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Original article

AGE, BODY MASS INDEX AND SEX AS DETERMINANTS OF PERIOPERATIVE BLOOD LOSS, DRAINAGE, AND TRANSFUSION IN TOTAL HIP ARTHROPLASTY WITH AND WITHOUT TRANEXAMIC ACID: A SECONDARY ANALYSIS

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Abstract

Introduction: Intravenous tranexamic acid (TXA) reduces blood loss and transfusion requirements in total hip arthroplasty (THA), but whether age, body mass index (BMI), and sex modify its effect or independently influence perioperative bleeding remains unclear. This secondary analysis investigated associations between these demographic factors and perioperative outcomes.

Materials and methods: This hypothesis-generating secondary analysis included 80 patients from a prospective comparative study of primary uncemented THA: 40 received 1 g intravenous TXA before incision and 40 served as controls. Within each group, associations of age and BMI with hematological and blood-loss outcomes were assessed using Pearson correlation, while sex-based differences were evaluated using Student's t-test and chi-square test. Statistical significance was set at $p<0.05$.

Results: In the TXA group, age correlated with total drain volume ($r=0.355$, $p=0.025$) but not with other outcomes. In controls, age correlated with preoperative hemoglobin ($r= 0.326$, $p=0.040$), but not with postoperative or blood-loss outcomes. BMI was not significantly associated with any outcome in either group. In controls, males had greater total drain volume than females (769.6±189.0 *vs*. 590.1±189.1 mL, $p=0.005$); this difference was not significant with TXA (627.5±234.8 *vs*. 507.4±172.5 mL, $p=0.071$). No demographic factor significantly predicted transfusion.

Conclusion: Age, BMI, and sex showed limited and inconsistent associations with perioperative bleeding and did not predict transfusion. TXA efficacy appeared broadly consistent across demographic subgroups, although larger adequately powered studies are required to confirm these findings.

Keywords: tranexamic acid; total hip arthroplasty; age; body mass index; sex differences; blood transfusion; secondary analysis

Introduction

Intravenous tranexamic acid (TXA) is now supported by a substantial body of randomized and observational evidence as an effective means of reducing blood loss and transfusion requirements in total hip arthroplasty (THA)[1,2]. Most of this evidence, however, addresses the average treatment effect of TXA across a study population, leaving open the question of whether demographic characteristics commonly recorded in routine practice-patient age, body mass index (BMI), and sex-meaningfully modify bleeding risk or the magnitude of hemostatic benefit of TXA.

Older age and higher BMI are frequently cited as risk factors for perioperative complications in arthroplasty generally[3,4], and sex-related differences in coagulation profile, muscle mass, and surgical exposure have been proposed as potential contributors to differential blood loss[5]. However, findings on whether these factors independently predict THA-specific blood loss or transfusion risk have been inconsistent across the literature, and few studies have examined whether such associations differ between patients who do and do not receive TXA. We therefore performed a secondary analysis of a prospective comparative cohort of patients undergoing primary uncemented THA, in which 40 patients received a single pre-incision 1 g intravenous dose of TXA and 40 did not. The purpose was to characterize the relationships between age, BMI, sex, and perioperative blood loss, drainage, and transfusion outcomes within each treatment arm.

Materials and methods

Relationship to primary study and design

This was a prespecified secondary analysis of the same 80-patient prospective comparative cohort reported in our primary study of intravenous TXA in primary uncemented THA (experimental group [EG], n=40, receiving 1 g intravenous TXA before skin incision; control group [CG], n=40, no antifibrinolytic), conducted at the University Clinic for Orthopedic Diseases, Skopje, between 2023 and 2025 [study cross-reference: Damjanovikj *et al*., companion manuscript]. Full details of eligibility criteria, surgical technique, TXA dosing, and outcome definitions have been reported in the primary manuscript and are summarized briefly below. This analysis re-uses the same patient sample to address a distinct, exploratory question-the role of demographic modifiers-and is reported transparently as a secondary analysis rather than as an independent trial.

Eligible patients were adults with radiographically confirmed coxarthrosis undergoing primary elective unilateral uncemented THA, ASA I-III, with normal hematological and hemostatic status. Total blood volume was calculated with the Nadler formula and total blood loss with the Mercuriali algorithm[6,7].

Variables analyzed

Within each treatment group separately, we assessed the correlation of patient age and BMI with: preoperative and postoperative day-5 erythrocyte count, hemoglobin, and hematocrit (including transfusion-independent values); erythrocyte volume loss; total blood loss; and total drain volume. We additionally compared these outcomes, plus transfusion frequency, between male and female patients within each group.

Statistical analysis

Pearson's correlation coefficient was used to assess linear association between age or BMI and continuous hematological/blood-loss variables. Continuous outcomes were compared between sexes using Student's t-test; categorical outcomes (e.g., transfusion yes/no) were compared using the chi-square test (Yates-corrected for small expected cell counts). All analyses were performed separately within the TXA and control groups. Significance was set

at p<0.05. Given the exploratory nature of this analysis and the modest sample size (n=40 per group), results should be interpreted as hypothesis-generating rather than confirmatory.

Results

Age

In the TXA group, age did not correlate significantly with preoperative or postoperative day-5 erythrocyte, hemoglobin, or hematocrit values, nor with erythrocyte loss or total blood loss (all p>0.35). Age correlated significantly and positively with total drain volume (r=0.355, p=0.025), indicating that older patients receiving TXA tended to have somewhat greater local wound drainage, despite no corresponding increase in total calculated blood loss.

In the control group, age correlated significantly with higher preoperative hemoglobin (r= 0.326, p=0.040) and was borderline associated with higher preoperative hematocrit (r=0.312, p=0.050); no other correlation reached significance, including drain volume, erythrocyte loss, and total blood loss (Table 1). Age also did not differ significantly between patients who did or did not require intraoperative or postoperative transfusion in either group.

Table 1. Correlation of age with hematological and blood-loss outcomes by treatment group

Outcome	EG (TXA) r (p)	CG (no TXA) r (p)
Preop. erythrocytes	-0.024(0.853)	-0.033(0.842)
Day-5 erythrocytes	0.048(0.765)	-0.194(0.239)
Preop. hemoglobin	0.045(0.782)	0.326(0.040)*
Day-5 hemoglobin	0.046(0.774)	0.114(0.485)
Preop. hematocrit	0.039(0.809)	0.312(0.050)
Day-5 hematocrit	0.014(0.934)	-0.016(0.923)
Erythrocyte loss	-0.148(0.361)	0.223(0.167)
Total blood loss	-0.138(0.396)	0.166(0.306)
Total drain volume	0.355(0.025)*	0.204(0.206)

*p<0.05, Values are Pearson r (p-value), EG-experimental group (TXA), CG-control group

Body mass index

BMI showed no statistically significant correlation with any hematological or blood-loss outcome in either the TXA group (r range -0.177 to 0.112; all p>0.27) or the control group (r range -0.243 to 0.222; all p>0.13) (Table 2). BMI also did not differ significantly between patients who did or did not receive intraoperative or postoperative transfusion in either group.

Table 2. Correlation of BMI with hematological and blood-loss outcomes, by treatment group

Outcome	EG (TXA) r (p)	CG (no TXA) r (p)
Preop. erythrocytes	-0.165(0.311)	0.209(0.195)
Day-5 erythrocytes	0.070(0.666)	-0.222(0.169)
Preop. hemoglobin	-0.177(0.274)	0.166(0.306)
Day-5 hemoglobin	0.053(0.744)	-0.208(0.197)
Preop. hematocrit	-0.124(0.446)	0.177(0.275)
Day-5 hematocrit	0.112(0.493)	-0.243(0.130)
Erythrocyte loss	-0.093(0.567)	0.198(0.220)
Total blood loss	-0.078(0.634)	0.203(0.210)
Total drain volume	-0.063(0.699)	-0.092(0.574)

Values are Pearson r (p-value), No correlation reached statistical significance, EG-experimental group (TXA), CG- control group

Sex

In the TXA group, male and female patients had similar total drain volume (627.5± 234.8 mL *vs*. 507.4±172.5 mL, p=0.071), erythrocyte loss (536.0±205.0 mL *vs*. 440.9±185.7 mL, p=0.132), and total blood loss (1423.3±582.3 mL *vs*. 1241.7±525.3 mL, p=0.306); males trended toward higher values for all three outcomes, but none reached significance. In the control group, the same pattern was present but reached statistical significance for total drain volume: males drained significantly more than females (769.6±189.0 mL *vs*. 590.1±189.1 mL, p=0.005), while erythrocyte loss (812.9±273.6 mL *vs*. 717.3±231.4 mL, p=0.240) and total blood loss (2205.1±743.7 mL *vs*. 2083.9±724.8 mL, p=0.605) did not differ significantly by sex (Table 3).

Table 3. Blood loss and drainage outcomes by sex within treatment group

Outcome	Group	Male	Female	p-value
Total drain volume, mL	EG (TXA)	627.5±234.8	507.4±172.5	0.071
Total drain volume, mL	CG (no TXA)	769.6±189.0	590.1±189.1	0.005*
Erythrocyte loss, mL	EG (TXA)	536.0±205.0	440.9±185.7	0.132
Erythrocyte loss, mL	CG (no TXA)	812.9±273.6	717.3±231.4	0.240
Total blood loss, mL	EG (TXA)	1423.3±582.3	1241.7±525.3	0.306
Total blood loss, mL	CG (no TXA)	2205.1±743.7	2083.9±724.8	0.605

*p < 0.05. EG, experimental group (TXA); CG, control group. Values are mean ± SD

Neither intraoperative nor postoperative transfusion frequency differed significantly by sex within the TXA group (intraoperative p = 0.219; postoperative p = 0.412) or the control group (intraoperative p = 0.744; postoperative p = 0.053, with a non-significant trend toward higher postoperative transfusion among women in the control group (75% *vs*. 45%).

Discussion

In this secondary analysis, age, BMI and sex showed, at most, limited and inconsistent associations with perioperative blood loss and transfusion outcomes after primary uncemented THA and none reliably predicted transfusion need in either treatment arm. This pattern is broadly consistent with prior work suggesting that surgical and hemostatic factors, rather than baseline demographic characteristics alone, are the dominant drivers of perioperative blood loss in THA, although some registry-based studies have reported modest independent associations between advancing age and transfusion risk at a population level[3,8].

The positive correlation between age and total drain volume observed within the TXA group (r=0.355, p=0.025), without a corresponding association with total calculated blood loss, suggests that any age-related increase in local wound exudate in this cohort was not of sufficient magnitude to translate into greater systemic blood loss once the antifibrinolytic effect of TXA was accounted for. This finding should be interpreted cautiously given the modest sample size and the number of correlations tested, which raises the possibility of a chance finding; it nonetheless may warrant closer attention to drain management in older patients receiving TXA in future, larger studies.

The association between older age and higher preoperative hemoglobin observed in the control group (r=0.326, p=0.040) is unlikely to reflect a causal relationship and more plausibly reflects incidental variation or selection characteristics of the patients enrolled at older ages in this cohort, since no corresponding association was present in the TXA group and age did not correlate with any postoperative or blood-loss outcome in either arm.

The sex-related difference in drainage volume-significant in the control group but attenuated to a non-significant trend in the TXA group-is an intriguing, hypothesis-generating observation. It is compatible with, but does not establish, the possibility that antifibrinolytic effect of TXA may partially attenuate an underlying sex-related difference in local surgical

bleeding; larger, adequately powered studies with sex as a pre-specified stratification variable would be needed to confirm whether this represents a genuine effect-modification or a chance finding in a modestly sized cohort. Reviews of blood management in total joint arthroplasty have noted that reported sex-based differences in blood loss are inconsistent across studies and are often confounded by differences in body size, baseline hemoglobin, and surgical approach[4,5], underscoring the need for cautious interpretation here.

The absence of a significant BMI association with any outcome in either group is consistent with some, but not all, of the existing literature; several studies of blood management in arthroplasty report that obesity may increase absolute blood loss due to greater surgical exposure and tissue trauma, while others find no independent effect once total blood volume is accounted for, as in the Nadler-based calculations used here[6,9].

This analysis shares the limitations of the parent cohort: a single-center design, a modest sample size for subgroup analysis (n=40 per arm, smaller still within sex strata), and the inherent multiplicity of testing numerous correlations, which increases the risk of at least one false-positive finding (e.g., the age–drain volume and age–preoperative hemoglobin associations reported here). As a secondary, exploratory analysis of a previously reported cohort, this study should be viewed as hypothesis-generating; the observed effect sizes should inform, rather than substitute for, the design of adequately powered, pre-registered studies addressing demographic effect modification of TXA efficacy in THA directly.

Conclusion

Within this cohort, age, BMI, and sex were not consistent, reliable predictors of perioperative blood loss or transfusion need after primary uncemented THA and the efficacy of intravenous TXA in reducing blood loss appeared broadly preserved across these subgroups. An isolated association between age and drain volume in the TXA group and a sex-related difference in drainage that was significant only in the absence of TXA are worth exploring in larger, purpose-designed studies but do not currently support demographic-based adjustment of TXA dosing or patient selection in routine practice.

Conflict of interest statement. None declared.

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