REVIEW PAPER

UROLOGICAL ONCOLOGY

Safety and efficacy of tranexamic acid in radical cystectomy: a systematic review and meta-analysis

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Introduction Perioperative blood transfusion (BT) is often required in radical cystectomy (RC) due to significant blood loss. Tranexamic acid (TXA), an antifibrinolytic agent, reduces bleeding, but concerns about thromboembolic risks persist. This systematic review and meta-analysis evaluate TXA's efficacy and safety in RC.

Material and methods A systematic search was conducted in PubMed, Embase, and Cochrane Central databases. Randomized controlled trials (RCTs) and retrospective studies comparing TXA versus controls in RC were included. Primary outcomes were perioperative, intraoperative, and postoperative BT rates. Secondary outcomes included estimated blood loss (EBL) and thromboembolic events (PROSPERO; CRD420251013502).

Results Four studies totaling 1,656 patients were included. TXA significantly reduced perioperative transfusion rates (OR = 0.40; 95% CI: 0.30–0.51; p < 0.00001). However, intraoperative (OR = 0.87; 95% CI: 0.50–1.52; p = 0.63) and postoperative transfusion rates (OR = 0.51; 95% CI: 0.21–1.23; p = 0.13) were not significantly different. No significant difference was found in EBL (MD = –9.31; 95% CI: from –82.50 to 63.87; p = 0.80). Safety analysis showed no increased risk of deep vein thrombosis (OR = 1.14; 95% CI: 0.54–2.41; p = 0.72) or pulmonary embolism (OR = 1.49; 95% CI: 0.69–3.24; p = 0.31).

Conclusions TXA reduces perioperative transfusion needs in RC without significantly affecting intraoperative or postoperative transfusion rates, EBL, or thromboembolic risk. Further RCTs are needed to optimize TXA use in RC.

Key Words: blood loss ‹› surgical ‹› blood transfusion ‹› cystectomy ‹› tranexamic acid ‹› venous thromboembolism

INTRODUCTION

Bladder cancer (BC) is projected to be the fourth most prevalent malignancy among males in the United States in 2025, based on modeled estimates [1]. Radical cystectomy (RC) plays an established role in the treatment of muscle-invasive BC and of non-invasive BC refractory to intravesical therapies, and it remains a cornerstone of curative-intent management aimed at reducing disease-specific mortality in this population [2]. Beyond its medical and oncological significance, RC is a highly complex surgical procedure that demands advanced expertise from urological surgeons [3].

Among the most frequently discussed perioperative concerns in contemporary literature are intraoperative blood loss and the consequent need for blood transfusion (BT) [4], especially in RC [5]. In this regard, perioperative BT is sometimes an essential strategy to manage severe bleeding [6]; and, more

critically, may be associated with worse oncologic outcomes [7] and potential risks, despite the use of modern blood screening protocols [8]. In this context, tranexamic acid (TXA) has emerged as a valuable and effective strategy to reduce bleeding and minimize the need for hemodynamic interventions, such as perioperative BT [9].

TXA is a lysine synthetic analogue that inhibits fibrinolysis by blocking plasminogen binding to fibrin, preventing its activation into plasmin and subsequent fibrin degradation [10]. This antifibrinolytic action enhances hemostasis and limits perioperative blood loss [10]. A previous study [11] has shown that even at high concentrations of plasminogen activators, TXA continues to inhibit clot formation, which could provide increased safety in patients with hypercoagulable conditions or those with different hemodynamic profiles who require surgery. However, one major concern regarding the administration of TXA is the risk of thrombosis, particularly in complex surgeries, such as emergency or trauma-related procedures [12]. Under these circumstances, the administered dose may play a crucial role in balancing the benefits of clot prevention with the potential risk of thrombosis [12].

Although most urological surgeries are elective and minimally invasive, and therefore associated with a lower risk of thrombosis [13], RC is still characterized by persistently significant morbidity and mortality rates [14, 15], as well as high postoperative complication rates [16]. In this context, the use of TXA presents considerable potential in the field of urologic surgery [13]. A previously published meta-analysis [13] evaluated the benefits of TXA in urological procedures such as percutaneous nephrolithotomy, transurethral resection of the prostate, and radical prostatectomy, demonstrating reductions in blood loss and transfusion requirements. However, it did not specifically focus on RC and included an insufficient number of studies dedicated to this procedure.With the emergence of new clinical research addressing this issue, this investigation has become crucial, systematically analyzing its efficacy and safety in this specific context and providing a comprehensive evaluation of its clinical outcomes.

MATERIAL AND METHODS

This systematic review and meta-analysis were conducted and reported following the *Cochrane Collaboration Handbook of Systematic Review of Interventions and the Preferred Reporting Items for the Systematic Reviews and Meta-analysis* (PRISMA) statement guidelines [17, 18]. The study protocol was prospectively registered with the International Prospective Register of Systematic Reviews (PROSPERO; CRD420251013502).

Search strategy

We systematically searched PubMed (MEDLINE), Embase, and Cochrane Central Register of Controlled Trials from inception to February 2025. With the aim of minimizing the risk of missing relevant studies, our search strategy included the terms "tranexamic acid", "cystectomy", and their variations, combined using both "AND" and "OR" operators to maximize the number of results obtained and avoid unnecessary restrictions. The complete search strategy is detailed in Suppl. Table 1. Two authors (F.R.C.S. and V.S.A) independently screened titles and abstracts and fully evaluated the studies for eligibility. Discrepancies were settled in a discussion panel with a third author (F.J.A-N.).

Eligibility criteria

We restricted the inclusion in this study to articles that met all the following eligibility criteria: (I) randomized clinical trials (RCTs) or retrospective studies; (II) studies evaluating the use of TXA in RC, comparing it with control groups; and (III) reported any outcomes of interest. Studies published solely as conference abstracts, reviews, case reports or studies not written in English were excluded from the analysis.

Data extraction

Data extraction was performed independently by two authors (F.R.C.S. and V.S.A.), adhering to established search parameters and quality evaluation standards. The extracted data included article characteristics (publication year, inclusion criteria, authors, country, follow-up duration, and type of study), population characteristics (age, sex, body mass index (BMI), perioperative BT requirement, and intervention used), intervention characteristics (dose and timing of application), and outcomes, as specified below.

Outcomes and definitions

The prespecified efficacy outcomes were the requirement for intraoperative BT, the requirement for postoperative BT, the requirement for perioperative BT, the mean number of units transfused intraoperatively, and the mean number of units transfused postoperatively, and estimated blood loss (EBL). Intraoperative BT referred to transfusions admin-

istered during the surgical procedure. Postoperative BT referred to transfusions administered after surgery, with the postoperative period defined as either up to 30 days after surgery or limited to the duration of the postoperative hospital stay, depending on the study. Perioperative BT encompassed any transfusion administered intraoperatively or postoperatively, according to the parameters described above. The safety outcomes analyzed included deep vein thrombosis (DVT); pulmonary embolism (PE); concurrent DVT and PE; and either DVT or PE. The analyses were stratified by comparison between the TXA group and control groups. In retrospective studies [9, 19, 20], the control group consisted of patients who did not receive additional antifibrinolytic treatment. In the RCT study [21], it included those who received 0.9% sodium chloride as placebo, matching TXA in infusion volume and schedule.

Statistical analysis

Statistical analyses were conducted using Review Manager 5.4.1. Binary outcomes were reported using odds ratios (OR) with 95% confidence intervals (CI) as the effect size measure. Mean differences (MD) with 95% CI were used for continuous outcomes. Heterogeneity was assessed with the Cochran Q test and I^2 statistics. $I^2 \geq 50\%$ was considered substantial heterogeneity [17]. The Restricted Maximum Likelihood random-effects model was applied. We also conducted a subgroup analysis based on medication dose: patients receiving 1 g preoperatively; patients receiving 10 mg/kg preoperatively, followed by 2 mg/kg/h intraoperatively; and patients receiving 10 mg/kg preoperatively, followed by 5 mg/kg/h intraoperatively.

Quality Assessment

The risk of bias and quality assessment in non-randomized studies were evaluated with the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool [22]. Randomized studies were assessed using the Risk of Bias 2 (RoB 2) tool [23]. This evaluation was conducted independently by two blinded reviewers (P.A.S.C and F.E.B.M). Disagreements were resolved through a consensus with a third reviewer (F.J.A-N.).

RESULTS

Study selection and characteristics

After a search of the literature, 215 studies were found. From these, 196 studies were eligible for title and abstract screening after duplicate removal. Out of these, 18 studies were eligible for full-text screening. Finally, as a direct consequence of our well-defined inclusion criteria, only 4 studies met the eligibility requirements and were included in this meta-analysis (Figure 1) [9, 19–21].

A total of 1,656 patients underwent RC, with 781 (47,16%) receiving TXA and 875 (52,84%) not receiving TXA. The mean age was approximately 69.05 ±2.82 years in the TXA group and 66.71 ±3.38 years in the non-TXA group. The most commonly administered TXA regimen consisted of a preoperative intravenous bolus of 10 mg/kg followed by a continuous intraoperative infusion at 2 mg/kg/hour. A detailed summary of baseline characteristics across the included studies is presented in Table 1.

Blood transfusion

In the broad analysis, the requirement for perioperative BT was significantly lower in patients

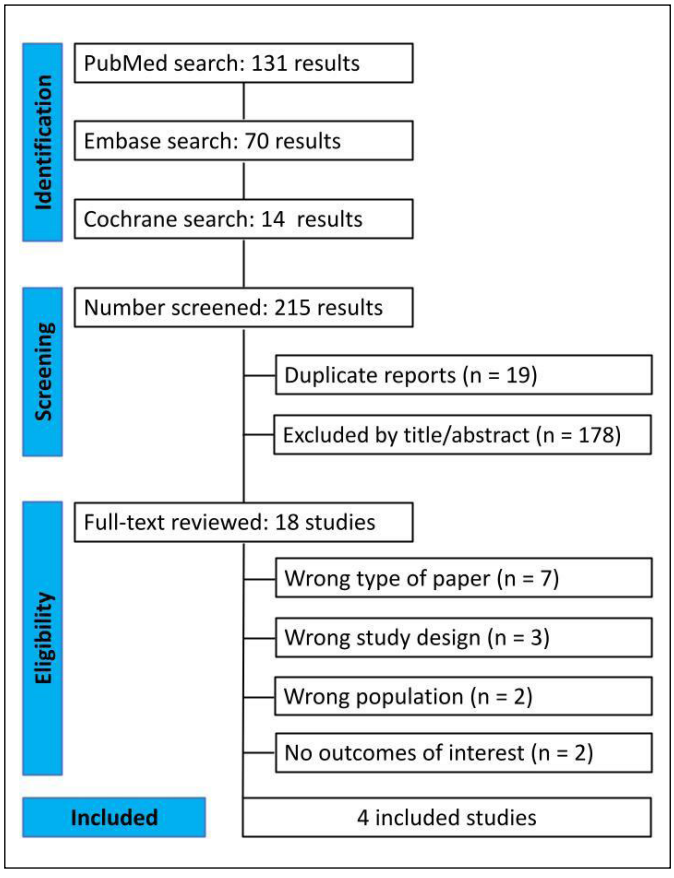


Figure 1. *Diagram showing the study selection process according to PRISMA guidelines. The diagram illustrates the identification, screening, eligibility and inclusion of studies for the meta-analysis, resulting in 4 included studies.*

who received TXA compared to the control group (OR = 0.40; 95% CI: 0.30–0.51; p < 0.00001; I^2 = 9%; Figure 2A). Subgroup analysis also demonstrated that, among patients who received 10 mg/kg preoperatively followed by 2 mg/kg/hour intraoperatively, the use of TXA was associated with a decreased requirement for perioperative BT (OR = 0.41; 95% CI: 0.33–0.52; p < 0.00001; I^2 = 0%; Figure 2A – subgroup analysis 1.1.2).

The requirement for intraoperative BT (OR = 0.87; 95% CI: 0.50–1.52; p = 0.63; I^2 = 43%; Figure 2B) showed no difference between groups. Likewise,

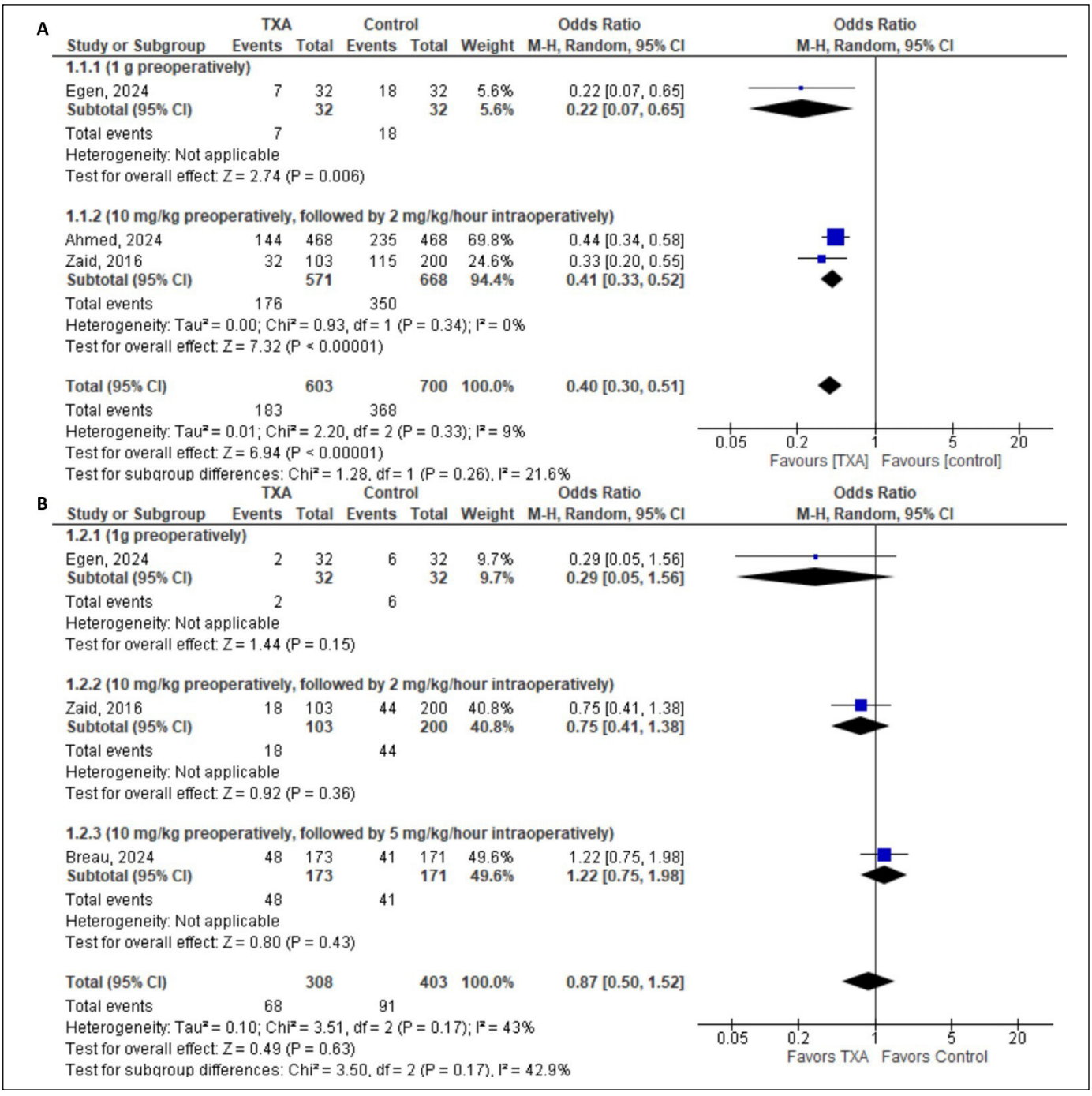


Figure 2. *Forest plot of the requirement for perioperative BT and the requirement for intraoperative BT. Forest plot comparing:* **A)** *requirement for perioperative BT, and* **B)** *requirement for intraoperative BT between patients undergoing radical cystectomy who did or did not receive tranexamic acid.*

CI – confidence interval; TXA – tranexamic acid

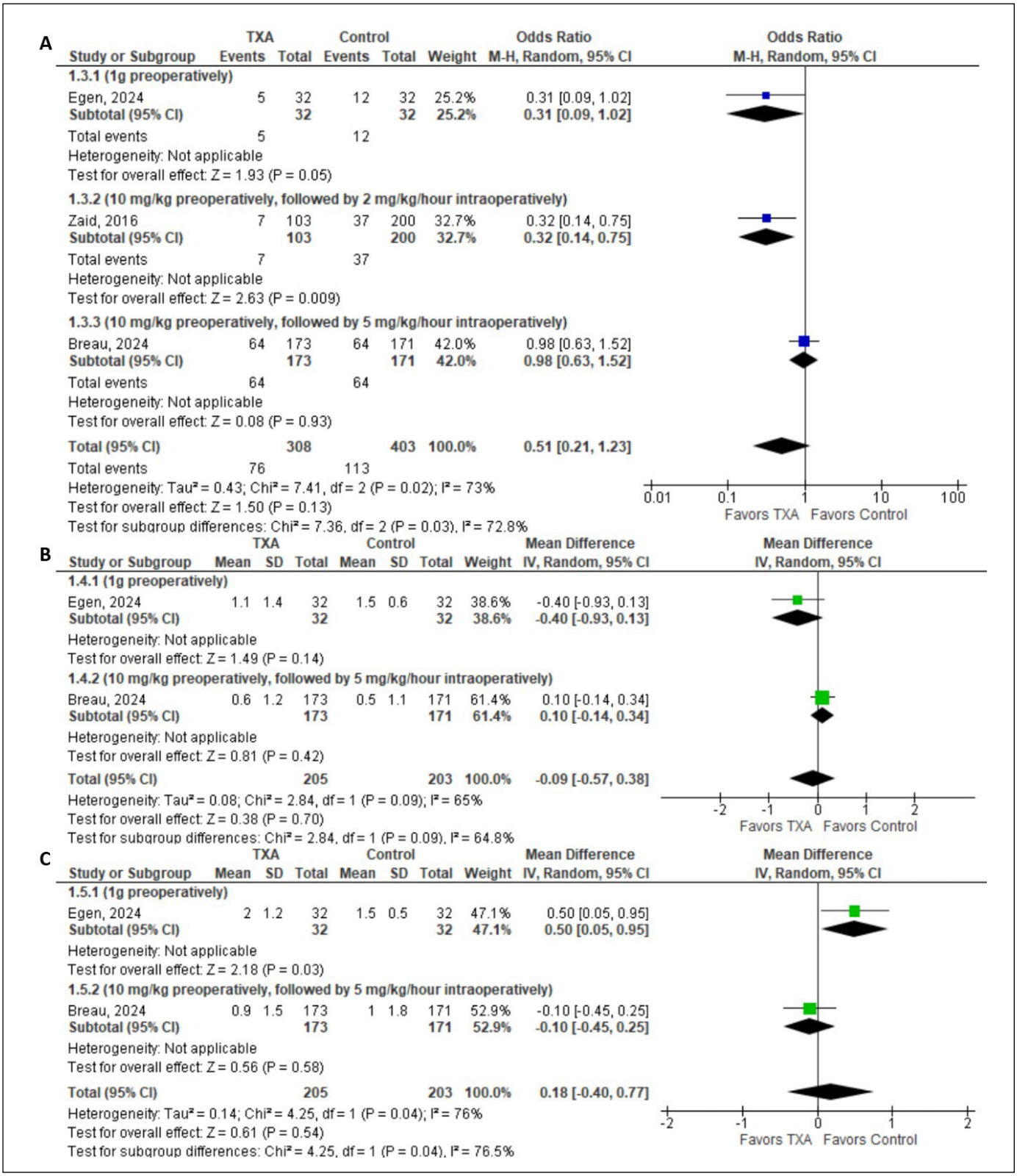


Figure 3. *Forest plot of the requirement for postoperative BT, the mean number of units transfused intraoperatively, and the mean number of units transfused postoperatively. Forest plot comparing:* **A)** *the requirement for postoperative BT,* **B)** *the mean number of units transfused intraoperatively, and* **C)** *the mean number of units transfused postoperatively between patients undergoing radical cystectomy who did or did not receive tranexamic acid.*

CI – confidence interval; TXA – tranexamic acid

the requirement for postoperative BT also revealed no significant difference (OR = 0.51; 95% CI: 0.21–1.23; p = 0.13; I^2 = 73%; Figure 3A), with this analysis exhibiting substantial heterogeneity. There was substantial heterogeneity and no significant differences in the mean number of units transfused intraoperatively (MD –0.09; 95% CI: from –0.57 to 0.38; p = 0.70; I^2 = 65%; Figure 3B) or postoperatively (MD = 0.18; 95% CI: from –0.40 to 0.77; p = 0.54; I^2 = 76%; Figure 3C).

Estimated blood loss

Our analysis of EBL revealed no statistical difference between intervention and control groups (MD = –9.31; 95% CI: from –82.50 to 63.87; p = 0.80; I^2 = 0%; Figure 4A).

Safety

In our safety analysis, overall, no difference was found in DVT events (OR = 1.14; 95% CI: 0.54–2.41; p = 0.72; I^2 = 3%; Figure 5A) and PE (OR = 1.49; 95% CI: 0.69–3.24; p = 0.31; I^2 = 0%; Figure 5B). Likewise, the subgroup analysis of patients who received 10 mg/kg preoperatively followed by 2 mg/kg/hour intraoperatively demonstrated no significant differences between the groups regarding DVT (OR = 1.05; 95% CI: 0.32–3.44; p = 0.94; I^2 = 51%; Figure 5A – subgroup analysis 1.7.1) or PE events (OR = 1.56; 95% CI: 0.63–3.85; p = 0.34; I^2 = 0%; Figure 5B – subgroup analysis 1.8.1). The subgroup analysis for DVT also demonstrates substantial heterogeneity.

We also analyzed composite safety outcomes in the general analysis, such as concurrent DVT

Table 1. *Baseline characteristics of included studies (TXA/Control)*

Author, year	Country	Type of study	Surgical indication	Sample	Dose	Perioperative BT requirement (%)	Male sex no. (%)	Mean age ±SD	BMI ±SD	Mean months Follow-up
Zaid et al. 2016 [20]	USA	Retrospective	RC for bladder cancer	103 / 200	Patients receiving 10 mg/kg preoperatively, followed by 2 mg/kg/h intraoperatively	32 (31.1) / 115 (57.5)	91 (88.3) / 161 (80.5)	68.8 ±2.7 / 68.6 ±2.6	27.4 ±1.3 / 27.4 ±1.2	1
Ahmed et al. 2024 [19]	USA	Retrospective	RC for bladder cancer	468 / 468	Patients receiving 10 mg/kg preoperatively, followed by 2 mg/kg/h intraoperatively	144 (30.8) / 235 (50.2)	NA	68.9 ±1.8 / 65 ±1.9	NA	3
Breau et al. 2024 [21]	Canada	RCT	RC for bladder cancer	178 / 175	Patients receiving 10 mg/kg preoperatively, followed by 5 mg/kg/h intraoperatively	NA	132 (74.2) / 131 (74.9)	69.8 ±2 / 68.2 ±2.5	27.3 ±1 / 27.9 ±1.2	1
Egen et al., 2024 [9]	Germany	Retrospective with PSM	RC for bladder cancer	32 / 32	Patients receiving 1 g preoperatively	6 (18.75) / 15 (46.88)	27 (84.4) / 21 (65.6)	68 ±10 / 72 ±9	28 ±5 / 27 ±5	1

BMI – body mass index; BT – blood transfusion; NA – not available; PSM – propensity score matching; RC – radical cystectomy; RCT – randomized clinical trial; SD – standard deviation; TXA – tranexamic acid

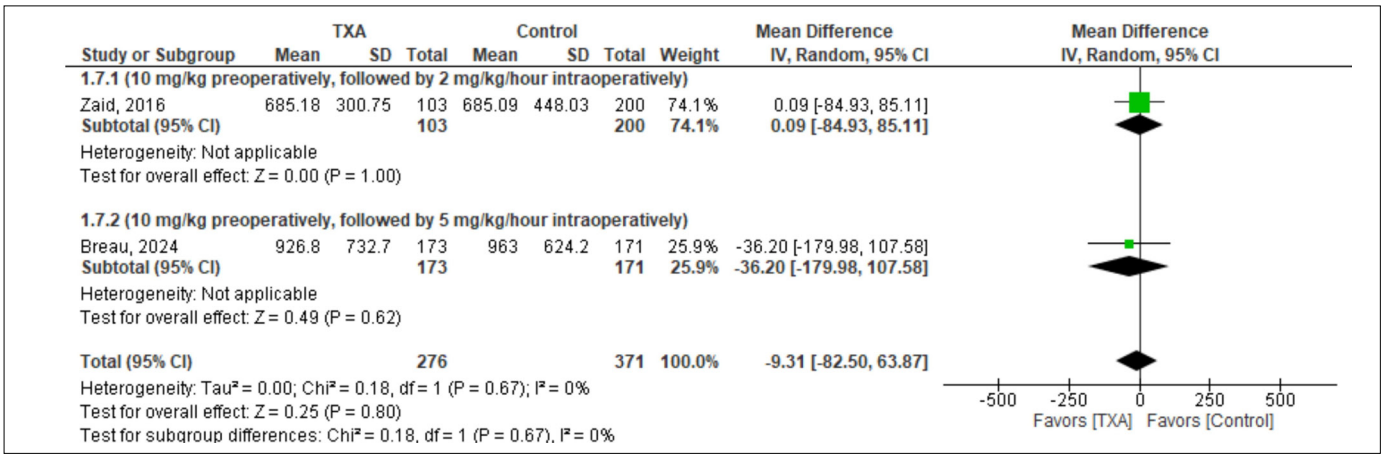


Figure 4. *Forest plot of EBL. Forest plot comparing EBL between patients undergoing radical cystectomy who did or did not receive tranexamic acid.*

CI – confidence interval; TXA – tranexamic acid

and PE (OR = 1.49; 95% CI: 0.74–3.01; p = 0.26; I^2 = 0%; Figure 6A) and either DVT or PE (OR = 1.58; 95% CI: 0.92–2.72; p = 0.10; I^2 = 0%; Figure 6B), but there were no significant differences between groups. In our subgroup analysis of patients who received 10 mg/kg preoperatively followed by 2 mg/kg/hour intraoperatively, neither group showed significantly fewer events of either DVT or PE (OR = 1.68; 95% CI: 0.90–3.14; p = 0.10; I^2 = 0%; Figure 6B – subgroup analysis 1.10.2).

Quality assessment

We analyzed the potential bias in the studies conducted by Ahmed et al. [9], Egen et al. [19], and Zaid et al. [20] using the ROBINS-I tool, assessing it across seven domains. The general risk for the first two studies was deemed moderate, while the last one was considered serious. Furthermore, the RoB 2 tool was utilized to examine the study by Breau et al. [21], which was evaluated across

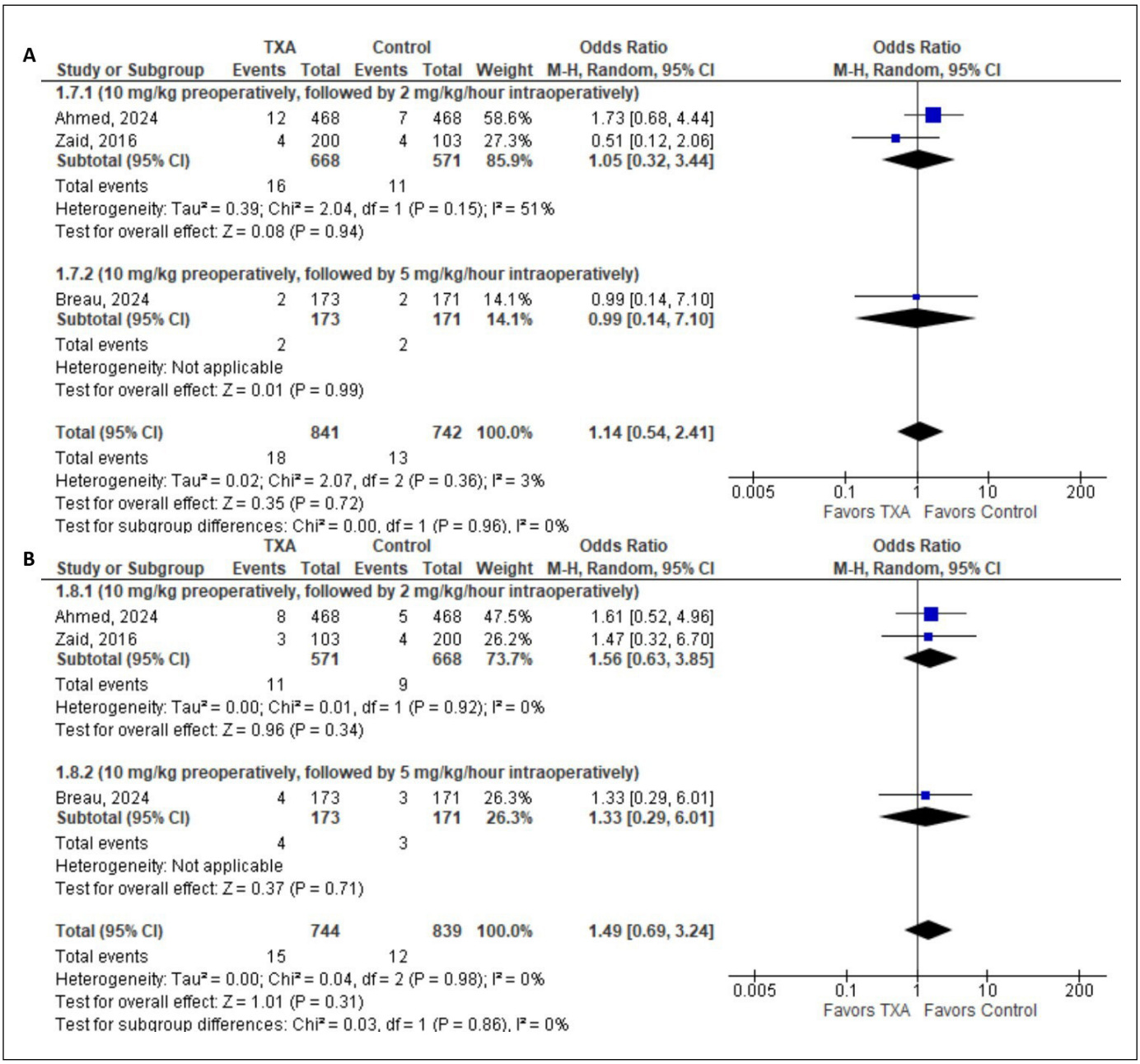


Figure 5. *Forest plot of DVT, and PE. Forest plot comparing:* **A)** *DVT, and* **B)** *PE between patients undergoing radical cystectomy who did or did not receive tranexamic acid.*

CI – confidence interval; TXA – tranexamic acid

five domains. This study was identified as low risk regarding overall bias. These ratings are depicted in the Summary Plot (Suppl. Figures 1 and 2) and the Traffic Light Plot (Suppl. Figures 3 and 4).

DISCUSSION

In this systematic review and meta-analysis comprising 4 studies and 1,656 patients we compared the efficacy and safety of TXA groups versus control groups of patients who underwent RC. Our main findings were as follows: (I) Overall analyses of TXA patients showed a significantly lower requirement for perioperative BT; (II) There was no significant difference between the experimental and control groups regarding postoperative or intraoperative BT; (III) The mean number of units transfused revealed no difference between groups and subgroups, both in the intraoperative and postoperative periods; (IV) Our analysis revealed no difference between groups of EBL; (V) None of the analyses, including subgroup analyses, of the safety outcomes showed

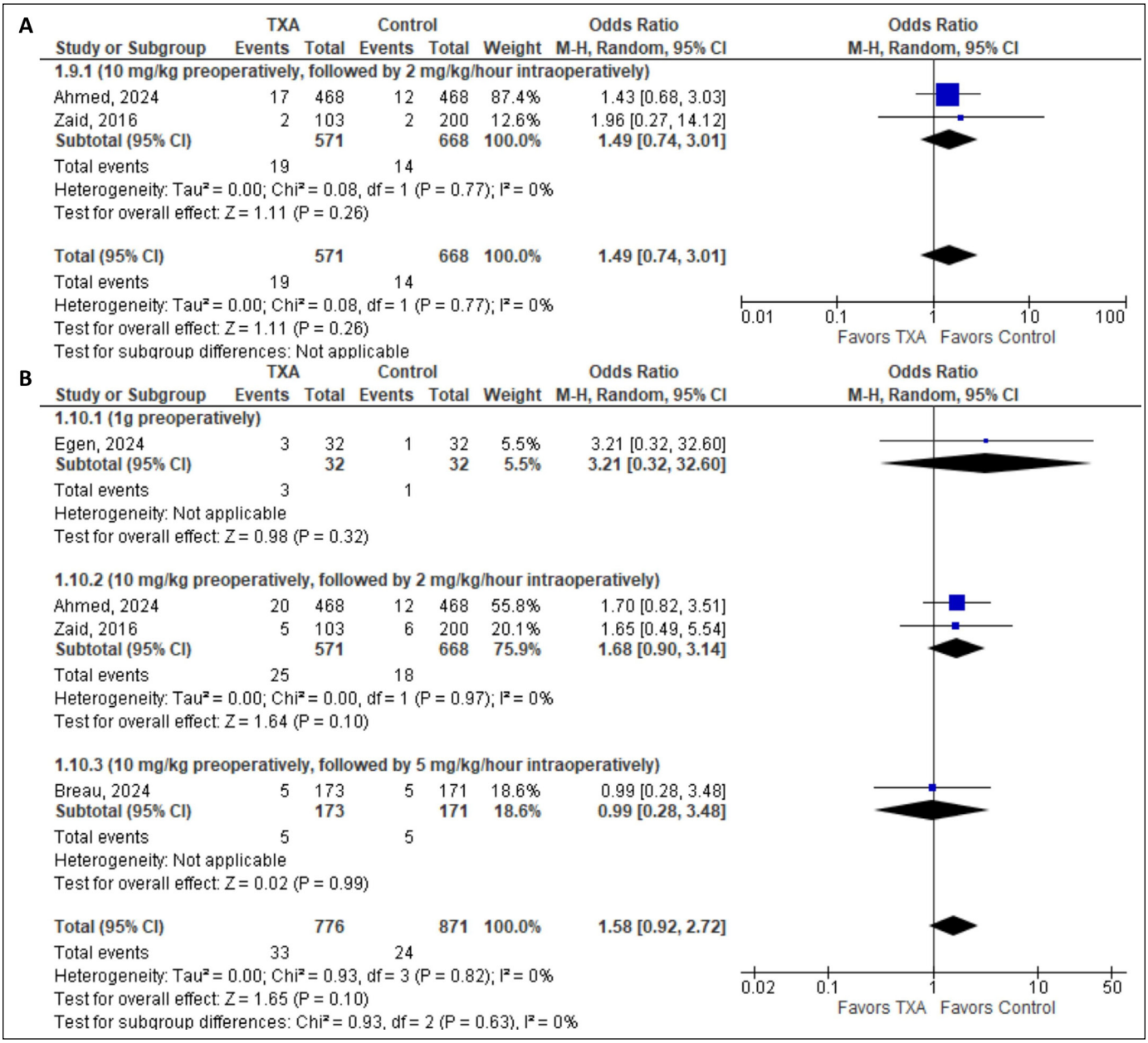


Figure 6. *Forest plot such as concurrent DVT and PE, and either DVT or PE. Forest plot comparing* **A)** *concurrent DVT and PE, and* **B)** *either DVT or PE between patients undergoing radical cystectomy who did or did not receive tranexamic acid.*

CI – confidence interval; TXA – tranexamic acid

a statistically significant difference between the use of TXA groups and the control groups.

RC is the standard treatment for clinically localized muscle-invasive BC [24]. Despite its curative potential, RC remains a complex and challenging procedure, consistently associated with significant morbidity and mortality [14, 15]. Complications are common, with wound-related, infectious, and gastrointestinal events being the most frequently reported, and overall complication rates exceeding 60% in some series [16, 25]. A cross-sectional study from The American College of Surgeons, analyzing data from over six million patients, indicated that individuals undergoing urological cancer surgeries are at a higher risk for perioperative BT [26]. In addition, current evidence indicates that perioperative BT in patients with BC who underwent RC may be linked to unfavorable oncologic outcomes [7], including reduced survival, higher risk of disease recurrence, and increased all-cause mortality [7, 27, 28]. Perioperative BT has been reported in up to 60% of RC patients and is associated with an increased risk of cancer recurrence and mortality [5, 29]. While further validation is needed, implementing strategies to minimize blood product utilization remains essential [29].

The use of TXA to mitigate intraoperative blood loss and subsequently reduce the need for perioperative BT has been evaluated in multiple studies [30–33]. A previous meta-analysis [30] examining the impact of TXA in surgical procedures across multiple subspecialties reported a significant reduction in blood loss. In the context of urological surgeries, a recent meta-analysis [13] found that, although there were insufficient data on RC at the time, TXA use was associated with decreased blood loss, lower transfusion rates, shorter hospital stays, and reduced operative duration.

The present meta-analysis included four studies with three different TXA dosing regimens in RC: 10 mg/kg of TXA before surgery followed by a continuous infusion of either 2 mg/kg/h [19, 20] or 5 mg/kg/h [21], or a single 1 g dose [9] administered preoperatively, following a protocol previously described for patients undergoing noncardiac surgery [33], to facilitate practical implementation. Notably, this variability in dosing strategies likely contributed to the increased heterogeneity observed in some pooled analyses. Although evidence suggests that administration methods varied across studies, these differences, along with dose variations, did not have a significant impact on blood loss [30]. Accordingly, our meta-analysis included all dosing regimens and conducted both an overall analysis across all studies, regardless of dose, as well as subgroup analyses based on different administration methods for each outcome.

In our analysis, the number of patients requiring perioperative BT was significantly higher in the control group compared to the TXA group during RC, regardless of the TXA dose administered [9, 19, 20]. However, when analyzed separately for intraoperative [9, 20, 21] or postoperative [9, 20, 21] BT, this difference did not reach statistical significance, except for postoperative BT with a dose of 10 mg/kg + 2 mg/kg/h, which significantly favored the TXA group but was based on a single study [20]. This discrepancy between the significant perioperative result and the nonsignificant intraoperative and postoperative findings may stem from inconsistencies in how the postoperative period was defined across studies. While two studies limited it to the hospital stay [9, 20], others extended it to 30 days [19, 21], creating variability in outcome measurement. This variation likely reduced the consistency of the postoperative analysis. In contrast, the perioperative outcome, by combining intraoperative and postoperative data, reflected a broader and more uniform timeframe, which may have improved the ability to detect the transfusion sparing effect of TXA.

Furthermore, when examining the mean number of units transfused, some studies indicate that individuals undergoing RC received a mean of two units in the perioperative setting [28,29]. Our analysis of the mean number of units transfused in both intraoperative and postoperative periods revealed no statistically significant difference specific to RC. A significant result was observed in the postoperative setting, based on a single study with a preoperative dose of 1 g [9], favoring the control group. Additionally, although previous literature has shown that TXA use in urological surgeries is associated with reduced EBL [13, 34], the present EBL analysis showed no significant differences between the groups. This result conflicts with our analysis of perioperative BT, which favored the TXA group, especially considering that the need for transfusion is commonly associated with EBL, as demonstrated in a previous meta-analysis [13] that found TXA to be associated with lower transfusion rates and reduced EBL. However, it is important to highlight that our perioperative BT analysis included three observational studies [9,19,20], whereas the EBL analysis was based on only two studies [20,21], one of which was not part of the perioperative BT analysis [21]. This difference in study composition may help explain the apparent inconsistency, reinforcing the need for further studies to clarify the impact of TXA in the context of cystectomy.

The perioperative use of TXA as an antifibrinolytic therapy is supported by solid pharmacological and clinical evidence [35]. There are various discussions in the medical literature regarding the safety of TXA and its potential role in increasing the risk of thromboembolic events. Some studies suggest a possible correlation between TXA and an independent increase in venous thromboembolism (VTE) risk among trauma patients [12, 36], while others report uncertain effects [6, 35]. Moreover, several studies have found no association between TXA use and a heightened risk of thrombotic adverse events [37, 38].

In the urological context, a study identified RC as having the second-highest incidence of postoperative VTE among all analyzed cancer types, underscoring the need for thorough risk assessment [39]. Two previous meta-analyses evaluating TXA use in urological surgeries, which lacked a sufficient number of cystectomy studies, suggested that TXA does not increase the risk of thromboembolic events [13, 34]. In our analysis, no significant differences were observed between the control and intervention groups regarding the development of DVT [19–21] or PE [19–21], including concurrent DVT and PE, or either DVT or PE [9, 19–21] across the included studies. These findings support the potential safety of TXA use in the context of RC.

Therefore, the use of TXA in RC may be a useful strategy to reduce perioperative transfusion requirements. While our findings demonstrated statistically significant results in this regard, clinical interpretation should consider the heterogeneity in study designs, dosing regimens, and outcome definitions. Still, the consistency of the effect in the overall analysis supports its potential benefit. TXA administration should be guided by individual patient risk profiles and institutional protocols, with clinical judgment considering the patient's current condition, history of thromboembolic events, and the treatment setting's capacity for intervention and transfusion. Future trials with standardized dosing regimens and outcome reporting are essential to strengthen the current evidence base and optimize clinical applicability.

This systematic review and meta-analysis have several limitations that should be acknowledged: (I) there is significant heterogeneity in the dosing regimens of TXA across the included studies, which complicates direct comparisons and may explain the increased heterogeneity in some analyses; (II) variation in how the postoperative period was defined across studies may have affected the consistency of outcome reporting, particularly for postoperative transfusion data; (III) the limited number of RCTs among the included studies represents a significant limitation, as observational and retrospective cohort designs are more susceptible to bias; (IV) furthermore, the criteria for allocating participants to the TXA and control groups varied among the included studies, potentially influencing reported outcomes; (V) three of the included studies implemented postoperative thromboprophylaxis, typically for approximately four weeks, which may influence the interpretation of the safety outcomes.

CONCLUSIONS

This systematic review and meta-analysis demonstrated that TXA significantly reduces the need for perioperative BT in patients undergoing RC, without increasing the risk of thromboembolic events. While no significant differences were observed in intraoperative or postoperative transfusion rates, EBL, or mean number of transfused units, the reduction in overall perioperative transfusion requirements highlights TXA's potential as a hemostatic adjunct in this high-risk surgical population. Nonetheless, the heterogeneity in dosing regimens and the predominance of non-randomized studies underscore the need for further high-quality RCTs to establish standardized protocols and confirm long-term safety and efficacy of TXA in RC.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

FUNDING

This research received no external funding.

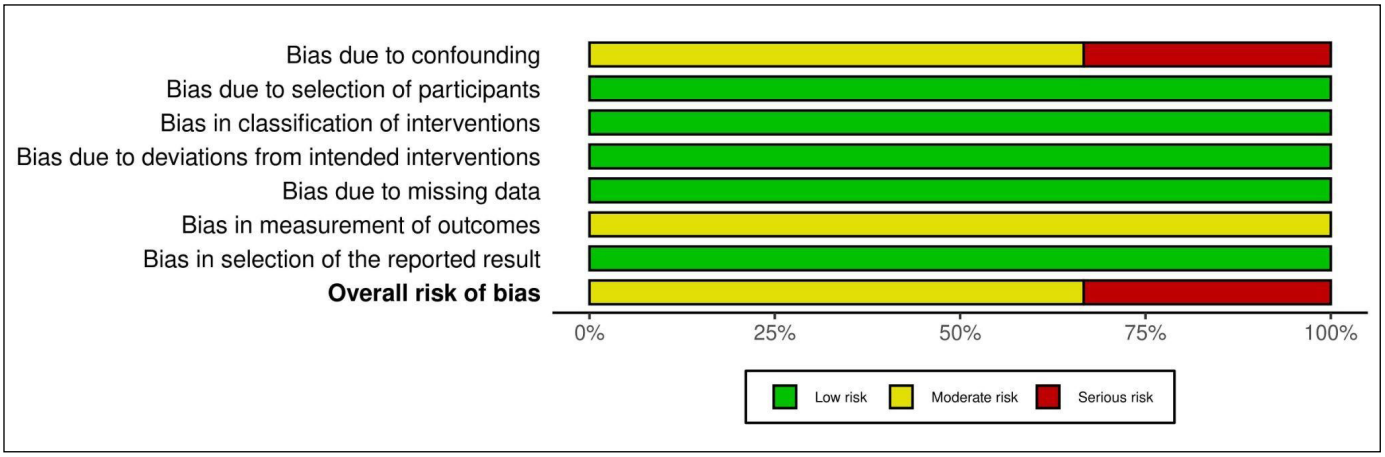
ETHICS APPROVAL STATEMENT

The ethical approval was not required.

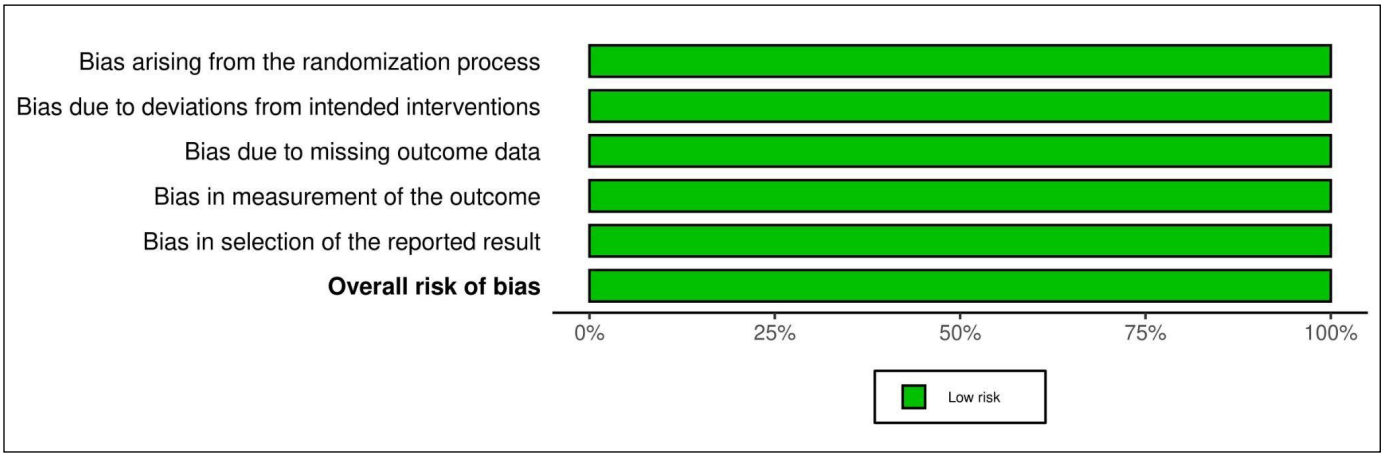
SUPPLEMENTARY MATERIAL

Suppl. Table 1. *Details of the search strategy according to the database*

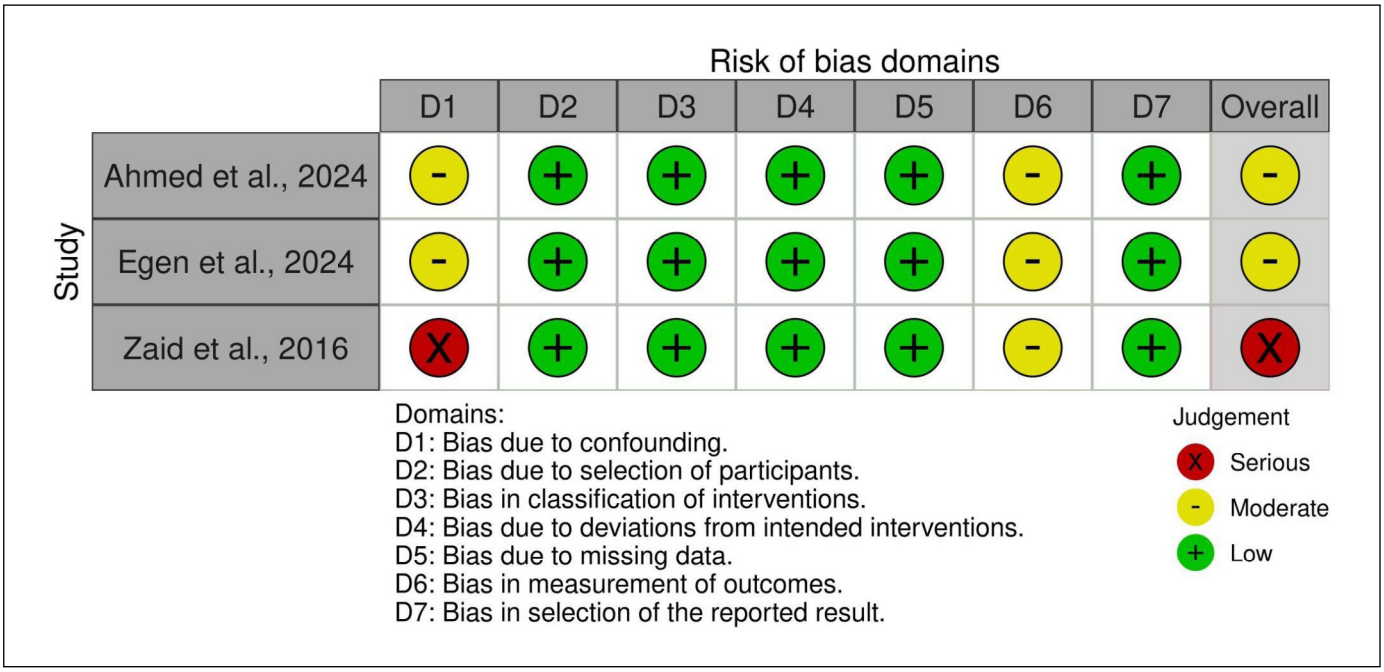
Database	Search strategy
PubMed/MEDLINE	("cystectomy"[mh] OR "radical cystectomy" OR "cystectomies" OR "urologic surgical procedures"[mh] OR "urologic surgical" OR "urologic surgical procedure") AND ("tranexamic acid"[mh] OR "transamin" OR "antifibrinolytic")
Embase	("cystectomy" OR "radical cystectomy" OR "cystectomies" OR "urologic surgical procedures" OR "urologic surgical" OR "urologic surgical procedure") AND ("tranexamic acid" OR "transamin" OR "antifibrinolytic")
Cochrane	("cystectomy" OR "radical cystectomy" OR "cystectomies" OR "urologic surgical procedures" OR "urologic surgical" OR "urologic surgical procedure") AND ("tranexamic acid" OR "transamin" OR "antifibrinolytic")



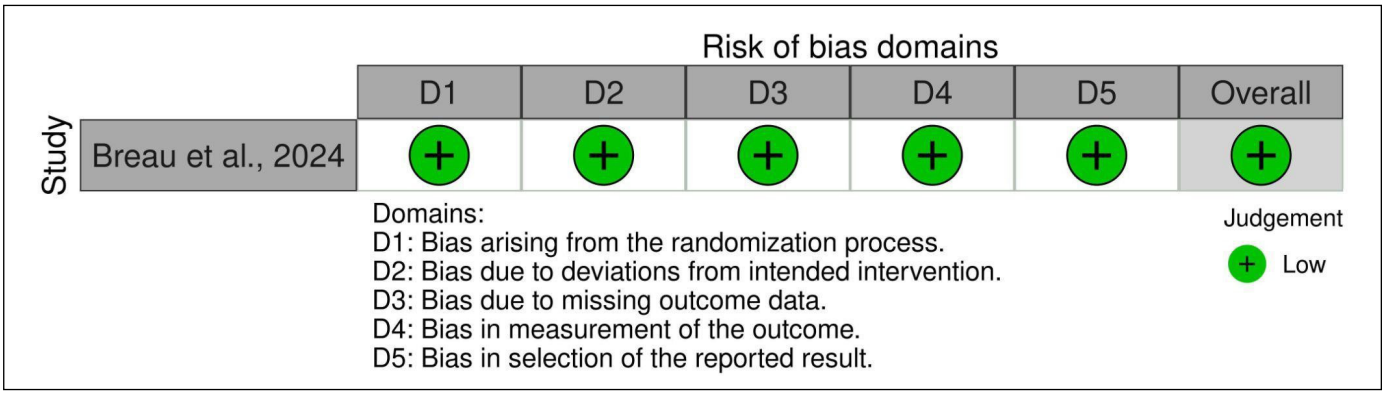
Suppl. Fig. 1. *Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) – assessment of non-randomized studies: summary plot.*



Suppl. Fig. 2. *Risk of Bias 2 (ROB2) – assessment of randomized studies: summary plot.*



Suppl. Fig. 3. *Risk Of Bias In Non-randomised Studies of Interventions (ROBINS-I) – assessment of non-randomized studies: traffic light plot.*



Suppl. Fig. 4. *Risk of Bias 2 (ROB2) – assessment of randomized studies: traffic light plot.*

References

1. Siegel RL, Kratzer TB, Giaquinto AN, Sung H, Jemal A. Cancer statistics, 2025. CA Cancer J Clin. 2025; 75: 10-45.
2. Hautmann RE. Urinary Diversion: Ileal Conduit to Neobladder. J Urol. 2003; 169: 834-842.
3. Yuh BE, Nazmy M, Ruel NH, et al. Standardized Analysis of Frequency and Severity of Complications After Robot-assisted Radical Cystectomy. Eur Urol. 2012; 62: 806-813.
4. Katsimperis S, Tzelves L, Tandogdu Z, et al. Complications After Radical Cystectomy: A Systematic Review and Meta-analysis of Randomized Controlled Trials with a Meta-regression Analysis. Eur Urol Focus. 2023; 9: 920-929.
5. Novara G, De Marco V, Aragona M, et al. Complications and Mortality After Radical Cystectomy for Bladder Transitional Cell Cancer. J Urol. 2009; 182: 914-921.
6. Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. BMJ. 2012; 344: e3054-e3054.
7. Uysal D, Egen L, Grilli M, et al. Impact of perioperative blood transfusions on oncologic outcomes after radical cystectomy: A systematic review and meta-analysis of comparative studies. Surg Oncol. 2021; 38: 101592.
8. Henry D, Moxey A, Carless P, et al. Anti-fibrinolytic use for minimising perioperative allogeneic blood transfusion. In: The Cochrane Collaboration, editor. The Cochrane Database of Systematic Reviews [Internet]. John Wiley & Sons, Chichester, UK 1999; p. CD001886.

9. Egen L, Keller K, Menold HS, et al. Tranexamic acid reduces perioperative blood transfusions following open radical cystectomy – a propensity-score matched analysis. World J Urol. 2024; 42: 477.

10. Colomina MJ, Contreras L, Guilabert P, Koo M, M Ndez E, Sabate A. Clinical use of tranexamic acid: evidences and controversies. Braz J Anesthesiol. 2022; 72: 795-812.

11. Wu G, Mazzitelli BA, Quek AJ, et al. Tranexamic acid is an active site inhibitor of urokinase plasminogen activator. Blood Adv. 2019; 3: 729-733.

12. Benipal S, Santamarina JL, Vo L, Nishijima D. Mortality and Thrombosis in Injured Adults Receiving Tranexamic Acid in the Post-CRASH-2 Era. West J Emerg Med. 2019; 20: 443-453.

13. Kim J, Alrumaih A, Donnelly C, Uy M, Hoogenes J, Matsumoto ED. The impact of tranexamic acid on perioperative outcomes in urological surgeries: A systematic review and meta-analysis. Can Urol Assoc J. 2023; 17. Available at: https://cuaj.ca/index.php/journal/article/view/8254

14. Lawrentschuk N, Colombo R, Hakenberg OW, et al. Prevention and Management of Complications Following Radical Cystectomy for Bladder Cancer. Eur Urol. 2010; 57: 983-1001.

15. Novotny V, Hakenberg OW, Wiessner D, et al. Perioperative Complications of Radical Cystectomy in a Contemporary Series. Eur Urol. 2007; 51: 397-402.

16. Richards KA, Steinberg GD. Perioperative outcomes in radical cystectomy: how to reduce morbidity? Curr Opin Urol. 2013; 23: 456-465.

17. Higgins JPT, Thomas J, Chandler J, et al. (eds.). Cochrane Handbook for Systematic Reviews of Interventions version 6.4 (updated August 2023), Cochrane, 2023. Available at: www.training.cochrane.org/handbook.

18. Moher D, Liberati A, Tetzlaff J, Altman DG; The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med. 2009; 6: e1000097.

19. Ahmed ME, Andrews JR, Mahmoud AM, et al. Intraoperative Tranexamic Acid in Radical Cystectomy: Impact on Bleeding, Thromboembolism, and Survival Outcomes. J Urol. 2025; 213: 447-454.

20. Zaid HB, Yang DY, Tollefson MK, et al. Efficacy and Safety of Intraoperative Tranexamic Acid Infusion for Reducing Blood Transfusion During Open Radical Cystectomy. Urology. 2016; 92: 57-62.

21. Breau RH, Lavallée LT, Cagiannos I, et al. Tranexamic Acid During Radical Cystectomy: A Randomized Clinical Trial. JAMA Surg. 2024; 159: 1355.

22. Sterne JA, Hernán MA, Reeves BC, et al. ROBINS-I: a tool for assessing risk of bias in non-randomised studies of interventions. BMJ. 2016; 355: i4919.

23. 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.

24. Alfred Witjes J, Lebret T, Compérat EM, et al. Updated 2016 EAU Guidelines on Muscle-invasive and Metastatic Bladder Cancer. Eur Urol. 2017; 71: 462-475.

25. Shabsigh A, Korets R, Vora KC, et al. Defining Early Morbidity of Radical Cystectomy for Patients with Bladder Cancer Using a Standardized Reporting Methodology. Eur Urol. 2009; 55: 164-176.

26. Montroy J, Lavallée LT, Zarychanski R, et al. The Top 20 Surgical Procedures Associated with the Highest Risk for Blood Transfusion. Br J Surg. 2020; 107: e642-e643.

27. Abel EJ, Linder BJ, Bauman TM, et al. Perioperative Blood Transfusion and Radical Cystectomy: Does Timing of Transfusion Affect Bladder Cancer Mortality? Eur Urol. 2014; 66: 1139-1147.

28. Sadeghi N, Badalato GM, Hruby G, Kates M, McKiernan JM. The impact of perioperative blood transfusion on survival following radical cystectomy for urothelial carcinoma. Can J Urol. 2012; 19: 6443-6449.

29. Linder BJ, Frank I, Cheville JC, et al. The Impact of Perioperative Blood Transfusion on Cancer Recurrence and Survival Following Radical Cystectomy. Eur Urol. 2013; 63: 839-845.

30. Ker K, Prieto-Merino D, Roberts I. Systematic review, meta-analysis and meta-regression of the effect of tranexamic acid on surgical blood loss. Br J Surg. 2013; 100: 1271-1279.

31. Tsantes AG, Trikoupis IG, Papadopoulos DV, et al. The Safety and Efficacy of Tranexamic Acid in Oncology Patients Undergoing Endoprosthetic Reconstruction and a ROTEM-Based Evaluation of Their Hemostatic Profile: A Pilot Study. Cancers. 2021; 13: 3951.

32. Houston BL, Uminski K, Mutter T, et al. Efficacy and Safety of Tranexamic Acid in Major Non-Cardiac Surgeries at High Risk for Transfusion: A Systematic Review and Meta-Analysis. Transfus Med Rev. 2020; 34: 51-62.

33. Devereaux PJ, Marcucci M, Painter TW, et al. Tranexamic Acid in Patients Undergoing Noncardiac Surgery. N Engl J Med. 2022; 386: 1986-1997.

34. Lin YH, Lee KC, Hsu CC, Chen KT. Efficacy and safety of intravenous tranexamic acid in urologic surgery: A systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore). 2023; 102: e34146.

35. Ng WCK, Jerath A, Wasowicz M. Tranexamic acid: a clinical review. Anestezjol Intensywna Ter. 2015; 47: 339-350.

36. Myers SP, Kutcher ME, Rosengart MR, et al. Tranexamic acid administration is associated with an increased risk of posttraumatic venous thromboembolism. J Trauma Acute Care Surg. 2019; 86: 20-27.

37. Weng S, Wang W, Wei Q, Lan H, Su J, Xu Y. Effect of Tranexamic Acid in Patients with Traumatic Brain Injury: A Systematic Review and Meta-Analysis. World Neurosurg. 2019; 123: 128-135.

38. Montroy J, Fergusson NA, Hutton B, et al. The Safety and Efficacy of Lysine Analogues in Cancer Patients: A Systematic Review and Meta-Analysis. Transfus Med Rev 2017; 31: 141-148.

39. Hammond J, Kozma C, Hart JC, et al. Rates of Venous Thromboembolism Among Patients with Major Surgery for Cancer. Ann Surg Oncol 2011; 18: 3240–3247.