

Review Article

Tranexamic Acid in Primary Total Hip Arthroplasty: Blood Loss and Transfusion Requirements

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Abstract

Background: Perioperative blood loss and allogeneic transfusion remain important sources of morbidity and cost after primary total hip arthroplasty (THA).

Objective: To synthesise evidence on tranexamic acid (TXA) administration routes, dosing regimens, and their effect on blood loss, transfusion, and thromboembolic safety in primary THA.

Methods: Narrative review of randomised trials, meta-analyses, network meta-analyses, cohort studies, and clinical practice guidelines on intravenous, topical, oral, and combined TXA regimens in primary THA.

Findings: TXA reduces total blood loss by roughly 300 mL and lowers transfusion rates by 50-70% regardless of route, with intravenous, topical, and oral regimens showing broadly equivalent efficacy. Pooled registry data show no significant increase in venous thromboembolism, even with prior thromboembolic events.

Conclusions: TXA is an effective, guideline-endorsed blood-conservation strategy in primary THA; route selection can reasonably be guided by cost and preference rather than expected differences in efficacy or safety.

Keywords: Tranexamic acid; Total hip arthroplasty; Blood loss; Transfusion; Venous thromboembolism

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Introduction

Primary total hip arthroplasty is associated with substantial perioperative blood loss, historically exposing 20-30% of patients to allogeneic red blood cell transfusion, with attendant risks of immunomodulation, infection, volume overload, and cost [1]. Tranexamic acid, a synthetic lysine analogue that competitively inhibits plasminogen activation and thereby stabilises fibrin clot, has become the cornerstone pharmacological blood-conservation strategy across elective orthopaedic surgery. Early randomised trials in cemented and cementless THA demonstrated that intravenous TXA meaningfully reduces both measured blood loss and

transfusion requirement without excess thromboembolic events [2], and this early signal has since been reproduced and extended across intravenous, topical (intra-articular), oral, and combined regimens, each with distinct pharmacokinetic and logistical profiles.

Despite this large evidence base, uncertainty persisted for years regarding the comparative efficacy of administration routes, the optimal dose and timing, and the safety of TXA in patients with pre-existing thromboembolic risk. Blood management strategies also carry direct economic consequences: each unit of allogeneic blood transfused adds acquisition, testing, and nursing costs, and postoperative anaemia has itself been linked to slower mobilisation and longer hospital stay after arthroplasty. These considerations, together with the drive toward enhanced-recovery and outpatient THA pathways, have made an effective, low-cost, easily administered blood-conservation agent a priority for arthroplasty surgeons and anaesthetists alike. This review synthesises randomised controlled trials, systematic reviews, network meta-analyses, large registry cohorts, and multi-society clinical practice guidelines addressing TXA use specifically in primary THA, with attention to route comparisons, dosing regimens, and venous thromboembolism (VTE) safety.

Pharmacology and Mechanism of Action

TXA reversibly binds lysine-binding sites on plasminogen, preventing its conversion to plasmin and thereby inhibiting fibrinolysis at the site of vascular injury. Because arthroplasty wounds generate substantial local fibrinolytic activity from exposed cancellous bone and synovium, antifibrinolytic therapy is mechanistically well suited to reducing surgical field bleeding. Systemic (intravenous or oral) administration achieves therapeutic plasma concentrations that also act at distant bleeding surfaces, whereas topical (intra-articular) delivery concentrates the drug at the wound with minimal

systemic absorption, a distinction that underlies much of the comparative safety and efficacy literature discussed below. Oral tablets are absorbed with a bioavailability of roughly 35-45%, which explains why oral doses are typically two to three times the equivalent intravenous dose to achieve comparable plasma exposure; this pharmacokinetic difference is central to interpreting the route-comparison trials that follow.

Dosing Regimens by Route

Reported regimens vary considerably across the literature (Table 1). Intravenous protocols range from a single weight-based or fixed dose (commonly 1 g or 10-15 mg/kg) given at incision to two- or three-dose regimens repeated postoperatively, while topical regimens typically instil 1.5-3 g of TXA diluted in 100-200 mL of saline into the wound before closure, as in the TRANX-H randomised trial, which used 3 g in 200 mL saline [3]. Oral regimens generally use 1-2 g given once or twice preoperatively, exemplified by a large enhanced-recovery cohort using 2 g orally two hours before surgery [4]. A multicentre randomised trial in revision THA found that additional intraoperative and postoperative intravenous doses beyond a single dose did not further reduce blood loss or transfusion [5], and a meta-analysis of single- versus double-dose intravenous regimens in hip and knee arthroplasty similarly found no significant efficacy advantage to repeat dosing [6]. A randomised comparison of TXA doses and routes in primary THA likewise found comparable blood-loss reduction across dose tiers once a minimum effective dose was reached [7]. Timing also matters: administration before tourniquet inflation or incision allows the drug to be present in the surgical field at the point of maximal fibrinolytic activation, and several trials have specifically dosed TXA 10-30 minutes preoperatively to maximise this window, an approach reflected in the TRANX-H and enhanced-recovery protocols summarised in Table 1.

Table 1: Representative tranexamic acid dosing regimens by administration route in primary total hip arthroplasty [3,4,5,6,7].			
Route	Representative regimen	Timing	Key trial(s)
Intravenous, single dose	1 g or 10-15 mg/kg	At incision	Zhou 2013 meta-analysis
Intravenous, repeat dose	1 g intraoperative + 1-2 further doses	Intraoperative and postoperative	Sershon 2020 (revision THA); Yang 2023 (no added benefit)
Topical (intra-articular)	1.5-3 g in 100-200 mL saline	Instilled into wound before closure	Alshryda 2013 (TRANX-H, 3 g/200 mL)
Oral	1-2 g	1-2 doses preoperatively	Irwin 2013 (2 g, 2 h preoperative)
Dose-response	Escalating IV/topical doses	Varies	Palijsa 2021 (comparable effect above minimum dose)

Efficacy: Blood Loss and Transfusion by Route

Across routes, TXA consistently reduces blood loss and transfusion relative to no treatment (Figure 1). A meta-analysis of nineteen randomised trials found intravenous TXA reduced total blood loss by approximately 305 mL and significantly lowered transfusion rates without increasing complications [1]. Topical TXA produces a similar magnitude of effect: a meta-analysis of fourteen studies found topical administration reduced total blood loss by approximately 298 mL with no increase in deep vein thrombosis or pulmonary embolism [8], a finding corroborated in a matched cohort of cementless THA [9] and in hip arthroplasty more broadly [10]. Head-to-head comparisons have generally found intravenous and topical routes statistically equivalent: a ten-trial systematic review and meta-analysis found no significant difference in blood loss or transfusion between routes [11], and a randomised noninferiority trial confirmed topical TXA was not inferior to intravenous administration [12]. A network meta-analysis ranking intravenous, topical, oral, and combined regimens concluded that no

single route was clearly superior and that combined intravenous-plus-topical administration ranked highest for blood-loss reduction without a safety penalty [13], a conclusion echoed by a dedicated meta-analysis of combined-versus-single-route regimens in primary THA [14]. Two companion network meta-analyses commissioned alongside a multi-society guideline similarly found all routes and most regimens statistically equivalent in efficacy [15].

Table 2: Selected comparative studies of TXA administration route in primary total hip arthroplasty reviewed here [11,12,13,14,16,18,19].			
Study	Comparison	Design	Key outcome
Fang 2021	IV vs topical	Meta-analysis (10 RCTs)	No significant difference in blood loss/transfusion
Zhou 2018	Topical vs IV	RCT, noninferiority	Topical noninferior to IV
Yoon 2018	IV vs topical vs oral vs combined	Network meta-analysis	Combined IV+topical ranked highest; no route clearly inferior
Zhang 2017	Combined vs single route	Meta-analysis	Combined regimen reduced blood loss further, no added VTE risk
Qi 2020	Oral vs IV	Meta-analysis of RCTs	Equivalent blood loss and transfusion
DeFrancesco 2023	Oral vs IV	Multicentre RCT, noninferiority	Oral noninferior to IV in hip and knee arthroplasty
Karayiannis 2022	24-hour extended IV vs single dose	RCT cost analysis (TRAC-24)	Extended dosing reduced blood-product costs

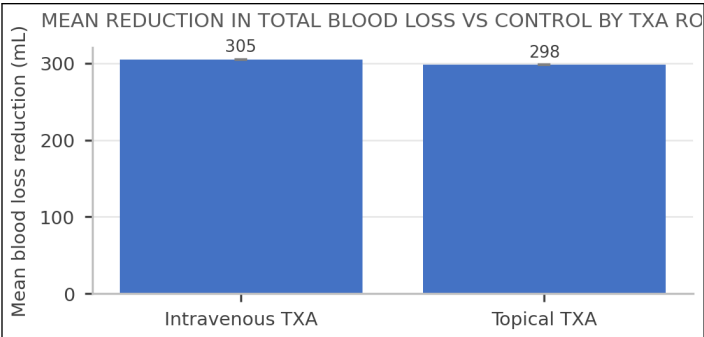


Figure 1: Mean reduction in total blood loss versus control with intravenous TXA (approximately 305 mL, pooled from 19 randomised trials) [1] and topical TXA (approximately 298 mL, pooled from 14 studies) [8].

Oral TXA has emerged as an attractive lower-cost alternative. A large retrospective cohort of 3,000 enhanced-recovery hip and knee replacements found the odds of transfusion were significantly higher with intravenous than oral TXA [4], and subsequent meta-analyses of randomised trials comparing oral and intravenous regimens in THA found equivalent blood loss and transfusion outcomes [16,17]. A large multicentre randomised non-inferiority trial confirmed oral TXA was non-inferior to intravenous TXA for the composite outcome of blood loss and transfusion in primary hip and knee arthroplasty [18]. A cost analysis from the TRAC-24 randomised trial additionally found that extending intravenous TXA dosing for 24 postoperative hours reduced blood-product costs relative to a single intraoperative dose (Table 2) [19]. Approach-specific analyses suggest the magnitude of benefit may vary modestly with surgical approach (direct anterior, posterior, or lateral), though TXA reduced bleeding across all approaches examined [20]. Taken together, the comparative literature indicates that the choice between intravenous, topical, and oral TXA in primary THA is best framed as a question of cost, convenience, and institutional workflow rather than a search for a superior agent, since all three routes achieve broadly similar reductions in blood loss and transfusion when appropriately dosed.

Safety and Venous Thromboembolic Risk

The principal safety concern with any antifibrinolytic is thromboembolic events, and this question has now been addressed at scale. A direct meta-analysis commissioned for the 2018 multi-society clinical practice guideline found no significant increase in deep vein thrombosis, pulmonary embolism, or death with TXA across pooled randomised trials in total joint arthroplasty [21], leading the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society to jointly recommend TXA for all patients undergoing arthroplasty who lack a documented contraindication [22]. A matched-outcome study specifically examining patients with a prior history of venous thromboembolism found recurrence was not significantly different with TXA (2.3%) than without it (1.8%) (Figure 2) [23], and a subsequent systematic review and meta-analysis concluded that TXA may even benefit patients with pre-existing thromboembolic risk by reducing bleeding-associated complications without raising thrombotic events [24]. A large administrative-claims matched cohort of 144,344 primary THA patients similarly found TXA use was not associated with increased venous thromboembolism, while transfusion and length of stay were significantly reduced [25]. An umbrella review pooling this evidence base concluded that both efficacy and safety of TXA in THA are now supported by high-certainty evidence across routes [26]. Because TXA is renally cleared, dose reduction or avoidance is generally advised in significant renal impairment, and caution is similarly recommended in patients with a seizure history, since high systemic doses have been associated with an excitatory cortical effect in cardiac surgical populations; topical administration, with its minimal systemic absorption, offers a practical alternative in such patients. Most reviewed trials also permitted concurrent mechanical and pharmacological

VTE prophylaxis, so the reassuring thromboembolic safety signal should be interpreted as additive to, rather than a replacement for, standard prophylaxis.

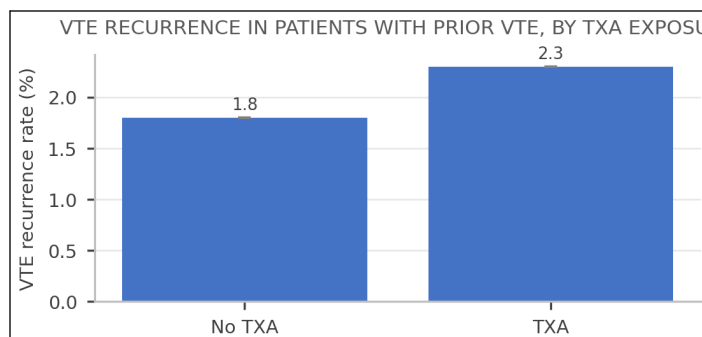


Figure 2: Venous thromboembolism recurrence in arthroplasty patients with a prior history of VTE, by TXA exposure, from a matched-outcome study of 1,620 procedures (258 TXA, 1,362 no TXA) [23].

Guidelines and Clinical Practice

Contemporary clinical practice guidelines endorse routine TXA use in primary THA irrespective of route, reserving route and dose selection for institutional cost, workflow, and patient-specific factors such as renal function or a history of seizure disorder [22]. Because efficacy is broadly route-equivalent, oral TXA is increasingly favoured where feasible given its markedly lower acquisition cost and ease of administration in enhanced-recovery pathways [4,16], while topical administration remains attractive when systemic exposure is a specific concern, and combined regimens may be reserved for patients at higher predicted blood loss [13]. Extending intravenous dosing into the first postoperative day, as trialled in TRAC-24, is a further option worth institutional consideration where transfusion avoidance and blood-product cost are both high priorities [19].

Conclusion

Two decades of accumulating randomised, meta-analytic, and large-cohort evidence establish tranexamic acid as an effective and safe blood-conservation strategy in primary total hip arthroplasty. Intravenous, topical, oral, and

combined regimens each reduce blood loss by roughly 300 mL and transfusion rates by half or more relative to no treatment, with no consistent efficacy advantage of one route over another and no demonstrated increase in venous thromboembolic risk, even among patients with prior thromboembolic disease. Remaining questions concern optimal dosing in specific high-risk subgroups and long-term cost-effectiveness comparisons between routes, but the weight of evidence now supports near-universal TXA use in primary THA absent a specific contraindication. Future work comparing route-specific cost-effectiveness within enhanced-recovery and outpatient THA pathways, and further defining safe use in patients with active or recent thromboembolic disease, will help refine rather than overturn this consensus.

References

1. Zhou, X.D., Tao, L.J., Li, J., Wu, L.D. (2013) Do we really need tranexamic acid in total hip arthroplasty? A meta-analysis of nineteen randomized controlled trials. *Archives of Orthopaedic and Trauma Surgery*, 133(7): 1017-1027.
2. Lemay, E., Guay, J., Côté, C., Roy, A. (2004) Tranexamic acid reduces the need for allogenic red blood cell transfusions in patients undergoing total hip replacement. *Canadian Journal of Anesthesia*, 51(1): 31-37.
3. Alshryda, S., Mason, J., Sarda, P., Nargol, A., Cooke, N., Ahmad, H., Tang, S., Logishetty, R., Vaghela, M., McPartlin, L., Hungin, A.P.S. (2013) Topical (intra-articular) tranexamic acid reduces blood loss and transfusion rates following total hip replacement: a randomized controlled trial (TRANX-H). *Journal of Bone and Joint Surgery American Volume*, 95(21): 1969-1974.
4. Irwin, A., Khan, S.K., Jameson, S.S., Tate, R.C., Copeland, C., Reed, M.R. (2013) Oral versus intravenous tranexamic acid in enhanced-recovery primary total hip and knee replacement. *Bone and Joint Journal*, 95-B(11): 1556-1561.
5. Sershon, R.A., Fillingham, Y.A., Abdel, M.P., Malkani, A.L., Schwarzkopf, R., Padgett, D.E., Vail, T.P., Nam, D., Nahhas, C., Culvern, C., Della Valle, C.J. (2020) The optimal dosing regimen for tranexamic acid in revision total hip arthroplasty: a multicenter randomized clinical trial. *Journal of Bone and Joint Surgery American Volume*, 102(21): 1883-1890.
6. Yang, Y.Z., Cheng, Q.H., Zhang, A.R., Yang, X., Zhang, Z.Z., Guo, H.Z. (2023) Efficacy and safety of single- and double-dose intravenous tranexamic acid in hip and knee arthroplasty: a systematic review and meta-analysis. *Journal of Orthopaedic Surgery and Research*, 18(1): 593.
7. Palija, S., Bijeljic, S., Manojlovic, S., Jovicic, Z., Jovanovic, M., Cvijic, P., Dragicevic-Cvjetkovic, D. (2021) Effectiveness of different doses and routes of administration of tranexamic acid for total hip replacement. *International Orthopaedics*, 45(4): 865-870.
8. Chen, S., Wu, K., Kong, G., Feng, W., Deng, Z., Wang, H. (2016) The efficacy of topical tranexamic acid in total hip arthroplasty: a meta-analysis. *BMC Musculoskeletal Disorders*, 17: 81.
9. Sanz-Reig, J., Mas Martinez, J., Verdu Roman, C., Morales Santias, M., Martinez Gimenez, E., Bustamante Suarez de Puga, D. (2018) Matched cohort study of topical tranexamic acid in cementless primary total hip replacement. *European Journal of Orthopaedic Surgery and Traumatology*, 28(7): 1335-1339.
10. Kang, J.S., Moon, K.H., Kim, B.S., Yang, S.J. (2017) Topical administration of tranexamic acid in hip arthroplasty. *International Orthopaedics*, 41(2): 259-263.
11. Fang, Y., Shang, X. (2021) Comparison of intravenous versus topical tranexamic acid in primary total hip arthroplasty: a systematic review and meta-analysis of ten randomized trials. *Journal of Comparative Effectiveness Research*, 10(14): 1089-1102.

12. Zhou, K., Wang, H., He, C., Liu, Z., Wang, Y., Feng, J. (2018) Is topical or intravenous tranexamic acid preferred in total hip arthroplasty? A randomized, controlled, noninferiority clinical trial. *PLoS ONE*, 13(10): e0204551.
13. Yoon, B.H., Kim, T.Y., Ko, Y.S., Lee, Y.K., Ha, Y.C., Koo, K.H. (2018) Optimal use of tranexamic acid for total hip arthroplasty: a network meta-analysis. *PLoS ONE*, 13(10): e0206480.
14. Zhang, P., Liang, Y., Chen, P., Fang, Y., He, J., Wang, J. (2017) Combined application versus topical and intravenous application of tranexamic acid following primary total hip arthroplasty: a meta-analysis. *BMC Musculoskeletal Disorders*, 18(1): 90.
15. Fillingham, Y.A., Ramkumar, D.B., Jevsevar, D.S., Yates, A.J., Shores, P., Mullen, K., Bini, S.A., Clarke, H.D., Schemitsch, E., Johnson, R.L., Memtsoudis, S.G., Sayeed, S.A., Sah, A.P., Della Valle, C.J. (2018) The efficacy of tranexamic acid in total hip arthroplasty: a network meta-analysis. *Journal of Arthroplasty*, 33(10): 3083-3089.e4.
16. Qi, Y., Li, Y., Wang, C., Chen, H., Rui, Y. (2020) Comparison of oral and intravenous tranexamic acid in total hip arthroplasty: a systematic review and meta-analysis. *Arthroplasty*, 2(1): 1-9.
17. Ye, W., Liu, Y., Liu, W.F., Li, X.L., Shao, J. (2020) The optimal regimen of oral tranexamic acid administration for primary total knee/hip replacement: a meta-analysis and narrative review of a randomized controlled trial. *Journal of Orthopaedic Surgery and Research*, 15(1): 457.
18. DeFrancesco, C.J., Reichel, J.F., Gbaje, E., Popovic, M., Freeman, C., Wong, M., DeMeo, D., Liu, J., Gonzalez Della Valle, A., Ranawat, A.S., Cross, M., Sculco, P.K., Haskins, S., Kim, D., Maalouf, D., Kirksey, M., Jules-Elysee, K., Soffin, E., Kumar, K., Beathe, J.C., Figgie, M.P., Inglis, A.E., Garvin, S., Alexiades, M.M., DelPizzo, K., Russell, L.A., Sideris, A., Saleh, J., Zhong, H., Memtsoudis, S.G. (2023) Effectiveness of oral versus intravenous tranexamic acid in primary total hip and knee arthroplasty: a randomised, non-inferiority trial. *British Journal of Anaesthesia*, 130(2): 234-241.
19. Karayiannis, P.N., Agus, A., Bryce, L., Hill, J.C., Beverland, D. (2022) Using tranexamic acid for an additional 24 hours postoperatively in hip and knee arthroplasty saves money: a cost analysis from the TRAC-24 randomized control trial. *Bone and Joint Open*, 3(7): 536-542.
20. Khorram, R., Borazjani, R., Khavandegar, A., Behjat, M., Rahmanipour, E., Vafadar, R., Vali, M., Parsa, A., Ghorbani, M. (2025) The efficacy of tranexamic acid in perioperative bleeding following total hip arthroplasty through different surgical approaches: systematic review and meta-analysis. *Journal of Orthopaedics*, 62: 112-121.
21. Fillingham, Y.A., Ramkumar, D.B., Jevsevar, D.S., Yates, A.J., Shores, P., Mullen, K., Bini, S.A., Clarke, H.D., Schemitsch, E., Johnson, R.L., Memtsoudis, S.G., Sayeed, S.A., Sah, A.P., Della Valle, C.J. (2018) The safety of tranexamic acid in total joint arthroplasty: a direct meta-analysis. *Journal of Arthroplasty*, 33(10): 3070-3082.
22. Fillingham, Y.A., Ramkumar, D.B., Jevsevar, D.S., Yates, A.J., Bini, S.A., Clarke, H.D., Schemitsch, E., Johnson, R.L., Memtsoudis, S.G., Sayeed, S.A., Sah, A.P., Della Valle, C.J. (2018) Tranexamic acid use in total joint arthroplasty: the clinical practice guidelines endorsed by the American Association of Hip and Knee Surgeons, American Society of Regional Anesthesia and Pain Medicine, American Academy of Orthopaedic Surgeons, Hip Society, and Knee Society. *Journal of Arthroplasty*, 33(10): 3065-3069.
23. Sabbag, O.D., Abdel, M.P., Amundson, A.W., Larson, D.R., Pagnano, M.W. (2017) Tranexamic acid was safe in arthroplasty patients with a history of venous thromboembolism: a matched outcome study. *Journal of Arthroplasty*, 32(9): S246-S250.
24. Duan, X., Li, M., Yu, Q., Jiang, J., Tang, J., Liu, Y. (2024) Tranexamic acid may benefit patients with preexisting thromboembolic risk undergoing total joint arthroplasty: a

systematic review and meta-analysis. *EFORT Open Reviews*, 9(6): 484-493.

25. Thapaliya, A., Mittal, M.M., Ratcliff, T.L., Mounasamy, V., Wukich, D.K., Sambandam, S.N. (2024) Usage of tranexamic acid for total hip arthroplasty: a matched cohort analysis of 144,344 patients. *Journal of Clinical Medicine*, 13(16): 4920.
26. Ghorbani, M., Sadrian, S.H., Ghaderpanah, R., Neitzke, C.C., Chalmers, B., Esmaeilian, S., Rahmanipour, E., Parsa, A. (2024) Tranexamic acid in total hip arthroplasty: an umbrella review on efficacy and safety. *Journal of Orthopaedics*, 54: 90-97.