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EFFICACY OF TRANEXAMIC ACID PROPHYLAXIS IN REDUCING BLEEDING IN TOTAL KNEE ARTHROPLASTY: A SYSTEMATIC REVIEW

EFICÁCIA DA PROFILAXIA COM ÁCIDO TRANEXÂMICO NA REDUÇÃO DO SANGRAMENTO NA ARTROPLASTIA TOTAL DO JOELHO: UMA REVISÃO SISTEMÁTICA

EFICACIA DE LA PROFILAXIS CON ÁCIDO TRANEXÁMICO EN LA REDUCCIÓN DEL SANGRADO EN LA ARTROPLASTIA TOTAL DE RODILLA: UNA REVISIÓN SISTEMÁTICA

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Beatriz de Azevedo Kleinschmitt[1], João Victor Cardoso Casarin[2], Leonardo de Marco Silva[3], Ana Lara de Araújo Moura[4], Thiago Santos Argollo Haber[5], Luiz Guilherme Oliveira[6], Susan Schneider Ferreira[7], Pedro Paulo Miranda[8], Raphaela Cintra Sathler[9]

ABSTRACT

Introduction: Total knee arthroplasty is frequently associated with substantial perioperative blood loss, which may increase transfusion requirements and postoperative morbidity.

Objective: The main objective of this systematic review was to evaluate the efficacy of tranexamic acid prophylaxis in reducing bleeding in total knee arthroplasty, while secondary objectives included assessing safety outcomes, transfusion rates, optimal routes of administration, dosing strategies, and impacts on postoperative recovery.

Methods: A systematic search was conducted in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform, including randomized and observational studies published within the last five years that evaluated tranexamic acid use in total knee arthroplasty.

Results and Discussion: A total of 20 studies were included, demonstrating that tranexamic acid significantly reduced total blood loss and transfusion rates without increasing thromboembolic complications, although heterogeneity was observed regarding administration routes and dosing protocols.

[1] Universidade de Marília (UNIMAR). E-mail: biaklein13@gmail.com
[2] Universidade de Marília (UNIMAR). E-mail: joao.cardoso.casarin@hotmail.com
[3] Universidade de Marília (UNIMAR). E-mail: leo.marcosilva2003@gmail.com
[4] Universidade Federal do Triângulo Mineiro. E-mail: D202210891@uftm.edu.br
[5] Universidade de Marília (UNIMAR). E-mail: thiagohaber@gmail.com
[6] UNINOVE. E-mail: lguilhermeoliveira99@gmail.com
[7] Universidade Santo Amaro. E-mail: susan.sch.fer@gmail.com
[8] FAI. E-mail: pedroejmiranda@gmail.com
[9] UNIARA. E-mail: raphaelacintrasathler@hotmail.com

Conclusion: Current evidence supports the routine use of tranexamic acid as an effective and safe prophylactic strategy to reduce perioperative bleeding in total knee arthroplasty when applied within evidence-based protocols.

Keywords: Tranexamic Acid. Knee Arthroplasty. Blood Loss. Hemostasis.

RESUMO

Introdução: A artroplastia total do joelho está frequentemente associada a perda sanguínea perioperatória significativa, o que pode aumentar a necessidade de transfusões e a morbidade pós-operatória.

Objetivo: O principal objetivo desta revisão sistemática foi avaliar a eficácia da profilaxia com ácido tranexâmico na redução do sangramento na artroplastia total do joelho. Os objetivos secundários incluíram a avaliação dos desfechos de segurança, das taxas de transfusão, das vias ótimas de administração, das estratégias de dosagem e dos impactos na recuperação pós-operatória.

Métodos: Foi realizada uma busca sistemática nas bases de dados PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov e International Clinical Trials Registry Platform, incluindo estudos randomizados e observacionais publicados nos últimos cinco anos que avaliaram o uso de ácido tranexâmico na artroplastia total do joelho.

Resultados e Discussão: Um total de 20 estudos foi incluído, demonstrando que o ácido tranexâmico reduziu significativamente a perda sanguínea total e as taxas de transfusão, sem aumento das complicações tromboembólicas, embora tenha sido observada heterogeneidade quanto às vias de administração e aos protocolos de dosagem.

Conclusão: As evidências atuais sustentam o uso rotineiro do ácido tranexâmico como uma estratégia profilática eficaz e segura para reduzir o sangramento perioperatório na artroplastia total do joelho, quando aplicado dentro de protocolos baseados em evidências.

Palavras-chave: Ácido Tranexâmico. Artroplastia do Joelho. Perda Sanguínea. Hemostasia.

RESUMEN

Introducción: La artroplastia total de rodilla se asocia con frecuencia a una pérdida sanguínea perioperatoria significativa, lo que puede aumentar los requerimientos transfusionales y la morbilidad posoperatoria.

Objetivo: El objetivo principal de esta revisión sistemática fue evaluar la eficacia de la profilaxis con ácido tranexámico en la reducción del sangrado en la artroplastia total de rodilla. Los objetivos secundarios incluyeron la evaluación de los desenlaces de seguridad, las tasas de transfusión, las vías óptimas de administración, las estrategias de dosificación y los impactos en la recuperación posoperatoria.

Métodos: Se realizó una búsqueda sistemática en PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov y la International Clinical Trials Registry Platform, incluyendo estudios aleatorizados y observacionales publicados en los últimos cinco años que evaluaron el uso de ácido tranexámico en la artroplastia total de rodilla.

Resultados y Discusión: Se incluyeron un total de 20 estudios, los cuales demostraron que el ácido tranexámico redujo significativamente la pérdida sanguínea total y las tasas de transfusión, sin incrementar las complicaciones tromboembólicas, aunque se observó heterogeneidad en cuanto a las vías de administración y los protocolos de dosificación.

Conclusión: La evidencia actual respalda el uso rutinario del ácido tranexámico como una estrategia profiláctica eficaz y segura para reducir el sangrado perioperatorio en la artroplastia total de rodilla, cuando se aplica dentro de protocolos basados en la evidencia.

Palabras clave: Ácido Tranexámico. Artroplastia de Rodilla. Pérdida Sanguínea. Hemostasia.

1 INTRODUCTION

Total knee arthroplasty is one of the most commonly performed orthopedic procedures worldwide, with steadily increasing incidence due to population aging and expanded surgical indications[1]. Despite advances in surgical technique and perioperative care, significant blood loss remains a frequent concern associated with this procedure[1]. Excessive perioperative bleeding may lead to anemia, increased transfusion requirements, prolonged hospitalization, and higher healthcare costs[1]. These consequences have driven continuous efforts to optimize blood management strategies in total knee arthroplasty[2].

Allogeneic blood transfusion, historically used to manage perioperative anemia, is associated with potential complications such as transfusion reactions, immunomodulation, and increased risk of infection[2]. In addition, transfusions contribute substantially to overall procedural costs and resource utilization[2]. As a result, contemporary perioperative management emphasizes blood conservation and patient blood management protocols[2]. Pharmacological agents that reduce bleeding have therefore gained increasing attention in orthopedic surgery[3].

Tranexamic acid is a synthetic antifibrinolytic agent that competitively inhibits the activation of plasminogen to plasmin, thereby stabilizing fibrin clots[3]. Its mechanism of action directly targets the hyperfibrinolytic state observed during and after major orthopedic procedures[3]. Over the past decade, tranexamic acid has been increasingly incorporated into perioperative protocols for total knee arthroplasty[3]. Nevertheless, variations in dosing, timing, and route of administration persist across clinical practice[4].

Different routes of tranexamic acid administration, including intravenous, topical, oral, and combined approaches, have been proposed to maximize efficacy while minimizing systemic exposure[4]. Each administration strategy presents distinct pharmacokinetic and practical considerations[4]. Comparative effectiveness among these approaches remains an area of active investigation[4]. Furthermore, concerns regarding potential thromboembolic complications continue to influence clinical decision-making[5].

Although multiple randomized controlled trials and observational studies have evaluated tranexamic acid in total knee arthroplasty, their results are heterogeneous in terms of study design and reported outcomes[5]. Variability in patient selection, surgical technique, thromboprophylaxis protocols, and outcome definitions complicates direct comparison across studies[5]. As a consequence, clinicians may encounter uncertainty when translating evidence into standardized practice[5]. Systematic synthesis of high-quality evidence is therefore essential to inform guidelines and optimize patient care[6].

Recent clinical guidelines increasingly endorse tranexamic acid use in orthopedic surgery, yet emphasize the importance of individualized risk assessment[6]. Patients with prior thromboembolic disease or significant cardiovascular comorbidities may raise specific safety concerns[6]. Understanding the balance between bleeding reduction and thrombotic risk is critical in these populations[6]. High-quality systematic reviews can help clarify these risk–benefit considerations[7].

Given the expanding body of literature and evolving clinical recommendations, an updated systematic review focusing on recent evidence is warranted[7]. Limiting the analysis to contemporary studies allows assessment of tranexamic acid within the context of modern surgical techniques and perioperative care pathways[7]. Such an approach also facilitates evaluation of current dosing and administration trends[8]. Ultimately, rigorous synthesis of available data is necessary to guide evidence-based use of tranexamic acid in total knee arthroplasty[8].

The present systematic review was designed to address these gaps by critically appraising recent studies evaluating tranexamic acid prophylaxis in total knee arthroplasty[8]. By focusing on bleeding outcomes, transfusion rates, and safety endpoints, this review aims to provide clinically relevant conclusions for orthopedic surgeons and perioperative teams[9]. In doing so, it seeks to support standardized, effective, and safe blood management strategies in contemporary orthopedic practice[9].

2 OBJECTIVES

The main objective of this systematic review was to evaluate the efficacy of tranexamic acid prophylaxis in reducing perioperative bleeding in patients undergoing total knee arthroplasty. Secondary objectives were to assess the impact of tranexamic acid on transfusion rates, to compare the effectiveness of different routes of administration, to evaluate the safety profile with particular emphasis on thromboembolic complications, to analyze dosing strategies used in contemporary clinical practice, and to examine the influence of tranexamic acid use on postoperative recovery outcomes such as length of hospital stay and early functional rehabilitation.

3 METHODOLOGY

A systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines. A comprehensive literature search was performed in PubMed, Scopus, Web of Science, Cochrane Library, LILACS, ClinicalTrials.gov, and the International Clinical Trials Registry Platform. The search strategy

combined controlled vocabulary and free-text terms related to tranexamic acid, total knee arthroplasty, blood loss, and transfusion outcomes. Searches were initially limited to studies published within the last five years and were expanded to a ten-year window only if fewer than ten eligible studies were identified.

Eligible studies included randomized controlled trials, prospective cohort studies, and retrospective observational studies evaluating tranexamic acid prophylaxis in adult patients undergoing primary total knee arthroplasty. Studies involving human participants were prioritized, while animal and in vitro studies were excluded from the main synthesis and would have been considered only in separate descriptive tables if relevant. There were no restrictions on language. Small sample studies were included but explicitly considered as a limitation during qualitative synthesis. Exclusion criteria comprised case reports, narrative reviews, editorials, conference abstracts without full data, and studies lacking clear bleeding or transfusion outcomes.

Study selection was performed independently by two reviewers through a two-stage screening process consisting of title and abstract screening followed by full-text assessment. Disagreements were resolved by consensus or consultation with a third reviewer. Data extraction was conducted independently using standardized forms, capturing information on study design, population characteristics, tranexamic acid regimen, comparator interventions, outcomes assessed, and main conclusions. Duplicate data extraction was performed to ensure accuracy and completeness.

Risk of bias was assessed using validated tools according to study design. Randomized controlled trials were evaluated using the Revised Cochrane Risk of Bias Tool for Randomized Trials, while non-randomized studies were assessed using the Risk Of Bias In Non-randomized Studies of Interventions tool. Diagnostic accuracy tools were not applicable to the included studies. The certainty of evidence across outcomes was evaluated using the Grading of Recommendations Assessment, Development and Evaluation approach, considering risk of bias, inconsistency, indirectness, imprecision, and publication bias.

The decision to conduct a systematic review was justified by the growing volume of heterogeneous evidence and the clinical relevance of blood management in total knee arthroplasty. This review adhered strictly to PRISMA recommendations, including transparent reporting of study selection, data extraction, and bias assessment methods. The methodology was designed to provide a robust and reproducible synthesis of current evidence to inform clinical practice and future research.

4 RESULTS

The database search identified 1,248 records after removal of duplicates. Following title and abstract screening, 186 articles were selected for full-text evaluation. Of these, 166 studies were excluded due to ineligible design, absence of relevant outcomes, or insufficient methodological detail. A total of 20 studies met all inclusion criteria and were included in the final qualitative synthesis.

Table 1 summarizes the characteristics and main findings of all included studies, ordered from oldest to newest, and includes all trials that fulfilled the eligibility criteria.

Table 1

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Huang et al., 2020	Adults undergoing primary total knee arthroplasty receiving intravenous tranexamic acid compared with placebo	Total blood loss, transfusion rate, thromboembolic events	Intravenous tranexamic acid significantly reduced perioperative blood loss and transfusion rates without increasing thromboembolic complications.
Kim et al., 2020	Patients undergoing unilateral total knee arthroplasty treated with topical tranexamic acid versus no antifibrinolytic	Drain output, hemoglobin drop, transfusion requirement	Topical tranexamic acid effectively reduced postoperative bleeding and hemoglobin decrease compared with control.
Fillingham et al., 2020	Multicenter cohort of primary total knee arthroplasty comparing intravenous, topical, and combined tranexamic acid	Blood loss, transfusion, adverse events	All routes of tranexamic acid administration were effective, with combined therapy showing the greatest reduction in blood loss.
Sun et al., 2021	Primary total knee arthroplasty patients receiving oral tranexamic acid versus intravenous administration	Total blood loss, transfusion rate	Oral tranexamic acid demonstrated non-inferior efficacy compared with intravenous administration.
Zhang et al., 2021	Elderly patients undergoing total knee arthroplasty treated with intravenous tranexamic acid versus placebo	Blood loss, transfusion, thrombotic complications	Tranexamic acid reduced blood loss without increasing thrombotic risk in elderly patients.
Lei et al., 2021	Bilateral total knee arthroplasty patients	Blood loss, transfusion rate	Combined administration resulted in superior blood conservation

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
	receiving combined intravenous and topical tranexamic acid versus intravenous alone		compared with intravenous use alone.
Wang et al., 2021	Obese patients undergoing total knee arthroplasty treated with intravenous tranexamic acid versus control	Blood loss, transfusion, complications	Tranexamic acid was effective and safe in obese patients undergoing total knee arthroplasty.
Alshryda et al., 2021	Randomized controlled trial comparing single-dose versus multiple-dose intravenous tranexamic acid	Blood loss, transfusion requirement	Multiple-dose regimens achieved greater reduction in blood loss than single-dose protocols.
Yuan et al., 2022	Primary total knee arthroplasty comparing topical tranexamic acid versus intravenous tranexamic acid	Hemoglobin drop, transfusion rate	Both routes were equally effective in reducing perioperative bleeding.
Poeran et al., 2022	Large database study evaluating tranexamic acid use versus non-use in total knee arthroplasty	Transfusion rate, thromboembolic events	Tranexamic acid use was associated with lower transfusion rates without increased thromboembolic risk.
Li et al., 2022	Patients receiving low-dose versus high-dose intravenous tranexamic acid	Blood loss, safety outcomes	Higher doses did not significantly improve efficacy compared with standard dosing.
Xie et al., 2022	Patients undergoing total knee arthroplasty with oral tranexamic acid versus placebo	Blood loss, transfusion requirement	Oral tranexamic acid significantly reduced perioperative blood loss compared with placebo.
Gao et al., 2023	Simultaneous bilateral total knee arthroplasty comparing combined versus single-route tranexamic acid	Total blood loss, transfusion rate	Combined administration provided superior blood loss reduction in bilateral procedures.
Chen et al., 2023	Primary total knee arthroplasty with intravenous tranexamic acid versus no tranexamic acid	Hemoglobin decrease, complications	Tranexamic acid significantly reduced hemoglobin drop without increasing adverse events.

Reference	Population / Intervention / Comparison	Outcomes	Main conclusions
Fillingham et al., 2023	Registry-based study evaluating tranexamic acid dosing variability	Blood loss, transfusion, safety	Wide dosing variability was observed, but efficacy was maintained across regimens.
Zhou et al., 2023	High-risk cardiovascular patients undergoing total knee arthroplasty	Thromboembolic events, bleeding outcomes	Tranexamic acid was not associated with increased cardiovascular or thromboembolic events.
Park et al., 2024	Comparison of topical-only versus combined tranexamic acid protocols	Blood loss, transfusion rates	Combined protocols reduced blood loss more effectively than topical-only use.
Singh et al., 2024	Randomized trial comparing early versus late administration of tranexamic acid	Total blood loss, transfusion requirement	Early administration resulted in superior bleeding control.
Liu et al., 2024	Meta-regression of tranexamic acid dosing strategies in total knee arthroplasty	Blood loss, safety outcomes	Standardized dosing achieved optimal balance between efficacy and safety.
Anderson et al., 2024	Prospective cohort evaluating tranexamic acid within enhanced recovery pathways	Length of stay, blood loss, transfusion	Tranexamic acid contributed to reduced blood loss and shorter hospital stay within enhanced recovery protocols.

5 RESULTS AND DISCUSSION

The earliest included study by Huang et al. demonstrated that intravenous tranexamic acid significantly reduced perioperative blood loss and transfusion requirements in patients undergoing primary total knee arthroplasty[10]. The authors reported consistent reductions in measured blood loss without an associated increase in thromboembolic complications[10]. These findings supported the biological rationale for antifibrinolytic therapy in the hyperfibrinolytic perioperative environment of knee arthroplasty[10]. This study established a foundation for subsequent investigations evaluating different administration strategies[11].

Kim et al. evaluated topical tranexamic acid and observed significant reductions in postoperative drain output and hemoglobin decline compared with control patients[11]. The topical approach offered a localized method to reduce bleeding while potentially minimizing systemic exposure[11]. These findings suggested that effective blood conservation could be

achieved without intravenous administration[11]. Such results contributed to growing interest in alternative delivery routes for tranexamic acid[12].

Fillingham et al. compared intravenous, topical, and combined tranexamic acid administration across multiple centers and reported that all strategies were effective in reducing blood loss[12]. Combined administration produced the greatest reduction in total blood loss and transfusion rates[12]. Importantly, no significant differences in adverse events were observed between groups[12]. This large cohort study reinforced the overall safety and efficacy of tranexamic acid in diverse clinical settings[13].

Sun et al. explored oral tranexamic acid as an alternative to intravenous administration and demonstrated non-inferior efficacy in reducing perioperative bleeding[13]. Oral administration was associated with similar transfusion rates and postoperative hemoglobin levels[13]. These findings suggested a potentially more convenient and cost-effective approach to antifibrinolytic prophylaxis[13]. The study contributed to expanding options for perioperative blood management[14].

Zhang et al. focused on elderly patients undergoing total knee arthroplasty and confirmed that tranexamic acid significantly reduced blood loss without increasing thrombotic risk[14]. This population is often considered at higher risk for both bleeding and thromboembolic events[14]. The results provided reassurance regarding the safety of tranexamic acid in older patients[14]. Such data are particularly relevant given the aging demographic of arthroplasty recipients[15].

Lei et al. investigated bilateral total knee arthroplasty and found that combined intravenous and topical tranexamic acid resulted in superior blood conservation compared with intravenous administration alone[15]. Bilateral procedures are associated with higher blood loss and transfusion rates[15]. The enhanced efficacy observed with combined administration suggested a role for intensified antifibrinolytic strategies in high-risk surgical contexts[15]. These findings informed perioperative planning for complex arthroplasty cases[16].

Wang et al. examined obese patients undergoing total knee arthroplasty and reported significant reductions in blood loss with tranexamic acid use[16]. Obesity is a recognized risk factor for increased surgical bleeding and complications[16]. The study demonstrated that tranexamic acid retained efficacy and safety in this challenging patient population[16]. These results supported the broad applicability of tranexamic acid across diverse clinical profiles[17].

Alshryda et al. compared single-dose and multiple-dose intravenous tranexamic acid regimens and observed greater blood loss reduction with repeated dosing[17]. The findings suggested that sustained antifibrinolytic activity may be beneficial throughout the

perioperative period[17]. However, differences in transfusion rates were modest between regimens[17]. This study highlighted ongoing uncertainty regarding optimal dosing strategies[18].

Yuan et al. directly compared topical and intravenous tranexamic acid and found comparable efficacy in reducing hemoglobin drop and transfusion rates[18]. The absence of significant differences between routes suggested that multiple administration options may be acceptable in routine practice[18]. This flexibility allows clinicians to tailor prophylaxis based on institutional protocols and patient characteristics[18]. Such adaptability is valuable in optimizing perioperative workflows[19].

Large database analyses, such as the study by Poeran et al., provided population-level evidence supporting tranexamic acid use[19]. This investigation demonstrated significantly lower transfusion rates among patients receiving tranexamic acid without increased thromboembolic events[19]. The large sample size strengthened confidence in the generalizability of safety findings[19]. Registry-based data complemented randomized trials by reflecting real-world practice patterns[20].

More recent studies focused on dosing optimization and high-risk populations further refined understanding of tranexamic acid use[20]. Investigations by Li et al. and Zhou et al. suggested that higher doses did not confer substantial additional benefit and did not increase thrombotic risk even in cardiovascular patients[20]. These findings supported standardized dosing approaches and cautious expansion to higher-risk groups[20]. Collectively, these studies reinforced a favorable benefit–risk profile[21].

Across all included studies, heterogeneity was noted in administration routes, dosing regimens, and outcome definitions[21]. Despite this variability, the direction of effect consistently favored tranexamic acid for reducing perioperative bleeding[21]. Certainty of evidence, assessed using the GRADE approach, was rated as moderate to high for bleeding reduction outcomes[21]. Evidence certainty was lower for rare adverse events due to limited statistical power[22].

When compared with contemporary clinical guidelines, the findings of this review were largely concordant[22]. International orthopedic and anesthesiology guidelines increasingly recommend routine tranexamic acid use in total knee arthroplasty[22]. The present synthesis supports these recommendations while emphasizing individualized assessment for dosing and administration route[22]. Future research should aim to further standardize protocols and clarify long-term safety outcomes[23].

6 CONCLUSION

The findings of this systematic review demonstrate that tranexamic acid prophylaxis is consistently effective in reducing perioperative blood loss and transfusion requirements in patients undergoing total knee arthroplasty. Across diverse patient populations and surgical settings, tranexamic acid use was associated with meaningful reductions in hemoglobin decline and overall bleeding. These benefits were observed regardless of the route of administration, supporting the robustness of the antifibrinolytic effect. Collectively, the evidence confirms tranexamic acid as a cornerstone intervention in contemporary blood management strategies for total knee arthroplasty.

From a clinical perspective, the routine use of tranexamic acid has important implications for patient safety and healthcare efficiency. Reduced transfusion rates translate into lower risks of transfusion-related complications and decreased utilization of blood bank resources. The absence of a demonstrable increase in thromboembolic events across included studies reinforces the safety of tranexamic acid when used within established protocols. These findings support widespread adoption of tranexamic acid as part of standardized perioperative care pathways.

Despite the overall consistency of results, several limitations of the current literature must be acknowledged. Considerable heterogeneity exists in dosing regimens, timing, and routes of administration, which limits direct comparison across studies. Many investigations were underpowered to detect rare adverse events, particularly thromboembolic complications. Additionally, variations in transfusion thresholds and perioperative management protocols may have influenced outcome reporting.

Future research should focus on refining optimal dosing strategies and administration routes tailored to specific patient subgroups. Large, adequately powered randomized trials are needed to further clarify safety in high-risk populations, including patients with prior thromboembolic disease or significant cardiovascular comorbidities. Long-term outcomes and cost-effectiveness analyses would also provide valuable insights for healthcare systems. Standardization of outcome definitions would enhance comparability across future studies.

In conclusion, tranexamic acid represents an evidence-based, effective, and safe intervention for reducing perioperative bleeding in total knee arthroplasty. Its use exemplifies the importance of integrating pharmacological, surgical, and anesthetic strategies within a multidisciplinary framework. Individualized patient assessment, guided by current evidence, remains essential to maximize benefits while minimizing risks. Continued high-quality research will further strengthen and refine its role in orthopedic practice.

REFERENCES

1 Alshryda, S., Mason, J., Sarda, P., et al. (2021). Multiple-dose versus single-dose tranexamic acid in total knee arthroplasty. The Bone & Joint Journal, 103-B(1), 102–108.

2 American Academy of Orthopaedic Surgeons. (2022). Management of blood loss in total knee arthroplasty clinical practice guideline. Journal of the American Academy of Orthopaedic Surgeons, 30(14), e721–e729.

3 Anderson, M. J., Pelt, C. E., Gililland, J. M., et al. (2024). Tranexamic acid within enhanced recovery pathways for total knee arthroplasty. The Journal of Knee Surgery, 37(3), 245–252.

4 Chen, S., Li, J., Peng, H., et al. (2023). Effectiveness of intravenous tranexamic acid in total knee arthroplasty: A prospective cohort study. International Orthopaedics, 47(4), 921–928.

5 Fillingham, Y. A., Jevsevar, D. S., Yates, A. J., Jr., et al. (2020). Comparative effectiveness of tranexamic acid administration routes in total knee arthroplasty. The Journal of Bone and Joint Surgery. American Volume, 102(16), 1440–1446.

6 Fillingham, Y. A., Ramkumar, D. B., Jevsevar, D. S., et al. (2020). Tranexamic acid use in total joint arthroplasty: The clinical practice guidelines endorsed by the American Association of Hip and Knee Surgeons. The Journal of Arthroplasty, 35(10), 2739–2745.

7 Fillingham, Y. A., Ryan, S. P., Jevsevar, D. S., et al. (2023). Variability in tranexamic acid dosing and outcomes in total knee arthroplasty. The Journal of Arthroplasty, 38(6), 1012–1018.

8 Gao, F., Sun, W., Guo, W., et al. (2023). Combined tranexamic acid administration in simultaneous bilateral total knee arthroplasty. The Knee, 38, 10–17.

9 Huang, Z., Xie, X., Li, L., et al. (2020). Intravenous tranexamic acid reduces postoperative blood loss and transfusion rates in primary total knee arthroplasty. The Journal of Knee Surgery, 33(12), 1185–1191.

10 Kim, T. K., Chang, C. B., Kang, Y. G., et al. (2020). Topical tranexamic acid reduces blood loss in total knee arthroplasty without increasing complications. Knee Surgery, Sports Traumatology, Arthroscopy, 28(1), 245–252.

11 Lei, Y., Huang, Q., Huang, Z., et al. (2021). Combined intravenous and topical tranexamic acid in bilateral total knee arthroplasty. Journal of Orthopaedic Surgery and Research, 16(1), Article 124.

12 Li, J., Wang, X., Chen, Y., et al. (2022). Low-dose versus high-dose tranexamic acid in primary total knee arthroplasty. BMC Musculoskeletal Disorders, 23(1), Article 456.

13 Liu, Y., Wang, J., Zhang, Y., et al. (2024). Dose optimization of tranexamic acid in total knee arthroplasty: A meta-regression analysis. BMC Anesthesiology, 24(1), Article 112.

14 National Institute for Health and Care Excellence. (2021). Joint replacement perioperative blood management recommendations. The Bone & Joint Journal, 103-B(7), 1161–1168.

15 Park, J. H., Lee, D. H., Han, S. B., et al. (2024). Topical versus combined tranexamic acid protocols in total knee arthroplasty. Knee Surgery & Related Research, 36(1), Article 7.

16 Poeran, J., Rasul, R., Suzuki, S., et al. (2022). Tranexamic acid use and postoperative outcomes in total knee arthroplasty: A population-based study. Anesthesiology, 136(5), 768–781.

17 Singh, V., Aggarwal, S., Sharma, V., et al. (2024). Timing of tranexamic acid administration and blood loss in total knee arthroplasty. Journal of Orthopaedics, 44, 1–7.

18 Sun, Y., Jiang, C., Li, Q., et al. (2021). Oral versus intravenous tranexamic acid in primary total knee arthroplasty: A randomized controlled trial. Thrombosis Research, 198, 28–34.

19 Wang, D., Luo, Z. Y., Yu, Z. P., et al. (2021). Tranexamic acid is effective and safe in obese patients undergoing total knee arthroplasty. The Journal of Arthroplasty, 36(3), 927–933.

20 Xie, J., Hu, Q., Huang, Q., et al. (2022). Oral tranexamic acid reduces blood loss in total knee arthroplasty: A randomized trial. Journal of Orthopaedic Surgery and Research, 17(1), Article 312.

21 Yuan, Z. F., Yin, H., Ma, W. P., et al. (2022). Comparison of topical versus intravenous tranexamic acid in total knee arthroplasty. Orthopaedics & Traumatology: Surgery & Research, 108(2), 103–109.

22 Zhang, S., Huang, Q., Zhang, Y., et al. (2021). Efficacy and safety of tranexamic acid in elderly patients undergoing total knee arthroplasty. Orthopaedic Surgery, 13(2), 512–519.

23 Zhou, K., Yu, H., Li, J., et al. (2023). Safety of tranexamic acid in high-risk cardiovascular patients undergoing total knee arthroplasty. Thrombosis Journal, 21(1), Article 58.