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# Investigating the dose-response of tranexamic acid for efficacy and safety in off-pump coronary artery bypass: A meta-analysis

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## ABSTRACT

**Introduction:** Off-pump coronary artery bypass (OPCAB) surgery carries a high risk of perioperative bleeding, often requiring blood transfusions. While tranexamic acid (TXA) is a standard antifibrinolytic agent, its ideal dosage for patients undergoing OPCAB has not been clearly established. The objective of this meta-analysis is to investigate the effectiveness, safety profile, and dose-response of TXA within this surgical context.

**Methods:** Following PRISMA guidelines, PubMed, ScienceDirect, and ClinicalTrials.gov were systematically searched for RCTs and observational studies comparing TXA with placebo or control. Primary efficacy measures included the volume of blood lost within 24 hours and the incidence of RBC or plasma transfusions. Safety profiles were monitored via all-cause mortality and thrombotic events, with data synthesis performed using fixed- and random-effects models and heterogeneity verified through I2 values. Pre-specified subgroup analyses by study design and administration regimen, as well as linear dose-response meta-regression, were conducted.

**Results:** Fourteen studies, including 5,899 patients, were analyzed. TXA significantly reduced 24-hour blood loss (MD: −193.48 mL; 95% CI: −262.86 to −124.10) and decreased RBC (RR: 0.66; 95% CI: 0.50–0.86) and plasma transfusion (RR: 0.60; 95% CI: 0.48–0.76) without increasing mortality or thromboembolic events (RR: 1.05; 95% CI: 0.69–1.59). Dose-response analysis showed no significant linear association between higher TXA doses and additional bleeding reduction ($p = 0.779$). Subgroup analyses indicated that the bolus-plus-continuous-infusion regimen may provide greater reductions in RBC transfusion (RR 0.57; $p = 0.005$) and a trend toward lower blood loss (MD −208.7 mL), whereas bolus-only showed smaller, non-significant effects.

**Conclusion:** TXA is safe and effective in OPCAB surgery for reducing blood loss and transfusion requirements. Escalating the dose offers no additional hemostatic benefit. A bolus-plus-continuous-infusion regimen appears more effective than bolus-only, suggesting that maintaining a sustained therapeutic concentration is more important than the total dose administered.

**Keywords:** Blood transfusion, dose-response, meta-analysis, off-pump coronary artery bypass, tranexamic acid.
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## INTRODUCTION

Bleeding and the need for transfusion are common complications following cardiac surgery.[1] These complications not only increase postoperative morbidity but also the risk of mortality.[2] The initiation of cardiopulmonary bypass (CPB) in cardiac procedures has been shown to trigger the clotting cascade, deplete essential coagulation factors, and lead to both excessive fibrinolysis and impaired platelet function.[3] Although off-pump coronary artery bypass (OPCAB) may reduce the risk of bleeding compared to procedures involving cardiopulmonary bypass (CPB), significant surgical trauma and heparin exposure still activate the coagulation cascade, making blood transfusion a primary concern in OPCAB patients.[3,4]

As a powerful inhibitor of fibrinolysis, tranexamic acid (TXA) has demonstrated significant success in minimizing blood loss and the necessity for blood product administration during cardiac surgery procedures.[5] However, this benefit is counterbalanced by concerns about a potential increased risk of thrombotic events, such as coronary artery graft thrombosis and stroke. Some studies have even associated TXA with an increased risk of postoperative neurological events, which are suspected to have a thromboembolic basis.[6]

The dosage of TXA remains a crucial, unresolved variable. Evidence suggests that different dosing regimens significantly affect the balance between blood conservation and the risk of adverse events. Postoperative seizures have been associated with high TXA concentrations ranging from 61-259 mg/kg. To avoid such

complications, the study dose in major trials like ATACAS was reduced by half, from an original 100 mg/kg to a safer 50 mg/kg.[5,6]

Given this uncertainty, this systematic review and meta-analysis were conducted to comprehensively assess the dose-response relationship of TXA in OPCAB patients. This study specifically seeks to verify TXA's effectiveness in minimizing bleeding and transfusion needs, assess its safety regarding mortality and thromboembolic complications, and determine if increasing the dose offers further advantages.

## METHODS

The execution of this study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.[7] Our study protocol has been registered on PROSPERO (CRD420251123551).

### Data sources and search strategy

A comprehensive search strategy was executed in PubMed, ScienceDirect, and ClinicalTrials.gov databases from database inception until August 2025. This strategy utilized a combination of key search terms, including "Off-Pump Coronary Artery Bypass Grafting" and "Tranexamic Acid," which were supplemented with Medical Subject Headings (MeSH) and other synonyms to maximize search sensitivity. The articles were imported into Mendeley Desktop (version 1.19.8), where duplicates were detected and removed.

### Eligibility criteria

Study selection was guided by the PICO (Population, Intervention, Comparator, and Outcome) model. We incorporated both observational studies and randomized controlled trials that focused on adult patients undergoing OPCAB surgery. In these studies, intravenous TXA was administered via bolus-only or bolus-plus-infusion regimens and compared against a placebo or no-intervention control group. Primary outcomes were 24-hour blood loss, need for red blood cell transfusion, and need for plasma transfusion, while safety outcomes included all-cause mortality and thromboembolic events. Studies were excluded if they involved patients under 18 years, on-pump procedures or other surgeries, non-intravenous TXA administration, use of other antifibrinolytic agents, or were case reports, case series, reviews, or editorials. For studies that included mixed coronary artery surgery populations, data extraction was prioritized for patient groups relevant to OPCAB.

Studies with missing or incomplete outcome data were carefully evaluated during the screening process. We proactively searched for missing information within the supplementary materials and appendices of the original publications. If the primary data required for meta-analysis remained unavailable after this search, the study was excluded from the quantitative synthesis to ensure the reliability of the pooled estimates.

### Inclusion and exclusion criteria

Two reviewers (HAS, MIRR) independently evaluated the remaining articles for their relevance to the inclusion criteria. After screening the titles and abstracts, the full texts were thoroughly examined. Studies were included in our analysis if they met the specified criteria, with a third reviewer (SDK) serving as the final arbiter in case of any disagreements.

### Quality assessment and data extraction

Methodological quality was evaluated independently by two authors (HAS and MIRR). We employed the Cochrane Risk-of-Bias tool version 2 (RoB-2) to assess randomized trials, whereas the Newcastle-Ottawa Scale (NOS) was utilized for the appraisal of observational studies. Any disagreements between the reviewers were resolved through discussion until a consensus was reached. Relevant information was compiled into a standardized Google Sheets database for further synthesis. Data extraction focused on key study characteristics (author, year, country, and design) and clinical variables, including total sample size, mean participant weight and age, and the administered dose of TXA.

### Statistical analysis and data synthesis

Data synthesis was carried out using R software (version 4.5.1). We applied either random-effects or fixed-effects models for our pairwise meta-analyses, with the choice of model determined by the degree of heterogeneity measured through the $I^2$ statistic, where values exceeding 50% were considered significant. To represent treatment effects, we utilized Mean Difference (MD) for continuous variables like 24-hour hemorrhage volume, and Risk Ratios (RR) with 95% confidence intervals for binary endpoints, including safety outcomes and transfusion needs. Dose-response analysis was performed using linear meta-regression after standardizing total TXA dose into mg/kg; studies without weight data were excluded. In the event of substantial heterogeneity (defined as $I^2 > 50\%$), exploratory subgroup analyses were planned to investigate potential sources of variability, such as study design (RCT vs non-RCT) and administration regimen (bolus vs bolus plus continuous infusion).

## RESULTS

The initial database search yielded 593 articles. After removing duplicates and performing full-text screening, the final meta-analysis included 11 RCTs and 3 Cohorts in 10 countries, involving 5,899 patients.[5,8,17–20,9–16] The PRISMA flow diagram that outlines the literature search and screening process can be seen in Figure 1. The search keywords used in each database for the literature search process are presented in Table 1. Combinations of Boolean operators and relevant terms related to tranexamic acid and off-pump coronary artery bypass procedures were applied to comprehensively identify eligible studies.

Table 2 summarizes the baseline characteristics of the included studies, including study design, sample size, participant demographics, and tranexamic acid dosing regimens. Most studies were randomized controlled trials conducted across multiple countries, with intravenous tranexamic acid compared against saline, standard care, or control groups in patients undergoing off-pump coronary artery bypass surgery. The baseline demographic characteristics, including age and body weight, were generally comparable between the intervention and control groups across the included studies. According to the RoB-2 framework, 6 of

the included RCTs were judged to have a low risk of bias, with the rest raising some concerns. Quality assessment for the 3 observational studies yielded NOS scores of 7 to 9 stars, reflecting generally strong methodology across the board. Overall, the methodological assessment indicated that the included studies were generally of good quality based on both the RoB-2 and NOS evaluations.

### Meta-analyses for blood loss 24-hours

The use of TXA was proven to significantly decrease 24-hour blood loss by an average of 193.48 mL (95% CI: –262.86 to –124.10) (Figure 2). The high degree of detected heterogeneity ($I^2$= 73.6 %) indicates that there were notable differences in clinical outcomes across the various analyzed research centers. Subgroup analyses suggested that the reduction in blood loss was consistent across RCTs and non-RCTs (p for subgroup difference = 0.95). When stratified by regimen, bolus-plus-continuous infusion showed a numerically greater reduction (–208.7 mL) compared with bolus alone (–161.5 mL), although the difference did not reach statistical significance (p = 0.46) (Table 3).

### Meta-analyses for red blood cell and plasma transfusion

Our analysis of red blood cell (RBC) transfusion (Figure 2B) integrated data from twelve studies, yielding a pooled risk ratio of 0.66 (95% CI: 0.50–0.86). This result demonstrates that TXA administration lowers the likelihood of requiring an RBC transfusion by 34% relative to the control cohorts. Moderate heterogeneity was observed in this calculation ($I^2$ = 54.7%, p = 0.012), indicating some variability among the studies. While RCTs showed stable benefits (RR 0.61; 95% CI: 0.50–0.74), the effect in non-randomized studies was less definitive (RR 0.93; 95% CI: 0.17–2.33; p = 0.99). Notably, when categorized by administration method, the bolus-plus-continuous infusion regimen was linked to a more substantial decrease in transfusion needs (RR 0.57; 95% CI: 0.41–0.80) compared to the bolus-only approach (RR 0.93; 95% CI: 0.88–0.97). The significant difference between these subgroups (p = 0.005) suggests that maintaining therapeutic levels through sustained dosing may provide better hemostatic protection than bolus delivery alone (Table 3).

For plasma transfusion (Figure 2C), ten studies were analyzed. The pooled result demonstrated a significant reduction with TXA (RR 0.59; 95% CI 0.37–0.95), corresponding to a 41% lower risk compared with the control group. The heterogeneity was low to moderate ($I^2$ = 40.7%, p = 0.096), suggesting that the effect was relatively consistent across studies.

### Meta-analyses for mortality and thrombotic events

The safety profile of TXA was assessed across twelve studies (Figure 2D), resulting in a pooled risk ratio of 1.06 (95% CI: 0.69–1.62). Because the 95% confidence interval confidence interval crosses 1.0, there was no evidence of a statistically significant change in the risk of death or thromboembolic events associated with

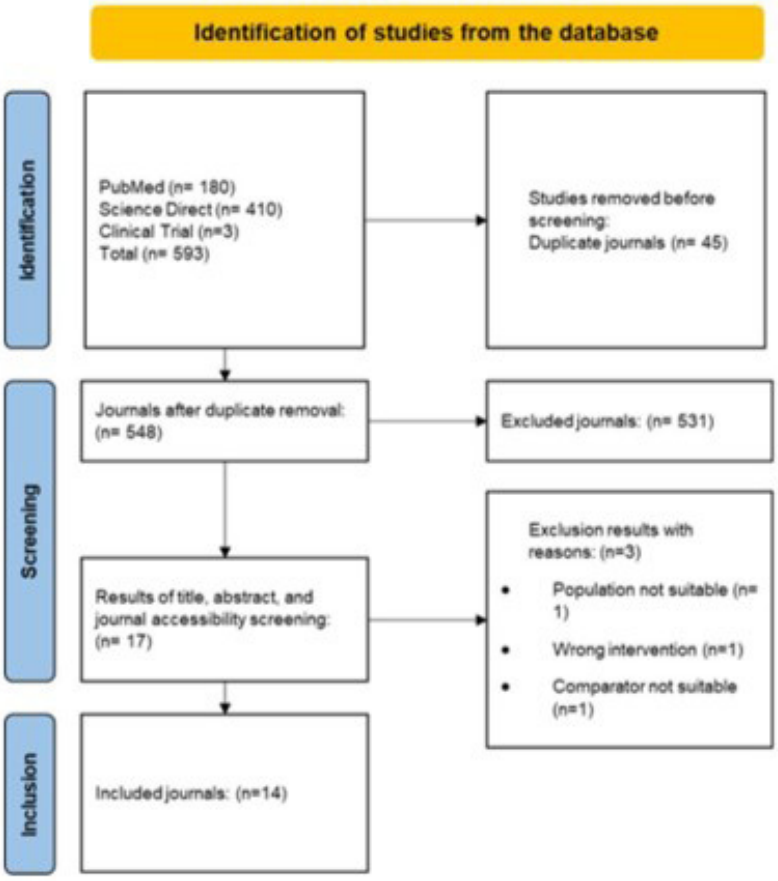



**Figure 1.** The PRISMA diagram illustrates the comprehensive study selection process for including studies in the systematic review and meta-analysis

**Table 1. Search strategy in each database**

| Database | Keyword |
|---|---|
| PubMed | (tranexamic OR TXA) AND (off-pump OR OPCAB OR "beating heart" OR "coronary bypass" OR "coronary artery bypass" OR "off pump") |
| ScienceDirect | ("tranexamic acid" OR TXA) AND ("off-pump" OR OPCAB) AND ("coronary artery bypass" OR CABG OR "myocardial revascularization") |
| ClinicalTrials.gov | ("tranexamic acid" OR TXA) AND ("off-pump" OR "off pump" OR OPCAB OR "beating heart surgery") AND ("coronary artery bypass" OR CABG OR "myocardial revascularization") |

**Table 2. Baseline characteristics**

| Author | Year | Country | Study Design | N | Age | Weight | Dose | Overall Risk of Bias (RoB-2) | NOS Score (out of 9) |
|---|---|---|---|---|---|---|---|---|---|
| Casati[8] | 2001 | Italy | RCT | 40 | TA: 64 ± 13<br>C: 62 ± 11 | TA: 71 ± 11<br>C: 72 ± 8 | TA: IV 1 g in 20 min + 400 mg/h<br>C: Saline | Some Concern | - |
| Casati[9] | 2004 | Italy | RCT | 51 | TA: 64 ± 12<br>C: 61 ± 11 | TA: 71 ± 12<br>C: 73 ± 10 | TA: IV 1 g in 20 min + 400 mg/h<br>C: Saline | Low Risk | - |
| Vanek[12] | 2005 | Czech Republic | RCT | 62 | TA: 68.4 (64.6, 72.2)<br>C: 68.9 (65.8, 72.0) | TA: 80.4 (74.9, 86.0)<br>C: 82.6 (77.7, 87.5) | TA: IV 1 g before incision + 200 mg/h<br>C: Saline | Low Risk | - |
| Murphy[13] | 2005 | Italy & UK | RCT | 100 | TA: 64.9 ± 7.0<br>C: 65.8 ± 8.7 | NR | TA: IV 2 g bolus 20 min after induction, before incision<br>C: Saline | Low Risk | - |
| Wei[14] | 2006 | China | RCT | 76 | TA: 62.8 ±7.9<br>C: 60.7 ± 8.0 | TA: 72.1 ± 7.6<br>C: 72.9 ± 10.0 | TA: IV 0.75 g in 20 min + 250 mg/h<br>C: Saline | Some Concern | - |
| Mehr-Aein[15] | 2007 | Iran | RCT | 66 | TA: 44 ± 10<br>C: 45 ±10 | NR | TA: IV 15 mg/kg before infusion of heparin + 15 mg/kg after protamine infusion<br>C: Saline | Some Concern | - |
| Taghaddomi[16] | 2009 | Iran | RCT | 100 | TA: 54.7 ± 10.9<br>C: 60.3 ± 10.2 | TA: 75.1 ± 14.0<br>C: 74.8 ± 13.9 | TA: IV 1 g in 20 min + 400 mg/h<br>C: Saline | Some Concern | - |
| Ahn[19] | 2012 | South Korea | RCT | 76 | TA: 69 ± 7<br>C: 67 ± 7 | NR | TA: IV 1 g in 20 min + 200 mg/h<br>C: Saline | Low Risk | - |
| Wang[20] | 2012 | China | RCT | 231 | TA: 60.5 ± 8.0<br>C: 60.0 ± 8.5 | TA: 71.1 ± 11.0<br>C: 73.5 ± 10.1 | TA: IV 1 g in 20 min + 400 mg/h<br>C: Saline | Low Risk | - |
| Chakravarthy[17] | 2012 | India | RCT | 48 | TA: 58 ± 4<br>C: 60 ± 6 | TA: 62 ± 9<br>C: 60 ± 6 | TA: IV 10 mg/kg over 30 min + 1 mg/kg/h for 12 hr<br>C: Ringer's Lactate | Some Concern | - |
| Myles[5] | 2017 | Australia | RCT | 143 | NR | NR | NR | Low Risk | - |
| Hulde[18] | 2019 | Germany | Cohort Retrospective with PSM | 4498 | TA: 67.2 ± 9.9<br>C: 67.2 ± 9.9 | NR | T: 1 g bolus | - | 9 |
| Khadanga[10] | 2020 | India | Cohort Prospective | 60 | TA: 57.5±7.89<br>C: 57.9±7.65 | TA: 71.9 ± 3.73<br>C: 73.46 ± 3.23 | T: 10 mg/kg over 10 minutes at the time of induction | - | 8 |
| Weingarten[11] | 2021 | Canada | Cohort Retrospective | 348 | TA: 66.6 ± 9.7<br>C: 65.6 ± 10.4 | TA: 84.9 ± 17.4<br>C: 81.4 ± 16.3 | Unspecified TXA dose<br>TXA dose mean 2.1 +- 1.5 g | - | 7 |

TXA use. Furthermore, the total absence of heterogeneity ($I^2$ = 0.0%, p = 0.96) demonstrates a highly uniform safety outcome throughout all analyzed trials.

### Linear dose-response meta-regression

Linear meta-regression was conducted to evaluate the dose-response relationship between standardized TXA dosage and its efficacy in reducing blood loss (Figure 3). For this analysis, studies were included only if they reported the mean and standard deviation for blood loss, as well as the mean patient weight necessary to standardize the total administered dose into mg/kg. Consequently, studies such as Vanek et al. (2005), which reported blood loss using geometric means and did not provide a standard deviation, were excluded from this specific analysis. The analysis, therefore, included studies with standardized doses ranging from approximately 10 mg/kg to 37 mg/kg.

Results of the meta-regression showed no statistically significant linear association between an increasing dose of TXA and a further reduction in 24-hour blood loss (regression coefficient B = -1.43; 95% CI: -12.78 to 9.92; p = 0.779). Visually, the bubble plot confirms this lack of a clear trend, with individual studies scattered widely around the nearly horizontal regression line. This suggests that within the evaluated dose range, escalating the dose of TXA does not confer additional hemostatic benefits in a predictable manner.

**Table 3. Subgroup analysis for Blood loss and RBC transfusion**

| Outcome | Subgroup | No. of Studies | Effect Estimate (95% CI) | Heterogeneity ($I^2$) | P for Subgroup Difference |
|---|---|---|---|---|---|
| 24-Hour Blood Loss (mL) | RCT only | 9 | MD -193.5 (-282.4, –104.2) | 75.2 % | 0.95 |
| | Non-RCT | 2 | MD -188.87 (920.7, 543.0) | 82.2% | |
| | Bolus | 3 | MD–161.5 (–375.3, 52.2) | 78.7% | 0.46 |
| | Bolus + continuous | 8 | MD –208.7 (–304.7, –112.8) | 71.4% | |
| RBC transfusion | RCT only | 10 | RR 0.61 (0.5; 0.74) | 9.7% | 0.99 |
| | Non-RCT | 2 | RR 0.93 (0.17; 2.33) | 51.8% | |
| | Bolus | 4 | RR 0.92 (0.88; 0.97) | 0% | 0.005 |
| | Bolus + continuous | 8 | RR 0.57 (0.46; 0.72) | 18.7% | |

## DISCUSSION

This systematic review and meta-analysis provide a comprehensive assessment of the efficacy, safety, and dose-response relationship of TXA in patients undergoing OPCAB surgery. Our principal findings confirm that TXA is an effective intervention for reducing postoperative blood loss and transfusion needs in OPCAB surgery, without increasing the risk of mortality or major thromboembolic events. Critically, our dose-response meta-regression revealed no significant linear association between escalating doses and further hemostatic benefit, suggesting a potential therapeutic ceiling for TXA's efficacy.

The efficacy of TXA in reducing blood loss is a consistent finding across the literature. Our pooled estimate of a 193.48 mL reduction in 24-hour blood loss supports this observation. This is in line with the results of numerous included RCTs. For instance, Casati et al. (2001) and Mehr-Aein et al. (2007) both demonstrated a significant reduction in postoperative bleeding in their respective placebo-controlled trials.[8,15] These observations align with the findings of Wang et al. (2012), whose large-scale RCT demonstrated that TXA administration was significantly more effective than placebo in reducing postoperative chest tube output during the first 24 hours.[20] Our findings of decreased transfusion requirements contrast with some evidence in the literature where results appear more variable. Specifically, research by Weingarten et al. (2021) and Wei et al. (2006) showed that TXA's success in reducing bleeding did not always translate into a significant reduction in blood product usage.[11,14]

A primary concern regarding antifibrinolytic therapy is the potential for increased thrombotic risk. Our meta-analysis provides reassuring evidence of TXA safety in the OPCAB population, showing no significant increase in the composite outcome of mortality and thromboembolic events. Importantly, compared with other antifibrinolytics, TXA holds a unique position in contemporary cardiac surgery. According to existing clinical recommendations, three primary agents are recognized: TXA, aprotinin, and epsilon-aminocaproic acid (EACA). However, the clinical utility of aprotinin has been restricted following its 2007 market withdrawal, and it is currently only authorized for on-pump CABG procedures within Europe. Meanwhile, the data supporting the use of EACA in this context remains insufficient. Consequently, TXA remains the most widely utilized and globally accepted option. Its efficacy is consistently demonstrated by high-quality evidence, including the landmark ATACAS randomized trial and multiple meta-analyses showing reductions in postoperative blood loss and transfusion requirements.[21] Our dose–response analysis revealed no significant linear association between escalating TXA doses (10–37 mg/kg) and further reductions in blood loss, suggesting a therapeutic ceiling in the OPCAB setting. This contrasts with ATACAS, where higher doses were associated with greater reductions in bleeding but also an increased risk of seizures. The discrepancy may reflect population differences, as ATACAS included both on-pump and off-pump procedures, whereas OPCAB alone induces less fibrinolysis, potentially reducing the

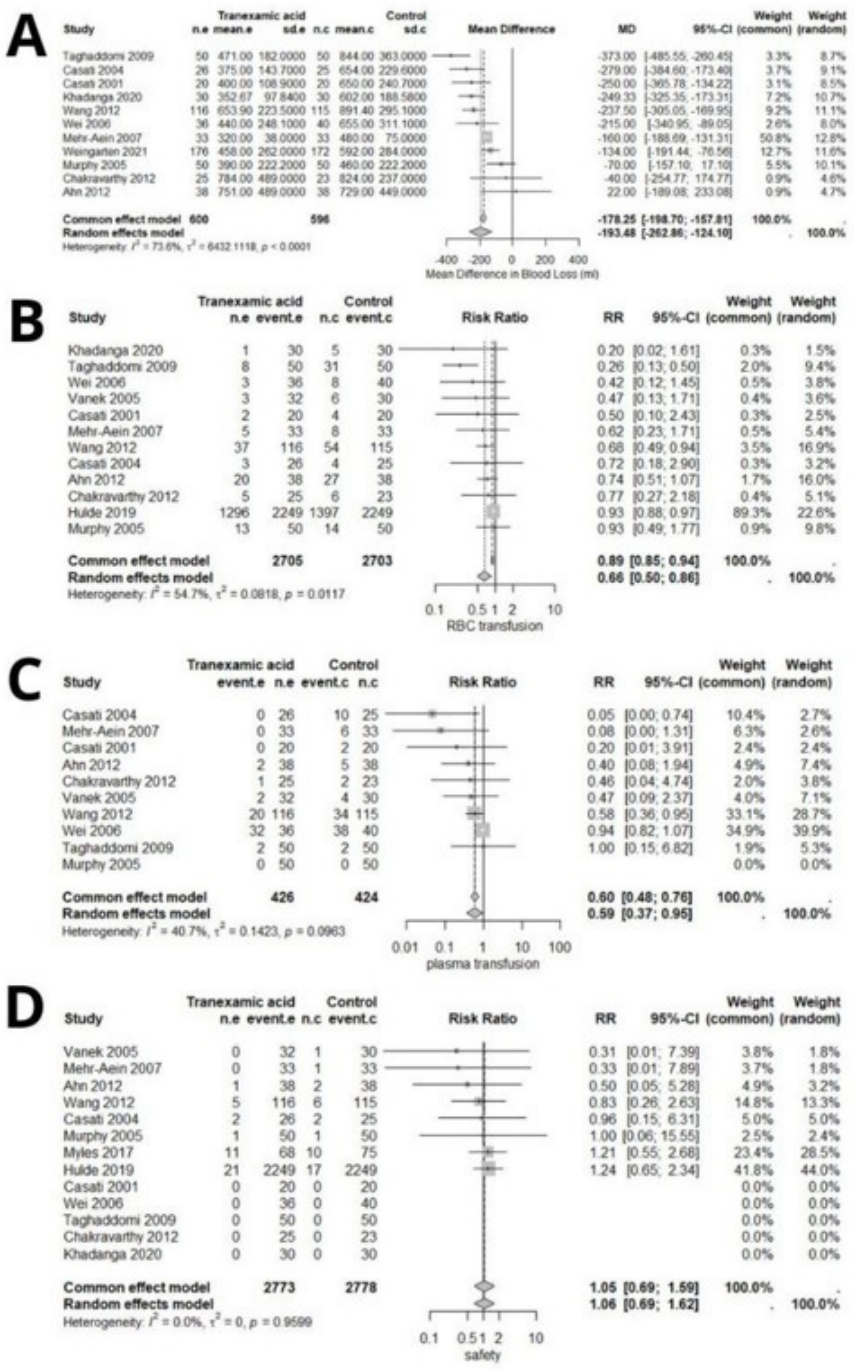



**Figure 2.** Forest plots of the meta-analysis showing the effect of tranexamic acid on the (A) 24-hour blood loss, (B) red blood cell transfusion, (C) plasma transfusion, and (D) mortality and thrombotic events. CI: Confidence Interval

need for higher doses. Similarly, Wang et al. (2022) examined a large mixed CABG cohort (≈42.6% on-pump after propensity matching). High-dose TXA (≥50 mg/kg) significantly reduced blood loss at 24 and 48 hours, but transfusion exposure and safety outcomes remained unchanged (primary p=0.238; seizures p=0.201).3

Subgroup analyses suggested a trend toward greater reductions in 24-hour blood loss with bolus-plus-continuous infusion (MD −208.7 mL) compared with bolus alone (MD −161.5 mL), although this difference was not statistically significant (P=0.46). For RBC transfusion, continuous infusion was associated with a significantly lower risk (RR 0.57 vs 0.92; P=0.005). Study design (RCT vs non-RCT) did not significantly influence outcomes. This clinical advantage may be explained by the pharmacokinetic profile of TXA; in patients with normal renal function, the effective half-life of TXA is relatively short, approximately 2 hours.[13] While a single bolus dose provides an initial plasma concentration sufficient to inhibit fibrinolysis, this protective effect may not be sustained throughout the duration of the surgery due to the drug's rapid clearance. By administering a continuous intraoperative infusion, a stable therapeutic plasma concentration is maintained.

This meta-analysis has several limitations. First, the primary outcome of 24-hour blood loss was associated with substantial heterogeneity, indicating variability in the magnitude of TXA's effect across studies. This variability likely comes from several factors, including differences in surgical expertise and techniques across the diverse international centers represented. Furthermore, variations in perioperative management protocols may have influenced the reported blood loss and transfusion outcomes. Second, our dose–response analysis was restricted to a linear model within a relatively narrow dosing range (10–37 mg/kg); although biologically a non-linear relationship may be more plausible, the available data distribution prevented stable modeling. Third, the inclusion of both randomized and non-randomized studies increases the risk of bias, even though our results were directionally consistent across designs. Fourth, variations in outcome definitions, perioperative co-interventions, and reporting practices across the included trials further limit the certainty of pooled estimates. Fifth, subgroup analyses suggested differences in efficacy between administration regimens (bolus vs bolus-plus-continuous infusion), particularly for transfusion requirements; however, trends for 24-hour blood loss were not statistically significant, and the limited number of studies in some subgroups reduces confidence in these findings. Sixth, publication bias was not formally evaluated, which may limit the assessment of potential small-study effects and

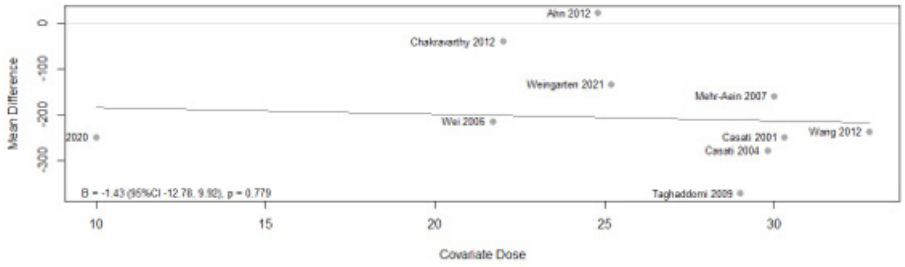



**Figure 3.** Dose-response meta-regression showing the linear relationship between standardized tranexamic acid (TXA) dose and the mean difference in 24-hour blood loss. Each circle represents an individual study. B, regression coefficient; CI, Confidence Interval

selective reporting. Finally, the included studies provided limited information on long-term outcomes and safety endpoints such as seizures, neurological events, or renal impairment, which remain important gaps for future research. Well-designed dose-finding randomized trials focused on OPCAB patients, with standardized outcome definitions and extended follow-up, are needed to confirm the optimal dosing strategy that balances efficacy and safety.

## CONCLUSION

In conclusion, this meta-analysis provides robust evidence that TXA is a safe and effective intervention for reducing postoperative blood loss and transfusion requirements in patients undergoing OPCAB surgery. The key finding of this study is that the method of administration is more critical than the total dose; a bolus-plus-continuous-infusion regimen provides optimal efficacy, while escalating the dose offers no additional hemostatic advantage, suggesting a clear therapeutic ceiling. These findings support a shift in clinical practice away from high-dose strategies towards optimizing the administration regimen to maximize the benefits of TXA.

## DISCLOSURES

### Ethical Considerations

Ethical approval was not required because this study used previously published data.

### Conflict of Interest

The authors have no conflict of interest.

### Funding

This study was self-funded by the authors without external grants.

### Author Contribution

HAS and MIRR conceived the study, designed the search strategy, performed data extraction and quality assessment, conducted the statistical analyses, and drafted the manuscript. SDK supervised the methodology and provided critical revisions to the manuscript.

### Use of Artificial Intelligence Generated Content

The use of generative artificial intelligence tools was restricted to minor language refinement, grammar correction, and readability enhancement during manuscript preparation. No AI-generated figures, datasets, analyses, or scientific interpretations were included in this work.

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None.

## REFERENCES

1. Pasrija C, Ghoreishi M, Whitman G, Ad N, Alejo DE, Holmes SD, et al. Mitigating the Risk: Transfusion or Reoperation for Bleeding After Cardiac Surgery. Ann Thorac Surg. 2020;110(2):457–63. Available from: http://doi.org/10.1016/j.athoracsur.2019.10.076.
2. Koch CG, Li L, Duncan AI, Mihaljevic T, Cosgrove DM, Loop FD, et al. Morbidity and mortality risk associated with red blood cell and blood-component transfusion in isolated coronary artery bypass grafting. Crit Care Med. 2006;34(6):1608–16. Available from: https://doi.org/10.1097/01.ccm.0000217920.48559.d8
3. Wang E, Yuan X, Wang Y, Chen W, Zhou X, Hu S, et al. Blood conservation outcomes and safety of tranexamic acid in coronary artery bypass graft surgery. Int J Cardiol. 2022;348:50–6. Available from: http://doi.org/10.1016/j.ijcard.2021.12.017.
4. Wang E, Wang Y, Li Y, Hu S, Yuan S. Tranexamic acid is associated with improved hemostasis in elderly patients undergoing coronary-artery surgeries in a retrospective cohort study. Front Surg. 2023;10:1117974. Available from: http://doi.org/10.3389/fsurg.2023.1117974.
5. Myles PS, Smith JA, Forbes A, Silbert B, Jayarajah M, Painter T, et al. Tranexamic Acid in Patients Undergoing Coronary-Artery Surgery. N Engl J Med. 2017;376(2):136–48. Available from: http://doi.org/10.1056/nejmoa1606424.
6. Myles PS, Smith JA, Kasza J, Silbert B, Jayarajah M, Painter T, et al. 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. Available from: https://doi.org/10.1016/j.jtcvs.2018.09.113.
7. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. BMJ. 2021;372:71. Available from: https://doi.org/10.1136/bmj.n71
8. Casati V, Gerli C, Franco A, Torri G, D'Angelo A, Benussi S, et al. Tranexamic acid in off-pump coronary surgery: a preliminary, randomized, double-blind, placebo-controlled study. Ann Thorac Surg. 2001;72(2):470–5. Available from: https://doi.org/10.1016/S0003-4975(01)02802-8.
9. Casati V, Della Valle P, Benussi S, Franco A, Gerli C, Baili P, et al. Effects of tranexamic acid on postoperative bleeding and related hematochemical variables in coronary surgery: Comparison between on-pump and off-pump techniques. J Thorac Cardiovasc Surg. 2004;128(1):83–91. Available from: http://doi.org/10.1016/j.jtcvs.2003.10.034.
10. Khadanga P, Kanchi M, Gaur P. Effectiveness of Tranexamic Acid in Reducing Postoperative Blood Loss in Patients Undergoing Off-Pump Coronary Artery Bypass Grafting. Cureus. 2020;12(12):e11924. Available from: http://doi.org/10.7759/cureus.11924.
11. Weingarten BR, Tran DTT, Mahaffey R, Sohmer B. Tranexamic acid for primary elective off-pump coronary artery bypass grafting surgery. Canadian journal of anaesthesia/Journal canadien d'anesthesie. 2021;68:1287–9. Available from: http://doi.org/10.1007/s12630-021-02013-2.
12. Vanek T, Jares M, Fajt R, Straka Z, Jirasek K, Kolesar M, et al. Fibrinolytic inhibitors in off-pump coronary surgery: a prospective, randomized, double-blind TAP study (tranexamic acid, aprotinin, placebo). Eur J cardio-thoracic Surg. 2005;28(4):563–8. Available from: http://doi.org/10.1016/j.ejcts.2005.06.027.
13. Murphy GJ, Mango E, Lucchetti V, Battaglia F, Catapano D, Rogers CA, et al. A randomized trial of tranexamic acid in combination with cell salvage plus a meta-analysis of randomized trials evaluating tranexamic acid

in off-pump coronary artery bypass grafting. J Thorac Cardiovasc Surg. 2006;132(3):475-480. Available from: http://doi.org/10.1016/j.jtcvs.2006.01.064.
14. Wei M, Jian K, Guo Z, Wang L, Jiang D, Zhang L, et al. Tranexamic acid reduces postoperative bleeding in off-pump coronary artery bypass grafting. Scand Cardiovasc J. 2006;40(2):105–9. Available from: http://doi.org/10.1080/14017430500519864.
15. Mehr-Aein A, Sadeghi M, Madani-civi M. Does tranexamic acid reduce blood loss in off-pump coronary artery bypass? Asian Cardiovasc Thorac Ann. 2007;15(4):285–9. Available from: http://doi.org/10.1177/021849230701500404.
16. Taghaddomi RJ, Mirzaee A, Attar AS, Shirdel A. Tranexamic acid reduces blood loss in off-pump coronary artery bypass surgery. J Cardiothorac Vasc Anesth. 2009;23(3):312–5. Available from: http://doi.org/10.1053/j.jvca.2008.09.018.
17. Chakravarthy M, Muniraj G, Patil S, Suryaprakash S, Mitra S, Shivalingappa B. A randomized prospective analysis of alteration of hemostatic function in patients receiving tranexamic acid and hydroxyethyl starch (130/0.4) undergoing off pump coronary artery bypass surgery. Ann Card Anaesth. 2012;15(2):105–10. Available from: http://doi.org/10.4103/0971-9784.95072.
18. Hulde N, Zittermann A, Deutsch M-A, von Dossow V, Gummert JF, Koster A. Tranexamic acid and convulsive seizures after off-pump coronary artery bypass surgery: the role of renal insufficiency. Interact Cardiovasc Thorac Surg. 2019;29(6):852–4. Available from: http://doi.org/10.1093/icvts/ivz188.
19. Ahn SW, Shim JK, Youn YN, Song JW, Yang SY, Chung SC, et al. Effect of tranexamic acid on transfusion requirement in dual antiplatelet-treated anemic patients undergoing off-pump coronary artery bypass graft surgery. Circ J. 2012;76(1):96–101. Available from: http://doi.org/10.1253/circj.cj-11-0811.
20. Wang G, Xie G, Jiang T, Wang Y, Wang W, Ji H, et al. Tranexamic acid reduces blood loss after off-pump coronary surgery: a prospective, randomized, double-blind, placebo-controlled study. Anesth Analg. 2012;115(2):239–43. Available from: http://doi.org/10.1213/ANE.0b013e3182264a11.
21. Casselman FPA, Lance MD, Ahmed A, Ascari A, Blanco-Morillo J, Bolliger D, et al. 2024 EACTS/EACTAIC Guidelines on patient blood management in adult cardiac surgery in collaboration with EBCP. J Cardiothorac Vasc Anesth. 2024;39(8):1964-2018. Available from: https://doi.org/10.1053/j.jvca.2024.10.006.

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