering the risk-benefit ratio, especially the risk of bleeding.[7,8,9]

DEVELOPMENT

Venous thromboembolic disease (VTE) is one of the leading causes of preventable in-hospital deaths and the third leading cause of death after acute myocardial infarction and stroke. VTE includes deep vein thrombosis (DVT) and pulmonary thromboembolism (PTE).[1]

It is estimated that at least 3 million deaths occur each year, with an estimated 300 000 deaths related to VTE in the United States and approximately 500 000 in Europe each year. There is little published information on the incidence of VTE in hospitalized patients, and we have not found any literature referring to its incidence in Argentina.[2]

Major orthopedic surgery, referring to total hip arthroplasty (THA) and total knee arthroplasty (TKA), without prophylaxis has a perioperative VTE rate of between 2 % and 4 % and above 50 % when detected by venography, which is associated with high morbidity and mortality. Therefore, its prevention is a fundamental aspect of the management of these patients.[3]

One of the leading causes of total hip and knee replacement is osteoarthritis, which causes pain and disability. THA is commonly recommended in patients with advanced osteoarthritis and has shown excellent results, improving the patient's quality of life. Although prophylaxis is recommended in all patients, symptomatic VTE occurs in approximately 2 % of patients after lower limb arthroplasty.[7]

The study by Johnson et al. of 7,959 patients undergoing TKA reported a non-fatal TEP rate of 7,89 % and a fatal TEP rate of 1,04 % in the first five postoperative weeks, making PTE the highest cause of mortality after TKA during the first postoperative weeks. In the study by Stulberg et al., a series of 638 patients undergoing TRAT was reported, in which 49 patients did not receive prophylaxis, and 83 % of these developed DVT. Following these results, safe and effective strategies were developed for the prophylaxis of VTE after major orthopedic surgery.

The estimated risk of DVT in patients undergoing TKA increases to more than 2 %, associated with an increased

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incidence in patients who smoke, have diabetes, chronic obstructive pulmonary disease, are older, are obese, have a history of trauma, prolonged intraoperative traction, or prolonged postoperative immobilization.[4]

Before administering thromboprophylaxis, each patient's case should be evaluated individually to ensure that the risk of bleeding does not outweigh the risk of developing VTE, thereby avoiding complications. In patients with a higher risk of thrombosis versus bleeding, thromboprophylaxis should not be delayed.[6]

According to the SECOT (Spanish Society of Orthopedic Surgery and Traumatology), risk factors related to the patient or the surgical procedure itself are described as follows:

1. Patient-related factors:

- Genetic factors
- Acquired factors:
- Patient-dependent: age, hypertension, COPD, obesity, history of VTE, etc.
- Dependent on the clinical situation: prolonged bed rest, heart failure, AMI, etc.

2. Factors related to the surgical procedure:

- Prolonged procedure: General anesthesia > 90 minutes due to surgical technique, type of approach, significant blood loss >3 g/dl, and time from trauma to surgery.

Risk levels, in turn, stratify these factors:

Table 1. Risk factors by level

Strong risk factors
• Hip or lower limb fracture
• Hip or knee arthroplasty
• Major surgery (especially abdominal, pelvic, or neurosurgical)
• Multiple trauma
• Spinal cord injury
• Hospitalization in the previous 3 months for heart failure, AMI, atrial fibrillation, or atrial flutter
• Previous history of venous thromboembolic disease
Moderate risk factors
• Arthroscopic knee surgery
• Neoplasms
• Congestive heart failure or respiratory failure
• Infections (pneumonia, urinary tract infection, and HIV) and sepsis
• Stroke with limb paresis/plegia
Weak risk factors
• High blood pressure
• Diabetes
• High cholesterol
• Obesity (BMI > 30 kg/m2)
• Varicose veins and chronic venous insufficiency

For risk staging, the Caprini scale is proposed, which was not initially validated for trauma patients. However, according to He et al., their study concludes that the scale has good predictive and discriminatory power in these patients. According to Krauss ES et al., in patients undergoing TKA or TTR, a score of 10 or higher is considered high risk, while a score of less than 10 is considered low risk. Luksameearunothai, K et al. recommend performing a Doppler ultrasound before surgery to assess the preoperative risk of DVT in elderly patients with hip fractures who have a score of 12 or higher.[10,11,12,13,14,15]

Drugs used for pharmacological thromboprophylaxis after DVT and/or PTE include oral anticoagulants (OACs), low molecular weight heparins (LMWHs), and aspirin (ASA). LMWHs, such as enoxaparin, have reported DVT rates for DVT of 3,4 to 20,8 % and non-fatal PTE rates of 0 to 0,5 %, and DVT rates for PTE of 23 to 45 % and non-fatal PTE rates of 0 to 0,2 % in the postoperative month; however, ASA has also been shown to be an effective prophylactic agent after these surgeries, with reported DVT rates of up to 2,6 % and non-fatal PTE rates between 0,14 and 0,6% in the postoperative month. It is also an effective prophylactic agent after these surgeries, with reported DVT rates of up to 2,6 % and non-fatal PTE rates between 0,14 and 0,6 % at 90 days postoperatively.

The meta-analysis by Jorge H. Nuñez et al. included a total of 248 461 patients, with 176 406 patients receiving thromboprophylaxis with LMWH and 72 055 patients receiving thromboprophylaxis with ASA. The mean age was 65,3 in patients receiving LMWH and 66,1 in patients receiving ASA. There were no significant differences in the risk of VTE, DVT, and PTE, the primary endpoints after CABG and/or ATR, between ASA and LMWH, nor were there any significant differences in the secondary endpoints of mortality, bleeding, or surgical wound complications between the two groups.[15,16,17] Due to the qualities of ASA, such as its low cost, safety, ease of administration, and evidence from observational studies, its use for thromboprophylaxis has increased in the US. The International Consensus on Venous Thromboembolism (ICM-VTE), published in 2021, strongly recommends using aspirin as prophylaxis after DVT or DVT.[5]

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Table 2. Caprini risk scale

1 point	2 point	3 point	5 point
• Age 41 to 60 yearss • Minor surgery, less than • 45 min) • BMI >25 kg/m2 • Edema in lower limbs • Varicose veins in lower limbs • Pregnancy or postpartum (1month) • History of unexplained or repeated miscarriages (more than 3) • Oral contraception or hormone replacement therapy • Sepsis (<1 month) • Severe lung disease, including pneumonia (<1 month) • Functional lung disorders • Diagnosis of acute heart failure or worsening of heart failure (<1 month) • Severe lung disease, including pneumonia (<1 month) • Functional lung disorders • Diagnosis of AMI or worsening of heart failure (<1 month) • History of inflammatory bowel disease • Patient undergoing conservative treatment, bedridden.	• Age 61-74 • Arthroscopic surgery • Major open surgery (>45 min) • Laparoscopic surgery (>45 min) • Malignant neoplasm • Bed rest (>72 h) • Immobilization of the limb with plaster cast (< 1 month) • Central venous catheter (< 1 month)	• Age ≥75 years • History of VTE • Family history of VTE • Malignant neoplasm or • chemotherapy • Antithrombin, protein C, or S deficiency • Carrier of factor V Leiden prothrombin gene mutation G20210A • Lupus anticoagulant Anticardiolipin antibodies • Antibodies against ß2 glycoprotein • Heparin-induced thrombocytopenia • Other congenital or acquired thrombophilia.	• Stroke (<1 month) • Hip or knee joint replacement • Fracture of the pelvic bones, femur, or tibia, multiple trauma • Acute spinal cord injury (<1 month)

ASA is a platelet cyclooxygenase-1 inhibitor that irreversibly inhibits platelet aggregation. Low doses of ASA, 81 mg twice daily, are as effective as higher doses. In addition, its use has been associated with a lower incidence of joint prosthesis infection than an anticoagulant such as warfarin; it may cause less bleeding and persistent drainage problems from the surgical wound, risk factors for prosthetic infection. LMWHs are more selective indirect inhibitors of factor Xa and, to a lesser extent, thrombin and have been shown to reduce the rate of VTE in patients undergoing major orthopedic surgery. In addition to pharmacological prophylaxis, there are complementary methods such as mechanical prophylaxis: early postoperative ambulation within 24 hours, graduated compression stockings, intermittent pneumatic compression, and foot vein pumps; all with the indication of combination with pharmacological prophylaxis, unless there is a high risk of bleeding.

The 2020 systematic review and meta-analysis by Matharu et al. concluded that thromboembolic prophylaxis with aspirin after elective hip or knee arthroplasty does not show statistically significant differences in terms of efficacy and safety compared to other drugs such as LMWH, warfarin, and oral anticoagulants. Other publications propose combined therapy with aspirin and mechanical measures, highlighting, in some cases, the lower frequency of readmissions due to bleeding complications, thromboembolic events, and wound complications associated with this combination compared to other treatments such as LMWH.[18,19,20]

An ASA dose of between 30 and 150 mg would be sufficient to inhibit COX-1 function, and a dose of 81 mg twice daily is as effective as 325 mg twice daily. Most symptomatic thromboembolic events occur within the first 2 weeks after surgery (94 %), with 89 % occurring in the first week. However, the thromboembolic risk in these patients is high for much longer, so the minimum duration should be 7 to 15 days after surgery. Still, most international guidelines recommend extending it to 35 days.[6]

According to the 2022 CRISTAL randomized trial, the rate of symptomatic VTE in the first 90 days was 3,45 % in the aspirin group and 1,82 % in the enoxaparin group (estimated difference, 1,97 %; 95 % CI, 0,54 %-3,41 %). This was significantly higher for enoxaparin (P = 0,007). Of the six secondary outcomes, including readmission, reoperation, major bleeding events, mortality within 90 days, reoperation within 6 months after surgery, and adherence rates assessed by audits, none were significantly better in the enoxaparin group than in the aspirin group.[8]

According to the systematic review and meta-analysis by Marrannes S. et al. 2021, which included 32 studies (9 RCTs and 23 observational studies) to compare the efficacy of aspirin prophylaxis after ATR with LMWH, vitamin K antagonists, and factor Xa inhibitors, no significant differences on the effectiveness of VTE prevention were found between aspirin, LMWH, and warfarin. Factor Xa inhibitors were more effective, but more bleeding complications were reported; however, the results were not statistically significant.[9,25,26,27]

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Table 3. Recommendations for thromboprophylaxis according to SECOT

Procedure	Thrombotic risk	Thromboprophylaxis
Elective total hip and knee arthroplasty	Low risk	Early ambulation + pharmacological prophylaxis: • Aspirin (100 mg twice daily) (for at least 4 weeks postoperatively) and mechanical measures (at least until discharge). • Low molecular weight heparin (for at least 4 weeks after surgery) and mechanical measures (at least until discharge). • Direct-acting oral anticoagulants as prescribed in the package insert (for at least 4 weeks after surgery) and mechanical measures (at least until discharge).
Elective total hip and knee arthroplasty	High risk	Early ambulation + pharmacological prophylaxis: • Low molecular weight heparin (for at least 4 weeks postoperatively) and mechanical measures (at least until discharge). • Direct-acting oral anticoagulants as prescribed in the package insert (for at least 4 weeks postoperatively) and mechanical measures (at least until discharge).
Revision hip and knee arthroplasty	Low and high	Early ambulation • Low molecular weight heparin (for at least 4 weeks postoperatively) and mechanical measures (at least until discharge).

The systematic review and meta-analysis by Juan E Farley et al. 2020 included four trials with 1 507 participants who underwent elective lower limb arthroplasty. There was no significant difference in overall VTE rates when comparing aspirin versus enoxaparin (RR, 0,84; 95 % CI: 0,41 to 1,75; p = 0,65).[28,29,30] There were no significant differences in the rates of all major bleeding events between the aspirin and enoxaparin groups (RR, 0,84; 95 % CI: 0,08 to 9,16) or lower (RR, 0,77; 95 % CI: 0,34 to 1,72). The included trials demonstrated a significant risk of bias and low quality of evidence for the primary outcomes and moderate to very low quality for the secondary outcomes.[10]

In the systematic review and meta-analysis by JY Cai et al. 2021, a total of 117 full-text studies were evaluated, and a total of 161 463 patients undergoing ATC with a mean age of 66,2 ± 5,0 years were identified in 14 studies. It was concluded that there are increased risks of venous thromboembolism (OR: 1,56; 95 % CI 1,21-2,01), pulmonary embolism (OR: 1,63; 95 % CI: 1,31-2,04), and overall mortality (OR: 1,35; 95 % CI 1,04-1,74) for patients receiving aspirin compared to direct oral anticoagulants. There were also mild bleeding complications for patients receiving direct oral anticoagulants compared with aspirin. This finding may have implications for developing best practice guidelines to reduce the risk of VTE complications in patients undergoing CTA or ATR.[11,30,31]

CONCLUSIONS

Venous thromboembolic disease (VTE), profound vein thrombosis (DVT), and pulmonary embolism (PE) represent a significant threat to patients undergoing major orthopedic surgery, particularly hip (THA) and knee (TKR) arthroplasty. Even with prophylaxis, the high incidence of thromboembolic events in these surgical procedures highlights the importance of adequate individual risk assessment and personalized selection of preventive strategies.

Various risk factors intrinsic to the patient and associated with the surgical procedure have been identified and classified into different risk levels. Tools like the Caprini scale have proven helpful in stratification and clinical decision-making, even in orthopedic and trauma populations. This assessment is essential to optimize the risk-benefit ratio between thromboprophylaxis and bleeding risk.

The pharmacological options available include low molecular weight heparins (LMWHs), direct oral anticoagulants (DOACs), and aspirin (ASA). Although LMWHs have traditionally been considered the gold standard, several studies and meta-analyses have shown that ASA can offer similar results in terms of VTE prevention, with advantages associated with its low cost, safety profile, and ease of administration. However, some recent studies suggest a slight superiority in the efficacy of DOACs, although an increased risk of bleeding may accompany this.

Current recommendations often favor a combined strategy, using pharmacological thromboprophylaxis and mechanical measures such as early ambulation, compression stockings, or intermittent pneumatic compression devices. In addition, the duration of treatment should be adjusted to the patient's individual risk, with prolonged prophylaxis of up to 35 days recommended in high-risk cases.

In conclusion, the approach to VTE in the context of major orthopedic surgery should be comprehensive, personalized, and based on the best available evidence. The choice of prophylactic agent should consider clinical factors, individual risks, patient characteristics, and the resources available at each institution. Although aspirin has gained ground as a valid option in certain groups, it does not entirely replace LMWH or ACOD in patients with high thrombotic risk. In the future, it will be necessary to continue generating local evidence, especially in countries such as Argentina, to adapt international guidelines to the specific realities of the healthcare system.

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The authors declare that there is no conflict of interest.

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