JAMA Surgery | Original Investigation

Perioperative Use of Tranexamic Acid in General Surgery
A Systematic Review and Meta-Analysis

Lucas Monteiro Delgado; Bernardo Fontel Pompeu, MD; Gabriel Henrique Acedo Martins; Mariana Lima Azevedo; Eric Pasqualotto; Thiago Celestino Chulam, MD; Sérgio Mazzola Poli de Figueiredo, MD

IMPORTANCE Tranexamic acid (TXA) is increasingly used to minimize perioperative bleeding. However, its efficacy and safety profile across general surgical procedures remains unclear.

OBJECTIVE To evaluate the efficacy and safety of prophylactic TXA in reducing intraoperative blood loss, need for transfusion, and major bleeding in general surgery, while assessing its association with thromboembolic events and mortality.

DATA SOURCES PubMed, Embase, and Cochrane Library were systematically searched from inception to April 3, 2025.

STUDY SELECTION Randomized clinical trials (RCTs) comparing TXA to placebo in adult patients undergoing general surgery and reporting at least 1 predefined outcome of interest were included.

DATA EXTRACTION AND SYNTHESIS Two reviewers independently extracted data and assessed risk of bias. Mean differences (MDs) and risk ratios (RRs) with 95% CIs were pooled using random-effects models. Heterogeneity was assessed using the I^2 statistic.

RESULTS Twenty-six RCTs with a total of 6976 patients were included. TXA use was associated with lower intraoperative blood loss (MD, −35.85 mL; 95% CI, −57.20 to −14.51 mL; I^2 = 91%; P = .001), reduced need for transfusion (RR, 0.75; 95% CI, 0.60-0.94; I^2 = 54%; P = .01), and fewer major bleeding events (RR, 0.72; 95% CI, 0.59-0.89; I^2 = 0%; P = .002). No significant differences were found in venous thromboembolism (RR, 1.09; 95% CI, 0.62-1.92; I^2 = 15%; P = .75), mortality (RR, 1.08; 95% CI, 0.72-1.61; I^2 = 0%; P = .71), and length of stay (MD, −0.54 days; 95% CI, −1.15 to 0.06 days; I^2 = 73%; P = .08). In the subgroup analysis restricted to abdominal procedures, the benefits observed in the overall population on intraoperative blood loss and need for transfusion were no longer present. In the hepatobiliary subgroup, TXA was associated with a significant reduction in major bleeding (RR, 0.59; 95% CI, 0.39-0.90; I^2 = 0%; P = .01), while no significant differences were observed for the other outcomes.

CONCLUSIONS AND RELEVANCE This systematic review and meta-analysis found that prophylactic TXA use was associated with lower intraoperative blood loss, transfusion requirements, and major bleeding without an observed increase in thromboembolic or mortality risk. Although these findings support the use of TXA in general surgery procedures, the decision to use TXA should be individualized considering individual patient characteristics and the specific procedure being performed.

Invited Commentary

Supplemental content

Author Affiliations: Universidade Federal de Minas Gerais, Belo Horizonte-MG, Brazil (Delgado, Martins, Azevedo); Department of Colorectal Surgery, Heliópolis Hospital, São Paulo-SP, Brazil (Pompeu); Universidade Municipal de São Caetano do Sul (USCS), São Paulo-SP, Brazil (Pompeu); Universidade Federal de Santa Catarina, Florianópolis-SC, Brazil (Pasqualotto); AC Camargo Cancer Center, São Paulo-SP, Brazil (Chulam); Universidade Federal do Espírito Santo, Vitória-ES, Brazil (Chulam); Department of Surgery, University of North Carolina, Chapel Hill, North Carolina (de Figueiredo).

Corresponding Author: Lucas Monteiro Delgado, 190 Prof. Alfredo Balena Avenue, Santa Efigênia, Belo Horizonte-MG, 30130-100, Brazil (ldelgado@ufmg.br).

JAMA Surg. doi:10.1001/jamasurg.2025.5498
Published online December 17, 2025.

Tranexamic acid (TXA) is an antifibrinolytic agent that inhibits the conversion of plasminogen to plasmin, disrupting fibrinolysis and enhancing the stability of fibrin clots.[1,2] While it promotes physiological hemostasis, its prothrombotic potential remains a theoretical concern.[3] The use of TXA has been well established in cardiac, orthopedic, and plastic surgeries[4-8]; however, the effectiveness of TXA in general surgery remains unclear.

General surgery encompasses a diverse range of procedures, each with distinct bleeding risk profiles and differing from other surgical specialties, such as cardiac, orthopedic, and plastic surgeries.[9] Major intraoperative bleeding is associated with increased transfusion needs, reinterventions, and prolonged hospital stays.[10] Thus, identifying effective strategies to minimize bleeding and reduce transfusion requirements is of significant clinical importance. A recent substudy from the Perioperative Ischemic Evaluation-3 (POISE-3) trial demonstrated reduced bleeding without increased cardiovascular risk,[3] underscoring the need for further investigation.

To date, no meta-analysis has specifically evaluated the efficacy and safety of TXA across general surgical procedures. We hypothesized that TXA would be associated with a reduction in bleeding-related outcomes without a corresponding increase in the risk of venous thromboembolism (VTE).

Key Points

Question Is prophylactic tranexamic acid associated with reduced blood loss in adult patients undergoing general surgery?

Findings In this systematic review and meta-analysis of 26 randomized clinical trials including 6976 patients, tranexamic acid was associated with lower intraoperative blood loss, reduced need for transfusion, and fewer major bleeding events, without increases in venous thromboembolism, mortality, or length of stay. However, these benefits did not remain consistent in subgroup analyses.

Meaning These findings suggest that prophylactic tranexamic acid is safe and is associated with reduced bleeding in general surgery, but its benefits may vary by procedure type and should not be generalized across all surgical contexts.

Methods

Protocol and Registration

This systematic review and meta-analysis was conducted in accordance with the Cochrane Handbook and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) reporting guideline.[11,12] The protocol was registered in PROSPERO (CRD420251038412).[13]

Search Strategy and Study Selection

We systematically searched PubMed, Embase, and the Cochrane Library from inception to April 3, 2025. Reference lists of included studies and relevant reviews were also screened for additional articles.[14] Full search strategies are provided in eTable 1 in Supplement 1. Two reviewers (G.H.A.M. and L.M.D.) independently screened records using Rayyan (Rayyan Systems Inc). After removing duplicates and irrelevant titles and abstracts, full texts were assessed for eligibility. Disagreements were resolved by a third reviewer (B.F.P.).

Eligibility Criteria

We included randomized clinical trials (RCTs) that compared TXA with placebo in adults (≥18 years) undergoing general surgery and that reported at least 1 predefined outcome. Exclusion criteria included single-arm studies, case reports, trial registrations without results, reviews, meta-analyses, and animal studies.

Data Extraction

Two reviewers (G.H.A.M. and M.L.A.) independently extracted data using a standardized form, including study identifiers (title, authors, year, registry, country, period), procedure type, TXA regimen (dose, timing, route), sample size, patient characteristics (age, sex), follow-up duration, and reported outcomes. Discrepancies were resolved by consensus. Patient-level data were not available because our analyses relied exclusively on aggregate results reported in the published studies, and no individual participant data were provided or accessible.

Outcomes and Subgroup Analyses

Primary outcomes included intraoperative blood loss, transfusion requirement, and major bleeding. Secondary outcomes were VTE, postoperative mortality, and length of hospital stay (LOS). Three subgroup analyses were conducted for the primary outcomes: (1) by surgical subcategory (abdominal vs head and neck), (2) restricted to hepatobiliary surgery, and (3) further restricted to liver resection and liver transplant.

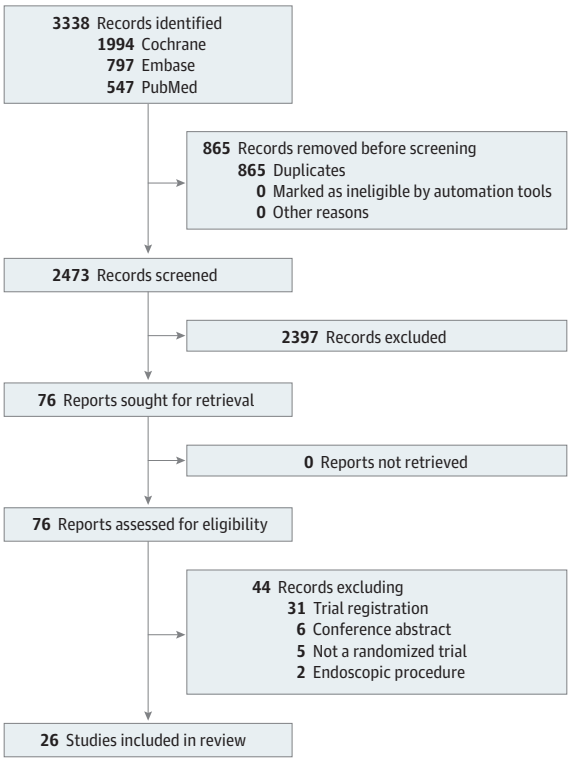
Risk of Bias and Evidence Quality Assessment

Two reviewers (L.M.D. and G.H.A.M.) independently assessed the risk of bias using the Cochrane RoB 2 tool, which covers 4 domains: randomization, deviations from intended interventions, missing data, outcome measurement, and selective reporting.[15] Disagreements were resolved by consensus. Overall risk of bias was determined by aggregating domain-level judgments. The certainty of evidence was evaluated using the GRADE approach and rated as high, moderate, low, or very low.[16] Publication bias was assessed using contour-enhanced funnel plots and the Egger regression test.[11,17]

Statistical Analysis

Continuous and binary outcomes were pooled as mean differences (MDs) or risk ratios (RRs), respectively, with 95% CIs. Pooled proportions were estimated using inverse-variance methods with logit or log transformations. Statistical significance was set at $P < .05$. A DerSimonian and Laird random-effects model was applied to all outcomes.[18] Heterogeneity was assessed using Cochran Q and I^2, with $I^2 > 25\%$ or $P < .10$ indicating substantial heterogeneity. Subgroup interactions were evaluated using a significance threshold of $P < .10$, as recommended by Cochrane.[11] All analyses were conducted in R, version 4.4.2 (R Foundation), and trial sequential analysis (TSA)

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Flow Diagram of Study Screening and Selection



was performed using TSA software, version 0.9.5.10 (Copenhagen Trial Unit).

Sensitivity Analysis

For outcomes with substantial heterogeneity ($I^2 \geq 25\%$), we conducted complementary analyses to test the robustness of results and explore potential sources of variability. Baujat plots were used to identify studies with disproportionate influence on both effect estimates and heterogeneity.[19] Leave-one-out analysis was performed by sequentially excluding each study to assess the stability of pooled outcomes.[20] We also performed TSA using the O'Brien-Fleming alpha-spending function to adjust for random errors; required information size was calculated assuming a 5% type I error and 20% type II error, incorporating the pooled mean difference and between-study variance.[21] Lastly, meta-regression was used to evaluate whether differences in TXA dosage or other study-level variables explained heterogeneity.[11,22]

Results

Study Selection and Characteristics

As detailed in **Figure 1**, the initial search identified 3338 results. Following the removal of duplicate records and an assessment of the studies based on title and abstract, 76 studies remained for full-text review, in accordance with the prespecified inclusion criteria. Of these, 26 RCTs were selected, including a total of 6976 patients.[3,23-47] Among these, 3553 patients (50.93%) received TXA, while 3423 patients (49.07%) did not. The baseline characteristics are detailed in the **Table**.

The abdominal subgroup included 16 RCTs[3,23-35,45,47] with a total of 6046 patients. Among these, 3065 patients (50.7%) received TXA, while 2981 (49.3%) did not. The procedures represented a broad range of abdominal operations, including liver resections, liver transplantation, pancreaticoduodenectomy, sleeve gastrectomy, colectomy, esophagectomy, and ventral or inguinal hernia repair. The head and neck subgroup comprised 10 RCTs,[36-44,46] totaling 930 patients. Among these, 488 patients (52.47%) received TXA, while 442 (47.53%) did not. The included procedures encompassed thyroid resections, tonsillectomies, endoscopic sinus surgeries, mastoidectomies, and head and neck cancer resections.

All included studies administered TXA intravenously, most commonly as a bolus-only regimen (n = 11),[3,23,31,35,36,38,40,42,44-46] followed by bolus plus rescue dosing (n = 6)[28,30,33,37,41,43] and bolus plus continuous infusion (n = 6).[26,27,29,32,34,38,39] Administration timing varied: preoperative (n = 5),[38,40,42,44,45] intraoperative (n = 11),[3,23-25,31,34-36,41,46,47] both preoperative and interoperative (n = 3),[27,28,39] or both intraoperative and postoperative (n = 7).[26,29,30,32,33,37,43] Dosing strategies included both fixed (eg, 1 g bolus) and weight-based (eg, 10-15 mg/kg) regimens. Complete protocol details are available in eTable 2 in Supplement 1.

Pooled Analysis

Primary Outcomes

TXA use was associated with lower intraoperative blood loss (MD, −35.85 mL; 95% CI, −57.20 to −14.51 mL; $P = .001$; $I^2 = 91\%$) (**Figure 2**), reduced need for transfusion (RR, 0.75; 95% CI, 0.60-0.94; $P = .01$; $I^2 = 54\%$) (**Figure 3**), and fewer major bleeding events (RR, 0.72; 95% CI, 0.59-0.89; $P = .002$; $I^2 = 0\%$) (**Figure 4**). All studies included in major bleeding event outcome analysis were abdominal surgeries.

Secondary Outcomes

There were no significant differences between groups in VTE (RR, 1.09; 95% CI, 0.62-1.92; $P = .75$; $I^2 = 15\%$) (eFigure 1 in Supplement 1), mortality (RR, 1.08; 95% CI, 0.72-1.61; $P = .71$; $I^2 = 0\%$) (eFigure 2 in Supplement 1), or LOS (MD, −0.54 days; 95% CI, −1.15 to 0.06 days; $P = .08$; $I^2 = 73\%$) (eFigure 3 in Supplement 1).

Sensitivity Analysis

In the leave-one-out sensitivity analysis, detailed in eFigures 4-6 in Supplement 1, exclusion of any single study did not significantly reduce heterogeneity or alter the results for intraoperative blood loss or need for transfusion, indicating the stability of the findings. For LOS, the exclusion of the study by Siddiqui et al[30] removed heterogeneity while shifting the results from nonsignificant to significant favoring TXA. We hypothesize that this influence is related to the fact that Siddiqui et al[30] was the only trial including ventral hernia repair, a low-risk general surgical procedure. Baujat plots, detailed in eFigures 7-9 in Supplement 1, were consistent with the findings of the leave-one-out analysis.

Table. Baseline Characteristics of the Included Studies

Source	Trial registration	Period	Country	General surgery subtype	Procedure	Patients, No.		Male, %		Age, mean, y	
						TXA	Control	TXA	Control	TXA	Control
Auvinen et al,[37] 1987	NA	NA	Finland, single-center	Head and neck	Thyroid resection	39	37	NA	NA	50	51
Boylan et al,[24] 1996	NA	1992-1994	Canada, single-center	Hepatopancreatobiliary	Liver transplant	25	20	56	55	49.2	48.8
Kaspar et al,[47] 1997	NA	NA	US, single-center	Hepatopancreatobiliary	Liver transplant	16	16	NA	NA	NA	NA
Dalmau et al,[25] 2000	NA	1997-1998	Spain, multicenter	Hepatopancreatobiliary	Liver transplant	42	42	73.8	61.9	58[a]	56[a]
Wu et al,[33] 2006	NA	2002-2004	Taiwan, single-center	Hepatopancreatobiliary	Hepatectomy	109	108	74.1	72.6	57	62
Chen et al,[39] 2008	NA	2006-2007	Taiwan, single-center	Head and neck	Various head and neck procedures	29	31	57.7	55.2	49.8	46.4
Alimian and Mohseni,[36] 2011	NA	2008-2009	Iran, single-center	Head and neck	Endoscopic sinus surgery	42	42	59.5	57.2	33	35
George et al,[40] 2011	NA	2007-2009	India, single-center	Head and neck	Tonsillectomy	50	50	46	58	NA	NA
NCT00827931[28]	NCT00827931	2009-2011	India, single-center	Hepatopancreatobiliary, upper GI and colorectal	Pancreatoduodenectomy, esophagectomy, colectomy, gastrectomy and biliary tract surgery	49	45	67.3	64.4	44.26[b]	48.56[b]
Alhomoud et al,[23] 2016	NA	2014	Kuwait, single-center	Upper GI	Sleeve gastrectomy	25	25	16		NA	
Kulkarni et al,[41] 2016	NA	NA	India, single-center	Head and neck	HNC surgery	108	111	74	79	51.3	20.7
Pannerselvam et al,[42] 2019	NA	2013	India, single-center	Head and neck	Endoscopic sinus surgery	56	28	71	53	32.2	33
Thakur et al,[43] 2019	NA	NA	India, single-center	Head and neck	Various head and neck procedures	43	48	37	35	42.8	48.5
Ziaei et al,[46] 2020	NA	2018	Iran, multicenter	Head and neck	Mastoidectomy	35	35	58.8	51.4	32.87	33.2
Babu et al,[38] 2021	NA	2018-2019	India, single-center	Head and neck	HNC surgery	56	30	80.4	71.4	48.1	44.3
Yang et al,[44] 2021	ChiCTR2100043139	2021	China, single-center	Head and neck	Endoscopic sinus surgery	30	30	53	40	44.1	44.2
Zaheer et al,[35] 2021	NA	2019-2020	Pakistan, single-center	Low risk general surgery	Inguinal hernia repair	40	40	100	100	41.5	39.3
Siddiqui et al,[30] 2022	NA	2022	Pakistan, single-center	Low risk general surgery	Ventral hernial repair	40	40	20	22	41.5	42.8
TAC-PD[32]	jRCTs041190062	2019-2021	Japan, multicenter	Hepatopancreatobiliary	Pancreaticoduodenectomy	110	110	56.5	59.1	71[a]	70[a]
Sermet et al,[29] 2023	NCT05696951	2022	Turkey, single-center	Upper GI	Sleeve gastrectomy	120	60	23.3	18.6	35.8	34.6
't Hart et al,[31] 2023	NL8029	2020-2021	Netherlands, single-center	Upper GI	Sleeve gastrectomy	56	56	22.4	19.2	36.0	36.8
Yang et al,[34] 2023	NA	NA	China, multicenter	Hepatopancreatobiliary	Hepatectomy	15	15	66.7	60	55.8	48.8
Shaker et al,[45] 2023	NCT03606785	2018-2020	Egypt, single-center	Colorectal	Explorative laparotomy	30	30	36.7	56.7	43.4	43.8
HeLiX[26]	NCT02261415	2014-2022	US and Canada, multicenter	Hepatopancreatobiliary	Hepatectomy	694	690	61.1	59.4	63.1	63.4
Luo et al,[27] 2025	ChiCTR2300076300	2021-2023	China, single-center	Hepatopancreatobiliary	Hepatectomy	59	59	42.4	50.8	51.4	53.6
POISE-3[3]	NCT03505723	2018-2021	International, multicenter	Major general surgery[c]	Major general surgery[c]	1635	1625	53	53.7	68.8	68.4

Abbreviations: GI, gastrointestinal; HNC, head and neck cancer; NA, not available; TXA, tranexamic acid.

[a] Median.

[b] Estimated from age group distribution using weighted midpoints.

[c] Includes hepatopancreaticobiliary, colorectal, upper GI, head and neck procedures, other major general, and other minor general surgeries.

Figure 2. Risk Ratios for Intraoperative Blood Loss

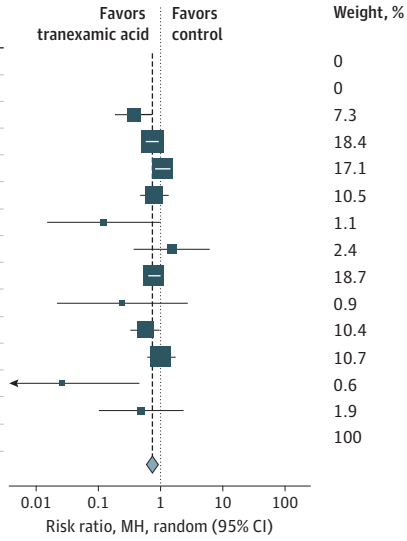
Study	Tranexamic acid		Control		Mean difference, IV, random (95% CI), mL	Weight, %
	Mean (SD) mL	Total, No.	Mean (SD) mL	Total		
Alimian and Mohseni,[36] 2011	184.00 (64.00)	42	312.00 (75.00)	42	-128.00 (-157.82 to -98.18)	11.8
Auvinen et al,[37] 1987	240.75 (183.73)	39	306.75 (269.36)	37	-66.00 (-170.20 to 38.20)	3.3
Boylan et al,[24] 1996	4904.94 (4245.00)	25	9754.90 (8616.70)	20	-4849.96 (-8976.68 to -723.23)	0
Chen et al,[39] 2008	86.50 (128.50)	29	115.50 (120.30)	31	-29.00 (-92.09 to 34.09)	6.6
George et al,[40] 2011	36.64 (587.18)	50	66.32 (934.48)	50	-29.68 (-335.59 to 276.23)	0.5
HeLiX[26]	817.30 (1065.00)	694	836.70 (1062.00)	690	-19.40 (-131.46 to 92.66)	2.9
Kulkarni et al,[41] 2016	785.00 (300.00)	120	1198.00 (1840.00)	120	-413.00 (-746.56 to -79.44)	0.4
Luo et al,[27] 2025	267.66 (189.97)	59	185.33 (151.97)	59	82.33 (20.25 to 144.41)	6.7
NCT00827931[28]	599.20 (419.58)	49	682.80 (555.52)	45	-83.60 (-283.96 to 116.76)	1.1
Pannerselvam et al,[42] 2019	36.10 (1.61)	56	68.93 (14.03)	28	-32.83 (-38.04 to -27.62]	15.2
Sermet and Ozsoy,[29] 2023	26.28 (15.27)	120	26.90 (14.81)	60	-0.62 (-5.26 to 4.02)	15.2
Shaker et al,[45] 2023	819.33 (322.25)	30	1027.00 (283.77)	30	-207.67 (-361.32 to -54.02)	1.7
TAC-PD[32]	659.00 (581.00)	110	701.00 (531.00)	110	-42.00 (-189.09 to 105.09)	1.9
Thakur et al,[43] 2019	135.93 (50.99)	43	131.67 (50.97)	48	4.26 (-16.72 to 25.24)	13.4
Wu et al,[33] 2006	381.09 (409.26)	109	719.99 (667.14)	108	-338.90 (-486.32 to -191.48)	1.8
Yang et al,[44] 2021	338.35 (270.89)	30	309.26 (175.92)	30	29.09 (-86.49 to 144.67)	2.8
Yang et al,[34] 2023	1244.50 (1717.57)	15	1363.35 (1431.31)	15	-118.85 (-1250.29 to 1012.59)	0
Ziaei et al,[46] 2020	60.20 (17.50)	35	90.40 (26.40)	35	-30.20 (-40.69 to -19.71)	14.8
Total		1655		1558	-35.85 (-57.20 to -14.51)	100
Heterogeneity: $\tau^2 = 773.116$; $\chi^2 = 193.49$ $df = 17$ ($P < .001$); $I^2 = 91\%$						
Test for overall effect: $z = -3.29$ ($P = .001$)						

A random-effects DerSimonian and Laird model was used to calculate the mean differences for intraoperative blood loss. Squares represent the point estimates of individual studies, and their sizes are proportional to the corresponding study weights in the meta-analysis. Horizontal lines indicate 95% CIs. Diamonds represent the overall pooled estimates. IV indicates inverse variance.

Figure 3. Risk Ratios for the Need for Transfusion

Study	Tranexamic acid Events	Tranexamic acid Total	Control Events	Control Total	Risk ratio,MH, random (95% CI)	Weight, %
Alhomoud et al,[23] 2016	0	25	0	25		0
Alimian et al,[36] 2011	0	42	0	42		0
Babu et al,[38] 2021	10	56	14	30	0.38 (0.19-0.76)	7.3
Dalmau,[25] 2000	29	42	37	40	0. 75 (0.60-0.93)	18.4
HeLiX[26]	101	694	91	690	1.10 (0.85-1.44)	17.1
Kulkarni et al,[41] 2016	22	120	27	120	0.81 (0.49-1.35)	10.5
Luo et al,[27] 2025	1	59	8	59	0.12 (0.02-0.97)	1.1
NCT00827931[28]	5	49	3	45	1.53 (0.39-6.04)	2.4
POISE-3[3]	141	1635	177	1625	0. 79 (0.64-0.98)	18.7
Sermet and Ozsoy,[29] 2023	1	120	2	60	0.25 (0.02-2.70)	0.9
Shaker et al,[45] 2023	12	30	20	30	0.60 (0.36-1.00)	10.4
TAC-PD[32]	25	110	24	110	1.04 (0.64-1.71)	10.7
Wu et al,[33] 2006	0	109	17	108	0.03 (0.00-0.46)	0.6
Yang et al,[34] 2023	2	15	4	15	0.50 (0.11-2.33)	1.9
Total	349	3106	424	2999	0. 75 (0.60-0.94)	100

Heterogeneity: $\tau^2 = 0.058$; $\chi^2 = 23.78$, $df = 11$ ($P = .01$); $I^2 = 54\%$
Test for overall effect: $z = -2.47$ ($P = .01$)

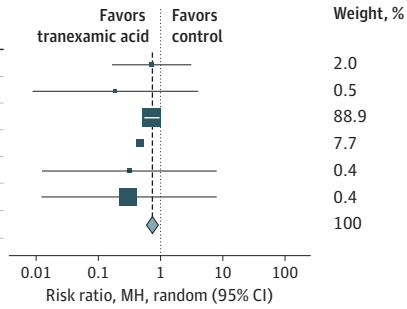


A random-effects DerSimonian and Laird model was used to calculate the risk ratio for intraoperative blood loss. Squares represent the point estimates of individual studies, and their sizes are proportional to the corresponding study weights in the meta-analysis. Horizontal lines indicate 95% confidence intervals. MH indicates Mantel-Haenszel method.

Figure 4. Risk Ratios for Major Bleeding

Study	Tranexamic acid Events	Tranexamic acid Total	Control Events	Control Total	Risk ratio, MH, random (95% CI)	Weight, %
Dalmau,[25] 2000	3	42	4	42	0.75 (0.18-3.15)	2.0
Luo et al,[27] 2025	0	59	2	59	0.20 (0.01-4.08)	0.5
POISE-3[3]	130	1635	171	1625	0.76 (0.61-0.94)	88.9
Sermet and Ozsoy,[29] 2023	12	120	12	60	0.50 (0.24-1.05)	7.7
't Hart et al,[31] 2023	0	56	1	56	0.33 (0.01-8.01)	0.4
TAC-PD[32]	0	110	1	110	0.33 (0.01-8.09)	0.4
Total	145	2022	191	1952	0.72 (0.59-0.89)	100

Heterogeneity: $\tau^2 = 0$; $\chi^2 = 2.27$, $df = 5$ ($P = .81$); $I^2 = 0\%$
Test for overall effect: $z = -3.11$ ($P = .002$)



A random-effects DerSimonian and Laird model was used to calculate the risk ratio for intraoperative blood loss. Squares represent the point estimates of individual studies, and their sizes are proportional to the corresponding study weights in the meta-analysis. Horizontal lines indicate 95% confidence intervals. MH indicates Mantel-Haenszel method.

Subgroup Analysis

In the subgroup analysis by surgical subcategory, TXA use was associated with lower intraoperative blood loss in head and neck surgery (MD, −41.89 mL; 95% CI, −65.62 to −18.15 mL; $P < .001$; $I^2 = 86\%$) (eFigure 10 in Supplement 1); however, no significant differences were observed in abdominal surgery (MD, −69.80 mL; 95% CI, −151.73 to 12.13 mL; $P = .09$; $I^2 = 80\%$) (eFigure 10 in Supplement 1). For need for transfusion, no significant differences were found between groups for either head and neck surgery (RR, 0.58; 95% CI, 0.28-1.21; $P = .15$; $I^2 = 68\%$) (eFigure 11 in Supplement 1) or abdominal surgery (RR, 0.77; 95% CI, 0.56-1.07; $P = .12$; $I^2 = 57\%$) (eFigure 11 in Supplement 1).

In the hepatobiliary subgroup, TXA use was associated with fewer major bleeding events (RR, 0.59; 95% CI, 0.39-0.90; $P = .01$; $I^2 = 0\%$) (eFigure 12 in Supplement 1); however, no significant differences were observed for the remaining outcomes (eFigures 13-17 in Supplement 1). In a further stratification of the hepatobiliary subgroup, restricted to liver resection and transplant, no significant differences were observed for any of the evaluated outcomes (eFigures 18-23 in Supplement 1).

Trial Sequential Analysis

TSAs confirmed the conclusiveness of findings for intraoperative blood loss and major bleeding, all reaching the required information size with low risk of random error. For need for transfusion and LOS, the data suggested a possible effect but remained inconclusive. VTE and mortality outcomes lacked sufficient information, limiting interpretability and highlighting the need for further high-powered studies. Detailed results of the TSAs are provided in eFigures 24-29 in Supplement 1.

Meta-Regression Analysis

Meta-regression analyses revealed no significant linear association between TXA dosage and intraoperative blood loss, suggesting a consistent treatment effect across the range of dosages used in the included studies. Similarly, no significant associations were identified for other prespecified moderators, including mean age, mean weight, sample size, and year of publication. Detailed results of the meta-regression analyses are provided in eFigures 30-34 in Supplement 1.

Risk of Bias and Quality Assessment

Risk of bias was assessed using the Cochrane RoB 2 tool (eFigure 35 in Supplement 1). Most trials were rated as low or having some concerns, with only a minority classified as high risk due to issues in randomization, allocation concealment, or blinding. Given the objective nature of the primary outcomes, the overall risk of bias was considered limited. Funnel plot analysis for intraoperative blood loss showed no major asymmetry, and the Egger test did not indicate significant small-study effects (t = −1.37, df = 16, P = .19; bias estimate = −1.24, SE = 0.90) (eFigure 36 in Supplement 1), suggesting low risk of publication bias. eTable 3 in Supplement 1 shows the summary of findings and certainty of evidence assessment according to the GRADE tool.

Discussion

This is, to our knowledge, the first meta-analysis to evaluate prophylactic TXA across a wide spectrum of general surgical procedures. Based on 26 RCTs with 6976 patients, TXA use was associated with lower intraoperative blood loss, decreased need for transfusion, and fewer major bleeding events. No significant differences were observed for VTE, mortality, or LOS. Leave-one-out sensitivity analyses demonstrated the stability of these findings, and TSA further confirmed the robustness and conclusiveness of our findings. Subgroup analyses showed that intraoperative blood loss reduction was confined to head and neck surgery. In abdominal surgery and hepatobiliary surgery, TXA was associated with a reduction in major bleeding, but this effect was not sustained when restricting the analysis to liver resection and transplant.

These results are consistent with the POISE-3 trial, the largest RCT of TXA in noncardiac surgery.[3] In its general surgery subgroup, TXA reduced life-threatening and major bleeding without increasing cardiovascular events. POISE-3 accounted for nearly 47% of our total sample and heavily influenced key outcomes, especially major bleeding and VTE. While reinforcing the validity of our findings, this also underscores the need for cautious interpretation of subgroup-driven effects.

Despite TXA use being associated with lower intraoperative blood loss overall, this effect was not observed in abdominal surgeries, suggesting it was potentially influenced by head and neck procedures. Although a trend toward transfusion reduction with perioperative TXA use was observed in the abdominal subgroup analysis, our overall TSA indicated that the cumulative evidence has not yet reached the required information size. This suggests that the current body of evidence remains inconclusive, and the inclusion of future studies may help reach a more definitive conclusion. A reduction in major bleeding was observed; however, this outcome was reported exclusively in abdominal surgery trials, as head and neck procedures seldom involve bleeding of such severity.

The hemostatic benefits of TXA observed in this study are consistent with evidence from other clinical settings. In trauma, the CRASH-2 trial showed that early TXA administration reduced all-cause and bleeding-related mortality without increasing vascular events,[48] supporting its widespread use in hemorrhage protocols. In gastrointestinal bleeding, while high-dose regimens may increase thrombotic risk without improving survival, low-dose or enteral TXA has been associated with decreased transfusion requirements and surgical interventions. Among patients with cirrhosis, TXA use has been linked to improved early bleeding control and lower rebleeding rates, despite no observed survival advantage.[49,50]

Beyond efficacy, we assessed TXA safety with a focus on VTE. Our meta-analysis found no significant difference in VTE incidence between groups, suggesting overall thrombotic neutrality in general surgery. However, this result was heavily influenced by POISE-3[3] and HeLiX,[26] which together accounted for most VTE events and nearly half the sample. Given the heterogeneity of surgical populations, caution remains warranted in prothrombotic settings such as malignancy, critical illness, and particularly hepatic surgery and transplant, which represent distinct contexts with unique hemostatic challenges. In a subgroup analysis restricted to hepatobiliary procedures, TXA did not significantly affect mortality, need for transfusion, or thromboembolic risk but was associated with a lower risk of major bleeding. However, when further stratified to liver resection and transplant only, no differences were observed in any of the evaluated outcomes.

Prior meta-analyses focusing solely on hepatic surgery, such as those by de Jesus et al[51] and Tanashat et al,[52] reported no benefit in terms of bleeding or mortality and raised concerns about an increased thromboembolic risk. However, the study by de Jesus et al[51] did not report a statistically significant difference in VTE occurrence and included only 3 studies with events, which weakens the basis for its overstated conclusion regarding a trend toward higher risk. Conversely, the meta-analysis by Tanashat et al[52] did not include the study by Luo et al,[27] a recent RCT on hepatectomy including 118 patients, whose inclusion could plausibly account for the change in results.

Another clinically important scenario is patients with cirrhosis. This represents a subgroup at particularly high risk, since cirrhosis is not a purely hypocoagulable state but rather a fragile re-equilibration of procoagulant and anticoagulant forces, making antifibrinolytic safety uncertain in this context.[53] Although our meta-analysis suggests a favorable safety profile in hepatic surgery overall, extrapolation from noncirrhotic populations may not be appropriate, and the use of TXA in this subgroup remains uncertain and warrants further dedicated evaluation.

Postoperative mortality was consistently low across the included studies, with the similar results between groups largely driven by the POISE-3 and HeLiX trials.[3,26] In addition, LOS, a

proxy for recovery and resource use, showed a nonsignificant trend favoring TXA. This may reflect its role in reducing blood loss, transfusion, and bleeding complications. However, LOS is influenced by nonclinical factors, such as discharge policies and bed availability, warranting cautious interpretation. Sensitivity analysis identified a single outlier study driving heterogeneity[30]; its exclusion rendered the reduction in LOS statistically significant in favor of TXA.

TXA is already incorporated into ERAS (enhanced recovery after surgery) protocols for cardiac surgery and is being explored in other fields for its ability to reduce transfusion, bleeding, and LOS.[54] Our results support its integration into similar pathways in general surgery, especially in elective and outpatient settings. Although cost is not directly assessed here, prior studies in trauma suggest TXA is cost-effective,[55] and its impact on bleeding and resource use may offer economic benefits in general surgery as well.

Limitations

This study has limitations. Significant heterogeneity likely reflects the inclusion of diverse surgical procedures with inherently different bleeding profiles and variable TXA protocols. Although subgroup analyses by procedure type helped address this heterogeneity, inconsistent dosing, timing, and routes limited identification of an optimal approach. While sensitivity analyses identified key sources of heterogeneity, some inconsistency remained. The absence of patient-level data precluded adjustment for individual predictors of efficacy or safety. Additionally, subgroup analyses were exploratory and unadjusted for multiple testing.

Conclusions

In summary, this systematic review and meta-analysis found that prophylactic administration of TXA in adult patients undergoing general surgery was associated with reduced intraoperative blood loss, transfusion requirements, and the risk of major bleeding, without an increase in the incidence of VTE or postoperative mortality. Although further research is needed to define its role in specific patient populations and procedures within general surgery, current evidence supports TXA as a safe and effective strategy for bleeding mitigation in general surgery settings.

ARTICLE INFORMATION

Accepted for Publication: October 19, 2025.

Published Online: December 17, 2025. doi:10.1001/jamasurg.2025.5498

Author Contributions: Mr Delgado had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Mr Delgado and Dr Pompeu contributed equally to this work.
Concept and design: Delgado, Pompeu, Martins, Azevedo, de Figueiredo.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Delgado, Pompeu, Pasqualotto, de Figueiredo.
Critical review of the manuscript for important intellectual content: All authors.
Statistical analysis: Delgado, Pompeu, Martins, Azevedo, Pasqualotto, de Figueiredo.
Administrative, technical, or material support: Delgado, Pompeu.
Supervision: Delgado, Pompeu, Chulam, de Figueiredo.

Conflict of Interest Disclosures: Dr de Figueiredo reported receiving honoraria from Intuitive and Distal Motion not related to this work. No other disclosures were reported.

Data Sharing Statement: See Supplement 2.

REFERENCES

1. Nilsson IM. Clinical pharmacology of aminocaproic and tranexamic acids. *J Clin Pathol Suppl (R Coll Pathol)*. 1980;14:41-47. doi:10.1136/jcp.s3-14.1.41

2. McCormack PL. Tranexamic acid: a review of its use in the treatment of hyperfibrinolysis. *Drugs*. 2012;72(5):585-617. doi:10.2165/11209070-000000000-00000

3. Park L, Marcucci M, Ofori S, et al. Safety and efficacy of tranexamic acid use in general surgery patients: a sub-study of the POISE-3 randomized controlled trial. *J Am Coll Surg*. 2024;239(5):S171. doi:10.1097/XCS.0000000000001163

4. Myles PS, Smith JA, Forbes A, et al; ATACAS Investigators of the ANZCA Clinical Trials Network. Tranexamic acid in patients undergoing coronary-artery surgery. *N Engl J Med*. 2017;376(2):136-148. doi:10.1056/NEJMoa1606424

5. Myles PS, Smith JA, Kasza J, et al; ATACAS investigators and the ANZCA Clinical Trials Network. Tranexamic acid in coronary artery surgery: one-year results of the Aspirin and Tranexamic Acid for Coronary Artery Surgery (ATACAS) trial. *J Thorac Cardiovasc Surg*. 2019;157(2):644-652.e9. doi:10.1016/j.jtcvs.2018.09.113

6. Goldstein K, Jones C, Kay J, Shin J, de Sa D. Tranexamic acid administration in arthroscopic surgery is a safe adjunct to decrease postoperative pain and swelling: a systematic review and meta-analysis. *Arthroscopy*. 2022;38(4):1366-1377.e9. doi:10.1016/j.arthro.2021.10.001

7. Alkhatib N, AlNouri M, Abdullah ASA, et al. Tranexamic acid use in anterior cruciate ligament reconstruction decreases bleeding complications: a systematic review and meta-analysis of randomized controlled trials. *Arthroscopy*. 2022;38(2):506-518.e6. doi:10.1016/j.arthro.2021.07.030

8. Rohrich RJ, Brown S, Brown T, Taub PJ. Role of tranexamic acid (TXA) in plastic and reconstructive surgery: a national perspective. *J Plast Reconstr Aesthet Surg*. 2025;102:373-383. doi:10.1016/j.bjps.2024.09.085

9. General surgery: global trends & opportunities. Life Science Intelligence. Accessed May 2, 2025. https://www.lifesciencemarketresearch.com/market-reports/general-surgery-global-trends-opportunities-2018

10. Smilowitz NR, Ruetzler K, Berger JS. Perioperative bleeding and outcomes after noncardiac surgery. *Am Heart J*. 2023;260:26-33. doi:10.1016/j.ahj.2023.02.008

11. Higgins JPT, Thomas J, Chandler J, et al. *Cochrane Handbook for Systematic Reviews of Interventions*, version 6.4. Updated August 22, 2024. Accessed April 5, 2025. http://www.training.cochrane.org/handbook

12. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372(71):n71. doi:10.1136/bmj.n71

13. Delgado L, Pompeu B, Martins G, Peñaranda L. Safety and efficacy of tranexamic acid in general surgery: a systematic review and meta-analysis of randomized controlled trials. PROSPERO 2025 CRD420251038412. April 23, 2025. Accessed November 11, 2025. https://www.crd.york.ac.uk/PROSPERO/view/CRD420251038412

14. Wohlin C. Guidelines for snowballing in systematic literature studies and a replication in software engineering. In: *Proceedings of the 18th International Conference on Evaluation and Assessment in Software Engineering*. EASE 2014. Association for Computing Machinery; 2014:1-10. doi:10.1145/2601248.2601268

15. Sterne JAC, Savović J, Page MJ, et al. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ*. 2019;366:l4898. doi:10.1136/bmj.l4898

16. Atkins D, Best D, Briss PA, et al; GRADE Working Group. Grading quality of evidence and strength of recommendations. *BMJ*. 2004;328(7454):1490. doi:10.1136/bmj.328.7454.1490

17. Egger M, Davey Smith G, Schneider M, Minder C. Bias in meta-analysis detected by a simple, graphical test. *BMJ*. 1997;315(7109):629-634. doi:10.1136/bmj.315.7109.629

18. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-188. doi:10.1016/0197-2456(86)90046-2

19. Baujat B, Mahé C, Pignon JP, Hill C. A graphical method for exploring heterogeneity in meta-analyses: application to a meta-analysis of 65

trials. *Stat Med*. 2002;21(18):2641-2652. doi:10.1002/sim.1221

20. Viechtbauer W, Cheung MWL. Outlier and influence diagnostics for meta-analysis. *Res Synth Methods*. 2010;1(2):112-125. doi:10.1002/jrsm.11

21. Shah A, Smith AF. Trial sequential analysis: adding a new dimension to meta-analysis. *Anaesthesia*. 2020;75(1):15-20. doi:10.1111/anae.14705

22. Thompson SG, Higgins JPT. How should meta-regression analyses be undertaken and interpreted? *Stat Med*. 2002;21(11):1559-1573. doi:10.1002/sim.1187

23. Alhomoud H. The effect of tranexamic acid on blood loss during laparoscopic sleeve gastrectomy. *World J Laparosc Surg*. 2016;9(1):30-33. doi:10.5005/jp-journals-10033-1266

24. Boylan JF, Klinck JR, Sandler AN, et al. Tranexamic acid reduces blood loss, transfusion requirements, and coagulation factor use in primary orthotopic liver transplantation. *Anesthesiology*. 1996;85(5):1043-1048. doi:10.1097/00000542-199611000-00012

25. Dalmau A, Sabaté A, Acosta F, et al. Tranexamic acid reduces red cell transfusion better than epsilon-aminocaproic acid or placebo in liver transplantation. *Anesth Analg*. 2000;91(1):29-34. doi:10.1097/00000539-200007000-00006

26. Karanicolas PJ, Lin Y, McCluskey SA, et al; HPB CONCEPT Team. Tranexamic acid in patients undergoing liver resection: the HeLiX randomized clinical trial. *JAMA*. 2024;332(13):1080-1089. doi:10.1001/jama.2024.11783

27. Luo JY, Zhou C, Shi SX, et al. Use of tranexamic acid in hepatectomy under controlled low central venous pressure: a randomized controlled study. *BMC Anesthesiol*. 2025;25(1):94. doi:10.1186/s12871-025-02935-0

28. Prospective randomized phase IV open label comparative study of tranexamic acid plus standard of care vs standard of care for the reduction of blood loss in patients undergoing major abdominal surgery. ClinicalTrials.gov identifier: NCT00827931. Updated April 26, 2012. Accessed April 20, 2025. http://clinicaltrials.gov/show/nct00827931

29. Sermet M, Ozsoy MS. Effect of tranexamic acid on postoperative bleeding in sleeve gastrectomy: a randomized trial. *Obes Surg*. 2023;33(12):3962-3970. doi:10.1007/s11695-023-06902-x

30. Siddiqui F, Umer F, Junaid T, Hamza M, Khan M, Shah S. Peri-operative use of transexamic acid in reduction of post operative seroma formation in patients undergoing ventral hernia repair. *Pak J Med Health Sci*. 2022;16(11):531-533. doi:10.53350/pjmhs20221611531

31. 't Hart JWH, Noordman BJ, Wijnand JMA, et al. Peroperative administration of tranexamic acid in sleeve gastrectomy to reduce hemorrhage: a double-blind randomized controlled trial. *Surg Endosc*. 2023;37(10):7455-7463. doi:10.1007/s00464-023-10232-5

32. Ishii K, Yokoyama Y, Yonekawa Y, et al. Tranexamic acid and blood loss in pancreaticoduodenectomy: TAC-PD randomized clinical trial. *Br J Surg*. 2023;110(2):159-165. doi:10.1093/bjs/znac382

33. Wu CC, Ho WM, Cheng SB, et al. Perioperative parenteral tranexamic acid in liver tumor resection: a prospective randomized trial toward a "blood transfusion"-free hepatectomy. *Ann Surg*. 2006;243(2):173-180. doi:10.1097/01.sla.0000197561.70972.73

34. Yang J, Zhang J, Luo J, et al. Safe and Effective Blood Preservation Through Acute Normovolemic Hemodilution and Low-Dose Tranexamic Acid in Open Partial Hepatectomy. *J Pain Res*. 2023;16:3905-3916. doi:10.2147/JPR.S426872

35. Zaheer F, Baloch Q, Abbas S, Naseer S, Muhammad O, Anees A. Single dose of IV tranexamic acid preoperatively reduces the incidence of post-operative scrotal edema following lichtenstein hernioplasty. a randomized prospective cohort analysis. *Medical Forum Monthly*. 2021;32(10):180-184.

36. Alimian M, Mohseni M. The effect of intravenous tranexamic acid on blood loss and surgical field quality during endoscopic sinus surgery: a placebo-controlled clinical trial. *J Clin Anesth*. 2011;23(8):611-615. doi:10.1016/j.jclinane.2011.03.004

37. Auvinen O, Baer GA, Nordback I, Saaristo J. Antifibrinolytic therapy for prevention of hemorrhage during surgery of the thyroid gland. *Klin Wochenschr*. 1987;65(6):253-255. doi:10.1007/BF01773442

38. Babu MJ, Neema PK, Reazaul Karim HM, Dey S, Arora R. Effect of two different tranexamic acid doses on blood loss in head and neck cancer surgery: a randomized, double-blind, controlled study. *Cureus*. 2021;13(12):e20190. doi:10.7759/cureus.20190

39. Chen CC, Wang CC, Wang CP, Lin TH, Lin WD, Liu SA. Prospective, randomized, controlled trial of tranexamic acid in patients who undergo head and neck procedures. *Otolaryngol Head Neck Surg*. 2008;138(6):762-767. doi:10.1016/j.otohns.2008.02.022

40. George A, Kumar R, Kumar S, Shetty S. A randomized control trial to verify the efficacy of pre-operative intra venous tranexamic acid in the control of tonsillectomy bleeding. *Indian J Otolaryngol Head Neck Surg*. 2011;63(1):20-26. doi:10.1007/s12070-010-0095-4

41. Kulkarni AP, Chaukar DA, Patil VP, Metgudmath RB, Hawaldar RW, Divatia JV. Does tranexamic acid reduce blood loss during head and neck cancer surgery? *Indian J Anaesth*. 2016;60(1):19-24. doi:10.4103/0019-5049.174798

42. Pannerselvam T, Kumar K, Karthekeyan R. Comparative study of two different intravenous doses of tranexamic acid with placebo on surgical field quality in functional endoscopic sinus surgery—a randomised clinical trial. *J Clin Diagn Res*. 2019;13(12):UC05-UC09. doi:10.7860/JCDR/2019/42939.13349

43. Thakur A, Gupta S, Thakur JS, et al. Tranexamic acid has no advantage in head and neck surgical procedures: a randomised, double-blind, controlled clinical trial. *J Laryngol Otol*. 2019;133(12):1024-1032. doi:10.1017/S0022215119002305

44. Yang W, Gou H, Li H, et al. Intravenous tranexamic acid improves the intraoperative visualization of endoscopic sinus surgery for high-grade chronic rhinosinusitis: a randomized, controlled, double-blinded prospective trial. *Front Surg*. 2021;8:771159. doi:10.3389/fsurg.2021.771159

45. Shaker EH, Fayek ES, Elrawas MM. Evaluation of efficacy and safety of a single dose tranexamic acid in reducing blood loss during colorectal cancer surgery: a randomised, placebo controlled, double-blinded study. *Indian J Anaesth*. 2023;67(2):194-200. doi:10.4103/ija.ija_576_22

46. Ziaei S, Joni SS, Shahriar R, Shahzamani M. Does intravenous tranexamic acid reduce bleeding during mastoidectomy? *Am J Blood Res*. 2020;10(3):46-51.

47. Kaspar M, Ramsay MA, Nguyen AT, Cogswell M, Hurst G, Ramsay KJ. Continuous small-dose tranexamic acid reduces fibrinolysis but not transfusion requirements during orthotopic liver transplantation. *Anesth Analg*. 1997;85(2):281-285. doi:10.1097/00000539-199708000-00007

48. CRASH-2 trial collaborators, Shakur H, Roberts I, 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. *Lancet*. 2010;376(9734):23-32. doi:10.1016/S0140-6736(10)60835-5

49. Dionne JC, Oczkowski SJW, Hunt BJ, et al; for ESICM Transfusion Taskforce and the GUIDE Group. Tranexamic acid in gastrointestinal bleeding: a systematic review and meta-analysis. *Crit Care Med*. 2022;50(3):e313-e319. doi:10.1097/CCM.0000000000005362

50. Kumar M, Venishetty S, Jindal A, et al. Tranexamic acid in upper gastrointestinal bleed in patients with cirrhosis: a randomized controlled trial. *Hepatology*. 2024;80(2):376-388. doi:10.1097/HEP.0000000000000817

51. de Jesus BGAS, Barreto ESR, Medrado Nunes GS, et al. Safety and efficacy of tranexamic acid in hepatic surgery: a meta-analysis of randomized controlled trials. *HPB (Oxford)*. 2025;27(8):1009-1019. doi:10.1016/j.hpb.2025.05.006

52. Tanashat M, Khalefa BB, Manasrah A, et al. Tranexamic acid in patients undergoing liver resection: an updated systematic review and meta-analysis of randomized controlled trials. *Clin Appl Thromb Hemost*. 2025;31:10760296251342467. doi:10.1177/10760296251342467

53. O'Leary JG, Greenberg CS, Patton HM, Caldwell SH. AGA clinical practice update: coagulation in cirrhosis. *Gastroenterology*. 2019;157(1):34-43.e1. doi:10.1053/j.gastro.2019.03.070

54. Salenger R, Arora RC, Bracey A, et al. Cardiac surgical bleeding, transfusion, and quality metrics: joint consensus statement by the enhanced recovery after surgery cardiac society and society for the advancement of patient blood management. *Ann Thorac Surg*. 2025;119(2):280-295. doi:10.1016/j.athoracsur.2024.06.039

55. Williams J, Roberts I, Shakur-Still H, Lecky FE, Chaudhri R, Miners A. Cost-effectiveness analysis of tranexamic acid for the treatment of traumatic brain injury, based on the results of the CRASH-3 randomised trial: a decision modelling approach. *BMJ Glob Health*. 2020;5(9):e002716. doi:10.1136/bmjgh-2020-002716