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Tranexamic Acid in Older Patients with Hip Fracture and Recent Nonacute Ischaemic Stroke: A Historical Control Cohort Study

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Abstract

Objective

To evaluate the effectiveness and safety of perioperative intravenous tranexamic acid (TXA) use in older patients who underwent surgery for hip fracture and who had a documented history of nonacute ischaemic stroke within the preceding year.

Methods

We retrospectively reviewed 843 older patients with unilateral hip fracture and ischaemic stroke who were treated between January 2012 and December 2023 before admission. Patients were stratified by fracture anatomy into femoral neck and intertrochanteric fracture cohorts, and they were then assigned to TXA or control groups according to intraoperative intravenous TXA use. Perioperative blood loss, transfusion rate, transfusion volume, postoperative haemoglobin level, and length of hospital stay were compared within each fracture cohort. New cerebrovascular events, cardiovascular events, lower limb deep vein thrombosis or pulmonary embolism, and all-cause mortality were recorded within 1 year after surgery.

Results

In the femoral neck fracture cohort, TXA patients (1 g before skin incision and 1 g before wound closure; n = 185) had significantly lower intraoperative blood loss, transfusion rate, and transfusion volume than controls (all $P < 0.01$). In the intertrochanteric fracture cohort, patients receiving the same regimen (n = 263) had reduced intraoperative blood loss ($P = 0.044$), with no significant differences in transfusion rate or volume (both $P > 0.05$). During 1-year follow-up, TXA was not associated with significant increases in new cerebrovascular events, cardiovascular events, lower limb deep vein thrombosis, pulmonary embolism, or all-cause mortality in either fracture cohort (all $P > 0.05$).

Conclusion

In older patients with hip fracture and stable nonacute ischaemic stroke, perioperative intravenous TXA use was not associated with an increased 1-year risk of thrombotic events or mortality. Its haemostatic effect, however, was anatomically heterogeneous: the benefit was robust in femoral neck fractures but substantially limited in intertrochanteric fractures.

Introduction

Hip fracture in older adults is not merely an isolated skeletal injury but a sentinel geriatric event that includes frailty, multimorbidity, urgent surgery, and sustained risks of death and functional decline[1]. In

this setting, perioperative anaemia is particularly common because fracture-related bleeding occurs before the operation and is complicated by surgical blood loss[2]. Observational data indicate that a substantial proportion of older patients with hip fracture require allogeneic red cell transfusion during the perioperative period[3].

Although transfusion remains an essential rescue intervention, it is not a neutral exposure[1, 4]. The FOCUS trial in high-risk patients after hip-fracture surgery and the AABB clinical practice guidelines support the implementation of restrictive, symptom-guided transfusion strategies; however, even with these strategies, effective blood conservation measures are still required in patients with limited physiological reserve[5–7]. With transfusion-related allergic reactions, circulatory overload, immune modulation, infection risk, increased resource use, and pressure on finite blood supplies, patient blood management has therefore become a central component of modern hip fracture care[8]. Adjunctive strategies, including erythropoietin in selected patients, TXA-mediated antifibrinolysis, and restrictive transfusion protocols, have been explored to reduce avoidable blood exposure while preserving tissue oxygen delivery[9].

TXA is a synthetic lysine analogue that inhibits the interaction between plasminogen and fibrin, thereby limiting plasmin-mediated fibrin degradation and stabilising the clot structure [9]. Its clinical value has been demonstrated across haemorrhagic and surgical settings; the CRASH-2 trial established the survival benefit of TXA in bleeding trauma patients without an increased risk of vascular occlusive events, and according to large orthopaedic datasets, TXA leads to reduced transfusion requirements after major joint surgery[10–12]. Several systematic reviews and meta-analyses suggest that in hip-fracture surgery specifically, TXA reduces transfusion exposure and perioperative blood loss without a clear signal of increased venous thromboembolism or other major thrombotic complications in unselected populations[13, 14].

Whether TXA exerts adverse effects in patients with prior cerebrovascular disease remains uncertain[12]. Survivors of ischaemic stroke frequently have atherosclerotic disease, endothelial dysfunction, advanced age, and long-term antiplatelet or anticoagulant exposure; moreover, secondary prevention guidelines emphasize their persistent vulnerability to recurrent vascular events[14]. Stroke recurrence remains clinically important within the first year after an index event, and the recurrence is associated with increased mortality and disability[15]. Moreover, noncardiac surgery after a previous stroke is associated with a time-dependent perioperative risk, with the highest risk occurring during the early poststroke period and decreasing thereafter. These considerations create a therapeutic paradox in hip fracture care: clinicians are most reluctant to administer an antifibrinolytic agent in patients who have the greatest need for blood conservation.

This dilemma cannot be fully resolved using the current evidence. Many TXA trials either excluded patients with recent thrombotic events or included patients with heterogeneous cardiovascular and thromboembolic risks in the same group, limiting inferences for patients with recent nonacute ischaemic stroke. Although studies of broader high-risk hip fracture cohorts demonstrated the benefits of TXA, they

generally combined patients with coronary artery disease, atrial fibrillation, venous thromboembolism, and cerebrovascular history in the same group, and they seldom focused on patients with recurrent stroke within 1 year[16]. We therefore conducted a historical control cohort study to evaluate perioperative intravenous TXA use in older patients with hip fracture and ischaemic stroke within the preceding year, excluding those with acute-phase stroke. We specifically examined 1-year cerebrovascular, cardiovascular, venous thromboembolic, and mortality outcomes, and further assessed whether the haemostatic effect of TXA differed between patients with femoral neck fractures and intertrochanteric fractures.

Materials and methods

Study design and participants

This retrospective observational study included older patients with hip fracture treated at our hospital between January 2012 and December 2023. The eligibility criteria were as follows: (1) unilateral fresh hip fracture within 2 weeks, (2) age ≥ 60 years, (3) a documented history of ischaemic stroke within 1 year before admission, (4) low-energy injury, and (5) surgical treatment of hip fracture. The exclusion criteria were as follows: (1) pathological fracture, (2) acute-phase stroke (< 1 month), (3) preoperative coagulation disorder, (4) severe renal insufficiency (creatinine clearance < 60 mL/min/1.73 m²), (5) follow-up < 1 year, or (6) incomplete clinical data.

Of 2267 patients with hip fracture who were screened during the study period, 843 met the eligibility criteria. The femoral neck fracture cohort included 365 patients—142 men and 223 women—173 with left-sided fractures and 192 with right-sided fractures; the age ranged from 6099 years, with a mean age of 80.54 ± 7.94 years. Comorbidities included hypertension in 246 patients (67.4%), coronary heart disease in 99 patients (27.1%), arrhythmia in 60 patients (16.4%), chronic obstructive pulmonary disease in 39 patients (10.7%), renal insufficiency in 24 patients (6.6%), dementia in 27 patients (7.4%), and diabetes mellitus in 117 patients (32.1%). The intertrochanteric fracture cohort included 478 patients: 179 men and 299 women. The age ranged from 60101 years, with a mean age of 81.39 ± 7.47 years. Comorbidities included hypertension in 320 patients (66.9%), coronary heart disease in 137 patients (28.7%), arrhythmia in 84 patients (17.6%), chronic obstructive pulmonary disease in 73 patients (15.3%), renal insufficiency in 47 patients (9.7%), dementia in 50 patients (10.5%), and diabetes mellitus in 155 patients (32.4%). This study was approved by the institutional ethics committee, and the requirement of informed consent was waived because of the retrospective design.

Treatment protocol

After admission, all patients routinely underwent electrocardiography, chest radiography, and lower limb vascular ultrasonography. Optimal treatment was implemented for medical comorbidities, deep vein

thrombosis was actively prevented, and surgery was performed as early as possible once no major contraindications were identified.

Patients with femoral neck fractures were placed in the supine position on a traction table. Nondisplaced fractures were treated directly; mildly displaced fractures were reduced under C-arm fluoroscopy through traction, adduction, and internal rotation. A longitudinal incision of approximately 5 cm was made distal to the lateral aspect of the greater trochanter, followed by dissection through the skin, subcutaneous tissue, and vastus lateralis. An anti-rotation guidewire was placed along the anterosuperior femoral neck. After satisfactory positioning of the first guidewire, a second guidewire was inserted into the inferomedial femoral neck under a 130 degree guide and advanced to the subchondral bone of the femoral head. After length measurement, a stepped drill was used for reaming along the guidewire, the dynamic component and locking screw were inserted, and an anti-rotation screw was placed after reaming along the anti-rotation guidewire. The final implant position was confirmed through C-arm fluoroscopy before layered wound closure.

Patients with intertrochanteric fractures were placed in the supine position on a traction table. Nondisplaced fractures were treated directly; mildly displaced fractures were reduced under C-arm fluoroscopy through traction, adduction, and internal rotation. A longitudinal incision of approximately 3 cm was made proximal to the greater trochanter to expose the trochanteric apex. A guidewire was inserted, the entry point was opened with a cannulated drill, and an appropriately sized intramedullary nail (Intertan or PFNA) was inserted according to the canal diameter. Distal locking was performed with the targeting device, and the implant position was confirmed through C-arm fluoroscopy before layered wound closure.

Standardized perioperative care was implemented. Low-molecular-weight heparin was administered subcutaneously beginning 8 h after surgery. Allogeneic blood transfusion was conducted when the haemoglobin concentration was < 80 g/L or when severe anaemia-related symptoms occurred. For infection prophylaxis, second-generation cephalosporin was administered intravenously within 24 h after surgery. Patients were encouraged to begin quadriceps contraction and hip and knee flexion exercises early and to ambulate as soon as clinically feasible.

Grouping

A historical control design was used. Since October 2016, intravenous TXA has been routinely administered intraoperatively as a haemostatic protocol for older patients undergoing hip-fracture surgery at our hospital. Before that date, no intraoperative haemostatic drugs were used. Patients in the TXA group (October 2016 to December 2023) received 1 g of intravenous TXA 10 minutes before skin incision and a second 1-g dose 10 minutes before wound closure. Patients in the control group (January 2012 to September 2016) did not receive TXA. In the femoral neck fracture cohort, 185 and 180 patients were assigned to the TXA and control groups, respectively. In the intertrochanteric fracture cohort, 263 and 215 patients were assigned to the TXA and control group, respectively.

Follow-up and outcomes

Follow-up visits were scheduled at 1, 3, 6, and 12 months after surgery. Thereafter, regular follow-up was not mandatory, and patients were observed until their last available follow-up visit in December 2024. Complications were recorded throughout the follow-up period and follow-up was terminated upon death when applicable.

The primary outcomes were postoperative transfusion rate, transfusion volume, and intraoperative blood loss. The secondary outcomes included length of hospital stay and complications over the follow-up period, such as cerebrovascular events (stroke recurrence), cardiovascular events (myocardial infarction or acute coronary syndrome), lower limb deep vein thrombosis or pulmonary embolism, and all-cause mortality. The detailed process of patient selection, fracture type stratification, and cohort allocation is shown in Fig. 1.

Statistical analysis

Statistical analyses were performed using SPSS version 21.0. Normally distributed continuous variables are presented as mean ± standard deviation and were compared between groups using the independent-samples *t* test. Nonnormally distributed variables are presented as medians (interquartile ranges) and were compared using the Mann—Whitney U test. Categorical variables are presented as numbers (%) and were compared using the chi-square test or Fisher's exact test, as appropriate. All tests were two-sided, and $P < 0.05$ was considered to indicate statistical significance.

Results

Baseline characteristics of patients with femoral neck fractures

The baseline perioperative characteristics of the femoral neck fracture cohort are shown in Table 1. Sex, age, comorbidities, laboratory results on admission, BMI, preinjury antithrombotic therapy, time from admission to surgery, anaesthesia type, operation duration, and procedure or prosthesis type did not significantly differ between the TXA and control groups (all $P > 0.05$).

Table 1
Baseline characteristics of patients with femoral neck fractures

Variable	TXA group (n = 185)	Control group (n = 180)	Test statistic	P value
Sex				
Male	77 (41.6%)	65 (36.1%)	1.166	0.280
Female	108 (58.4%)	115 (63.9%)		
Age (years)	80.08 ± 8.79	80.99 ± 6.99	1.090	0.277
Comorbidities				
Hypertension	117 (63.2%)	129 (71.7%)	2.946	0.086
Coronary heart disease	53 (28.6%)	46 (25.6%)	0.442	0.506
Arrhythmia	35 (18.9%)	25 (13.9%)	1.680	0.195
COPD	23 (12.4%)	16 (8.9%)	1.200	0.273
Dementia	16 (8.6%)	11 (6.1%)	0.858	0.354
Renal insufficiency	9 (4.9%)	15 (8.3%)	1.787	0.181
Diabetes mellitus	61 (33.0%)	56 (31.1%)	0.145	0.703
Laboratory variables	8.66 (7.28, 10.16)	8.78 (7.10, 10.64)	0.241	0.809
White blood cells	115.00 (99.00, 128.50)	111.00 (100.00, 122.00)	1.460	0.144
Haemoglobin	36.60 (34.30, 38.70)	36.95 (33.87, 38.85)	0.302	0.762
Albumin	69.00 (54.30, 84.00)	66.60 (55.00, 90.85)	0.066	0.948
Creatinine	7.28 (5.61, 9.40)	6.85 (5.20, 8.94)	1.590	0.112
Blood urea nitrogen				
BMI (kg/m²)	22.65 (20.38, 25.39)	23.30 (20.73, 26.12)	0.394	0.693
Admission-to-surgery time (days)	4.09 ± 1.93	3.83 ± 1.69	1.360	0.175
Preinjury antithrombotic therapy	161 (87.0%)	155 (86.1%)	0.066	0.797
Anaesthesia				
General	48 (25.9%)	53 (29.4%)	0.558	0.455
Regional	137 (74.1%)	127 (70.6%)		

Variable	TXA group (n = 185)	Control group (n = 180)	Test statistic	P value
Procedure/prosthesis type				
Hemiarthroplasty	118 (63.8%)	117 (65.0%)	0.059	0.808
Total hip arthroplasty	67 (36.2%)	63 (35.0%)		
Operation duration (min)	75 (70, 90)	75 (64, 86)	1.225	0.221

Outcomes in patients with femoral neck fractures

In the femoral neck fracture cohort, intraoperative blood loss, transfusion volume, and transfusion rate were significantly lower in the TXA group than in the control group (all $P < 0.05$), whereas postoperative haemoglobin levels were significantly higher in the TXA group ($P < 0.05$; Table 2). During follow-up, the length of hospital stay, 1-year mortality, cardiovascular events, cerebrovascular events, and lower limb deep vein thrombosis or pulmonary embolism did not significantly differ between the groups (all $P > 0.05$; Table 3).

Table 2
Primary outcomes in patients with femoral neck fractures

Outcome	TXA group (n = 185)	Control group (n = 180)	Test statistic	P value
Transfusion rate	104 (56.2%)	125 (69.4%)	6.829	0.009
Transfusion volume	2 (0, 4)	4 (1.6, 4)	4.431	< 0.001
Intraoperative blood loss (mL)	90 (70, 100)	120 (100, 150)	8.311	< 0.001
Postoperative haemoglobin (g/L)	107.5 (99, 118.5)	104 (94.25, 115)	2.160	0.031

Table 3
Secondary outcomes in patients with femoral neck fractures

Outcome	TXA group (n = 185)	Control group (n = 180)	Test statistic	P value
Length of stay (days)	11 (9, 13)	10 (8, 13)	1.810	0.070
All-cause mortality	31 (16.8%)	36 (20.0%)	0.640	0.424
Cardiovascular events	13 (7.0%)	12 (6.7%)	0.019	0.892
Cerebrovascular events	20 (10.8%)	17 (9.4%)	0.187	0.665
Lower limb DVT or PE	17 (9.2%)	15 (8.3%)	0.084	0.773

Baseline characteristics of patients with intertrochanteric fractures

The baseline perioperative characteristics of the intertrochanteric fracture cohort are provided in Table 4. Sex, age, comorbidities, laboratory results on admission, BMI, preinjury antithrombotic therapy, time from admission to surgery, anaesthesia type, operation duration, and internal fixation method did not significantly differ between the TXA and control groups (all $P > 0.05$).

Table 4
Baseline characteristics of patients with intertrochanteric fractures

Variable	TXA group (n = 263)	Control group (n = 215)	Test statistic	P value
Sex				
Male	102 (38.8%)	77 (35.8%)	0.445	0.505
Female	161 (61.2%)	138 (64.2%)		
Age (years)	81.61 ± 7.74	81.13 ± 7.12	0.701	0.483
Comorbidities				
Hypertension	168 (63.9%)	152 (70.7%)	2.486	0.115
Coronary heart disease	81 (30.8%)	56 (26.0%)	1.306	0.253
Arrhythmia	52 (19.8%)	32 (14.9%)	1.951	0.162
COPD	42 (16.0%)	31 (14.4%)	0.220	0.639
Dementia	33 (12.5%)	17 (7.9%)	2.720	0.099
Renal insufficiency	22 (8.4%)	25 (11.6%)	1.421	0.233
Diabetes mellitus	90 (34.2%)	65 (30.2%)	0.859	0.354
Laboratory variables	8.65 (7.29, 10.17)	8.62 (7.05, 10.55)	0.181	0.857
White blood cells	106.00 (90.00, 118.00)	103.00 (92, 115.00)	0.820	0.412
Haemoglobin	36.30 (33.90, 38.60)	37.00 (33.11, 38.80)	0.552	0.581
Albumin	70.00 (54.10, 85.00)	66.60 (56.00, 90.05)	0.050	0.960
Creatinine	7.18 (5.44, 9.40)	6.84 (5.10, 8.90)	1.646	0.100
Blood urea nitrogen				
BMI (kg/m²)	22.82 (20.76, 25.40)	23.43 (20.73, 26.22)	0.755	0.451
Admission-to-surgery time (days)	3.51 ± 1.89	3.64 ± 1.66	0.778	0.437
Preinjury antithrombotic therapy	230 (87.5%)	182 (84.7%)	0.780	0.377
Anaesthesia				
General	71 (27.0%)	60 (27.9%)	0.049	0.824
Regional	192 (73.0%)	155 (72.1%)		
Internal fixation method				

Variable	TXA group (n = 263)	Control group (n = 215)	Test statistic	P value
Intertan	163 (62.0%)	146 (67.9%)	1.820	0.177
PFNA	100 (38.0%)	69 (32.1%)		
Operation duration (min)	50 (40, 60)	48 (35, 55)	1.785	0.078

Outcomes in patients with intertrochanteric fractures

In the intertrochanteric fracture cohort, patients in TXA group exhibited lower intraoperative blood loss and higher postoperative haemoglobin levels than those in the control group (both $P < 0.05$). However, the transfusion volume and transfusion rate did not differ significantly between the groups (both $P > 0.05$; Table 5). During follow-up, the length of hospital stay, 1-year mortality, cardiovascular events, cerebrovascular events, and lower limb deep vein thrombosis or pulmonary embolism were comparable between the groups (all $P > 0.05$; Table 6).

Table 5
Primary outcomes in patients with intertrochanteric fractures

Outcome	TXA group (n = 263)	Control group (n = 215)	Test statistic	P value
Transfusion rate	149 (56.7%)	128 (59.5%)	0.403	0.526
Transfusion volume	2 (0, 4)	2 (0, 4)	1.745	0.081
Intraoperative blood loss (mL)	100 (80, 120)	120 (80, 150)	2.009	0.044
Postoperative haemoglobin (g/L)	106 (98, 106)	102 (93, 113)	2.349	0.019

Table 6
Secondary outcomes in patients with intertrochanteric fractures

Outcome	TXA group (n = 263)	Control group (n = 215)	Test statistic	P value
Length of stay (days)	10 (8, 12)	9 (7, 11)	1.458	0.097
All-cause mortality	61 (23.2%)	63 (29.3%)	2.297	0.130
Cardiovascular events	27 (10.3%)	24 (11.2%)	0.100	0.752
Cerebrovascular events	32 (12.2%)	30 (14.0%)	0.344	0.563
Lower limb DVT or PE	32 (12.2%)	25 (11.6%)	0.033	0.856

Discussion

Tranexamic acid (TXA) has been extensively validated as an effective blood-conservation agent in orthopaedic surgery through its competitive inhibition of plasminogen activation and subsequent attenuation of fibrinolysis [14]. Nevertheless, a history of thrombotic disease remains listed in drug labelling and several clinical guidance documents as a relative contraindication or at least a population requiring heightened caution [17]. In real-world practice, this concern may lead clinicians to withhold TXA administration from a substantial proportion of patients with hip fracture, who might otherwise derive meaningful haemostatic benefits, particularly those with a history of ischaemic stroke. Treatment in this subgroup remains uniquely challenging. Moreover, evidence from older high-risk patients undergoing hip-fracture surgery has shown that the transfusion strategy does not fully resolve postoperative morbidity; this observation indicates that, beyond transfusion thresholds alone, proactive blood conservation approaches should be implemented [5]. On the one hand, patients with ischaemic stroke often carry a high perioperative anaemia burden, partly because many patients receive long-term antiplatelet therapy and may experience greater hidden blood loss after fracture. On the other hand, their established vascular vulnerability raises concerns that antifibrinolytic therapy could lead to recurrent cerebrovascular or systemic thrombotic events. Thus, given the clinical intersection between the urgent need for blood conservation and the theoretical risk of thrombosis, these patients are left in a grey zone in which evidence is limited; yet, the potential benefit is considerable.

In the present study, we evaluated the effectiveness and safety of perioperative intravenous TXA in older patients with hip fracture and a documented history of recent nonacute ischaemic stroke. The principal finding is that TXA reduced perioperative bleeding without increasing the 1-year risk of major thrombotic events or all-cause mortality in this high-risk population. Importantly, the magnitude of its haemostatic benefit was heterogenous across fracture types. The effect was pronounced in femoral neck fractures but substantially limited in intertrochanteric fractures. This finding suggests that fracture anatomy and the timing of blood loss are critical determinants of TXA responsiveness. The following discussion therefore addresses the findings from two complementary perspectives: haemostatic effectiveness and thrombotic safety, with a particular emphasis on fracture-specific pathophysiology.

Haemostatic effectiveness of TXA should be interpreted according to fracture type

Our data indicate that the haemostatic effect of TXA in hip-fracture surgery is anatomically heterogenous. Rather, its clinical benefit appears to depend on the dominant source and timing of blood loss. This distinction is important because hip fractures are often treated as a single entity in perioperative blood management studies, although femoral neck and intertrochanteric fractures differ substantially in terms of vascular anatomy, fracture biology, surgical approach, and hidden blood loss patterns.

In patients with femoral neck fractures, intravenous TXA administration significantly reduced intraoperative blood loss, transfusion requirements, and transfusion volume, with statistically robust differences between the groups. These findings are consistent with those of previous studies showing that TXA can effectively decrease blood loss and transfusion exposure in patients undergoing surgery for femoral neck fractures or hip arthroplasty after fracture [18, 19]. Randomized evidence obtained in patients with hip-fracture surgery has also demonstrated that intravenous TXA administration can reduce erythrocyte transfusion requirements, although safety signals in high-risk vascular subgroups remain a key concern[20]. A plausible explanation lies in the anatomical characteristics of femoral neck fractures. As intracapsular injuries, femoral neck fractures tend to bleed predominantly from the fracture ends and intra-articular vascular structures. The surgical field is relatively confined, and the major bleeding component is more closely linked to the surgical procedure itself. Under these conditions, systemic TXA administered perioperatively may efficiently inhibit local fibrinolytic activity, thereby reducing both visible surgical bleeding and a portion of perioperative hidden blood loss.

In contrast, the haemostatic benefit of TXA was substantially limited in patients with intertrochanteric fractures. In this cohort, the administration of TXA was associated with a reduction in the median intraoperative blood loss, but it did not significantly reduce the transfusion rate or total transfusion volume. This pattern is consistent with previous evidence suggesting that the clinical effect of TXA in intertrochanteric fracture surgery may be less pronounced than that observed in other types of hip-fracture surgery [21]. The most likely explanation is that intertrochanteric fractures occur in a highly vascular extracapsular metaphyseal region rich in cancellous bone. Bleeding from this region is often diffuse, intramedullary, and substantial. More importantly, a major component of total blood loss may occur immediately after the fracture and before surgical intervention, rather than during the operation. This interpretation is supported by classic work showing that hidden blood loss represents a substantial fraction of total blood loss after hip-fracture surgery[22].

Our findings should be interpreted considering the timing of TXA administration. In the present study, TXA was administered intraoperatively 10 minutes before skin incision and 10 minutes before wound closure. Such a regimen can plausibly reduce active surgical-surface oozing, which explains the observed decrease in intraoperative blood loss. However, it cannot reverse blood loss that has already occurred within the fracture site and medullary cavity before drug administration. Consequently, when preoperative and fracture-related hidden blood loss dominates the overall blood-loss burden, the capacity of intraoperative TXA to influence downstream transfusion decisions may be inherently limited. The absence of a significant difference in transfusion rate and transfusion volume in the intertrochanteric cohort supports this interpretation.

These findings have direct clinical implications. They suggest that, compared with femoral neck fractures, intertrochanteric fractures may require a more tailored haemostatic strategy. Earlier administration of TXA, for example shortly after admission or during preoperative optimization, may theoretically target the ongoing fibrinolytic response induced by the fracture itself. In addition, multimodal blood management protocols combining early antifibrinolytic therapy, restrictive transfusion

thresholds, careful antithrombotic management, and standardized perioperative anaemia correction may be more appropriate for this anatomically high-bleeding-risk subgroup. Future prospective studies should therefore evaluate whether earlier or repeated TXA dosing can translate into a meaningful reduction in transfusion exposure among patients with intertrochanteric fractures.

TXA was not associated with increased thrombotic events or mortality in this high-risk population

The most clinically relevant safety finding of this study was that intravenous TXA administration did not significantly increase the incidence of recurrent stroke, new cardiovascular events, lower limb deep vein thrombosis, pulmonary embolism, or all-cause mortality within 1 year after surgery. These results were consistent across both the femoral neck fracture cohort and the intertrochanteric fracture cohort. For clinicians, this finding is important because it addresses a common but insufficiently evidenced concern: whether TXA should be routinely avoided in patients with a recent history of ischaemic stroke.

Although TXA use is contradicted in patients with a history of thrombosis, our data challenge the assumption that stable, nonacute ischaemic stroke should automatically preclude perioperative TXA administration. Several biological and clinical considerations may explain the absence of an observed excess thrombotic signal. First, ischaemic stroke is most commonly caused by atherosclerosis, platelet activation, and thrombus formation within a diseased arterial system. By contrast, TXA exerts its benefits primarily by inhibiting fibrinolysis; it does not directly activate platelets or initiate the coagulation cascade. Large-scale observational evidence derived from patients undergoing major orthopaedic surgeries similarly suggests that perioperative TXA is associated with lower transfusion exposure without a detectable increase in thromboembolic complications[23]. Second, many patients in this cohort continued antiplatelet or anticoagulant therapy during the perioperative period, which may have provided a background protective effect against thrombosis. Third, standard postoperative prophylaxis with low-molecular-weight heparin after hip-fracture surgery may have further reduced the theoretical prothrombotic risk associated with antifibrinolytic therapy. Fourth, all included patients were outside the acute phase of stroke. This distinction is clinically important because contemporary secondary stroke-prevention guidelines emphasize that recurrent vascular risk is strongly influenced by stroke mechanisms, vascular risk control, and antithrombotic management, rather than by a single historical diagnosis of stroke[24]. This is a critical distinction because the acute phase of stroke, particularly within the first month, is characterized by higher inflammatory activation, haemodynamic instability, and prothrombotic vulnerability.

Our findings should also be interpreted in the context of previous studies. Porter et al. [25] reported that TXA was not associated with increased complications in high-risk patients with intertrochanteric fractures. However, in that study, the definition of ‘high-risk’ included a heterogeneous group of patients with coronary artery disease, atrial fibrillation, venous thromboembolism, and other thrombotic risk factors. Such heterogeneity limits the ability to draw stroke-specific conclusions. Similarly, Viberg et al. [26] evaluated TXA use in high-risk hip fracture patients, but the timing and clinical stability of prior

ischaemic stroke were not clearly specified. Therefore, these data could not be used to determine whether TXA use is safe in patients with recent but nonacute ischaemic stroke. By focusing specifically on patients with ischaemic stroke within the preceding year while excluding patients with acute-phase stroke, the present study bridges this evidence gap and provides more directly applicable data for clinical decision-making.

However, these findings should not be overinterpreted as proof of universal safety. Rather, they support a more nuanced conclusion: in older patients with hip fracture and stable, nonacute ischaemic stroke, perioperative intravenous TXA use was not associated with an excess 1-year risk of major thrombotic complications or mortality. This distinction is essential because the safety profile observed in patients with stable stroke may not apply to patients with acute stroke, severe neurological disability, uncontrolled vascular risk factors, or markedly impaired renal clearance.

Limitations

This study has several limitations. First, because of its retrospective historical control design, selection bias and unmeasured confounding cannot be fully excluded, even though baseline characteristics were broadly balanced between groups. Second, this was a single-centre study, and the findings should be extrapolated cautiously to institutions with different perioperative blood management protocols, transfusion thresholds, or antithrombotic strategies, particularly in patients receiving direct oral anticoagulants. Third, the study population was not stratified according to stroke severity, infarct volume, stroke subtype, or residual neurological disability. Therefore, this study cannot determine whether the same safety profile applies to patients with severe stroke-related disability or to those in the acute phase of ischaemic stroke. Fourth, patients with renal insufficiency received only dose adjustment, and no dedicated subgroup analysis was performed. Because TXA is predominantly renally eliminated, this subgroup may theoretically have higher drug exposure and thrombotic risk. Fifth, routine repeated screening for lower limb venous thrombosis was not performed throughout the follow-up period, which may have resulted in the underdetection of asymptomatic venous thromboembolic events.

Conclusions and future perspectives

In summary, perioperative intravenous TXA use appears to be a clinically useful blood conservation strategy in older patients with hip fracture and a history of ischaemic stroke, without an observed increase in 1-year thrombotic events or all-cause mortality in this stable, nonacute stroke population. Its haemostatic benefit, however, is fracture-type dependent. TXA produced a clear and comprehensive benefit in patients with femoral neck fractures, where blood loss is more closely related to the operative field and intraoperative bleeding. In contrast, in intertrochanteric fractures, its effect was substantially limited, probably because a substantial proportion of blood loss had already occurred before surgery within the highly vascular extracapsular and intramedullary fracture environment. These findings support a more individualized approach to TXA use in patients with prior ischaemic stroke, and they also suggest that clinical expectations regarding haemostatic benefits should be calibrated according to fracture

anatomy. Future prospective studies should examine optimized dosing schedules, earlier administration strategies, and multimodal blood management protocols, particularly for intertrochanteric fractures.

Declarations

Authors' contributions

Zhang SH wrote the manuscript and created tables and figures. He YM and Zhang SH performed the statistics. He YM and Xu CY performed the dataextractions. Wang XW and Chen XB supervised the whole process and revised the manuscript. All authors read the final version.

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Data availability

No datasets were generated or analysed during the current study.

Ethics approval and consent to participate

This study was conducted in accordance with the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee of Beijing Tongren Hospital, Capital Medical University (Approval No. TREC2025-KY053). Owing to the retrospective design of the study and the use of anonymized clinical data, the requirement for written informed consent was waived by the Ethics Committee of Beijing Tongren Hospital, Capital Medical University.

Consent for publication

All authors consent to the publication of this manuscript and all associated data.

Competing interests

The authors declare no competing interests.

Consent to Participate declaration

Not applicable.

Clinical trial number

Not applicable.

References

1. Arshi A, et al. Blood transfusion rates and predictors following geriatric hip fracture surgery. Hip Int. 2021;31(2):272–9.
2. Haentjens P, et al. Meta-analysis: excess mortality after hip fracture among older women and men. Ann Intern Med. 2010;152(6):380–90.
3. Simunovic N, et al. Effect of early surgery after hip fracture on mortality and complications: systematic review and meta-analysis. CMAJ. 2010;182(15):1609–16.
4. Jang SY, et al. Blood Transfusion for Elderly Patients with Hip Fracture: a Nationwide Cohort Study. J Korean Med Sci. 2020;35(37):e313.
5. Carson JL, et al. Liberal or restrictive transfusion in high-risk patients after hip surgery. N Engl J Med. 2011;365(26):2453–62.
6. Carson JL, et al. Clinical Practice Guidelines From the AABB: Red Blood Cell Transfusion Thresholds and Storage. JAMA. 2016;316(19):2025–35.
7. Carson JL, et al. Red Blood Cell Transfusion: 2023 AABB International Guidelines. JAMA. 2023;330(19):1892–902.
8. Kim JH, et al. Effect of a Patient Blood Management Program on the Appropriateness of Red Blood Cell Transfusion and Clinical Outcomes in Elderly Patients Undergoing Hip Fracture Surgery. J Korean Med Sci. 2023;38(8):e64.
9. Zhang Y, et al. Intervention with erythropoietin in sarcopenic patients with femoral intertrochanteric fracture and its potential effects on postoperative rehabilitation. Geriatr Gerontol Int. 2020;20(2):150–5.
10. Suh YS, et al. Hip Fracture Surgery without Transfusion in Patients with Hemoglobin Less Than 10 g/dL. Clin Orthop Surg. 2021;13(1):30–6.
11. Williams-Johnson JA, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2) A randomised, placebo-controlled trial. West Indian Med J. 2010;59(6):612–24.
12. Liu W, Deng S, Liang J. Tranexamic acid usage in hip fracture surgery: a meta-analysis and meta-regression analysis of current practice. Arch Orthop Trauma Surg. 2022;142(10):2769–89.
13. Ker K, et al. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. BMJ. 2012;344:e3054.
14. Leverett GD, Marriott A. Intravenous tranexamic acid and thromboembolic events in hip fracture surgery: A systematic review and meta-analysis. Orthop Traumatol Surg Res. 2023;109(2):103337.
15. Xu J, et al. Trends and Risk Factors Associated With Stroke Recurrence in China, 2007–2018. JAMA Netw Open. 2022;5(6):e2216341.
16. Flach C, et al. Risk and Secondary Prevention of Stroke Recurrence: A Population-Base Cohort Study. Stroke. 2020;51(8):2435–44.
17. Kahan JB, et al. Expanded use of tranexamic acid is safe and decreases transfusion rates in patients with geriatric hip fractures. OTA Int. 2021;4(4):e147.

18. Watts CD, et al. Tranexamic Acid Safely Reduced Blood Loss in Hemi- and Total Hip Arthroplasty for Acute Femoral Neck Fracture: A Randomized Clinical Trial. J Orthop Trauma. 2017;31(7):345–51.
19. Pinzón-Florez CE, Vélez Cañas KM, Díaz DM, Quijano. Efficiency of tranexamic acid in perioperative blood loss in hip arthroplasty: a systematic literature review and meta-analysis. Rev Esp Anestesiol Reanim. 2015;62(5):253–64.
20. Zufferey PJ, et al. Tranexamic acid in hip fracture surgery: a randomized controlled trial. Br J Anaesth. 2010;104(1):23–30.
21. Kanthasamy S, et al. The efficacy of intravenous tranexamic acid administration at induction in definitive hip fracture surgery: Is there a role? Injury. 2021;52(8):2361–6.
22. Foss NB, Kehlet H. Hidden blood loss after surgery for hip fracture. J Bone Joint Surg Br. 2006;88(8):1053–9.
23. Poeran J, et al. Tranexamic acid use and postoperative outcomes in patients undergoing total hip or knee arthroplasty in the United States: retrospective analysis of effectiveness and safety. BMJ. 2014;349:g4829.
24. Kleindorfer DO, et al. 2021 Guideline for the Prevention of Stroke in Patients With Stroke and Transient Ischemic Attack: A Guideline From the American Heart Association/American Stroke Association. Stroke. 2021;52(7):e364–467.
25. Porter SB, et al. Tranexamic Acid Was Not Associated with Increased Complications in High-Risk Patients with Intertrochanteric Fracture. J Bone Joint Surg Am. 2022;104(13):1138–47.
26. Viberg B et al. Is tranexamic acid use in patients with a hip fracture safe? Bone Joint J, 2021. 103–b(3): pp. 449–455.

Figures

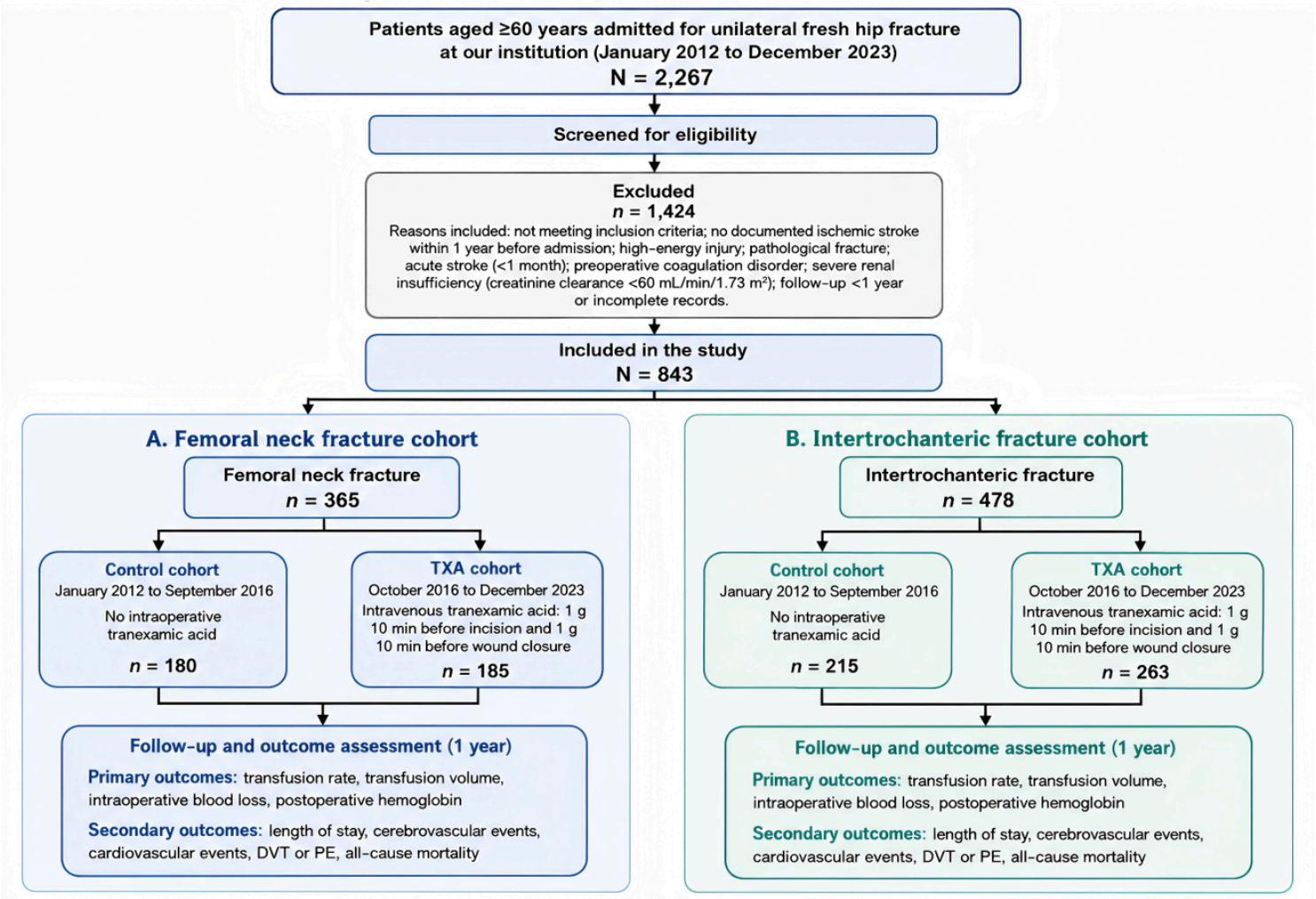


Figure 1

Flowchart of patient selection and cohort allocation