J Shoulder Elbow Surg (2022) 31, 2211–2216

ELSEVIER

Journal of Shoulder and Elbow Surgery

www.elsevier.com/locate/ymse

SHOULDER

The effect of tranexamic acid for visualization on pump pressure and visualization during arthroscopic rotator cuff repair: an anonymized, randomized controlled trial

Thema A. Nicholson, MS[a], Jacob M. Kirsch, MD[b], Ryan Churchill, MD[c], Mark D. Lazarus, MD[a], Joseph A. Abboud, MD[a], Surena Namdari, MD, MSc[a,*]

[a]*Rothman Orthopaedic Institute at Thomas Jefferson University, Philadelphia, PA, USA*
[b]*Boston Sports and Shoulder Center at New England Baptist Hospital, Boston, MA, USA*
[c]*New England Orthopedic Specialists, Peabody, MA, USA*

Background: Tranexamic acid (TXA) has been used surgically to decrease blood loss. The ability of TXA to improve arthroscopic visualization and allow for reduction in pump pressure is unknown. The purpose of this study was to determine the effect of intravenous (IV) TXA on change in pump pressure and visualization during arthroscopic rotator cuff repair.

Methods: This was a single-center, prospective, randomized, double-anonymized controlled trial. Patients with full-thickness rotator cuff tears undergoing operative repair were enrolled. Patients were randomized to receive 1 g of IV TXA preoperatively or no TXA (control group). All patients underwent arthroscopy using saline irrigation fluid with 3 mL epinephrine injected into the first 1000-mL saline bag. Total operative time, final pump pressure, number of increases in pump pressure, total amount of irrigation fluid used, blood pressure and anesthesia medical interventions for blood pressure were recorded. Visualization was measured by a visual analog scale (VAS) completed by the surgeon at the end of the case. Postoperative VAS pain scores were obtained 24 hours after surgery. The primary aim of this study was to investigate the effect that IV TXA has on change in pump pressure (ΔP) during shoulder arthroscopy, with a ΔP of 15 mm Hg set as a threshold for clinical significance.

Results: There were 50 patients randomized to the TXA group and 50 patients in the no TXA group. No significant differences were found between the TXA group and the control group regarding any measure of pump pressure, including the final arthroscopic fluid pump pressure (44.5 ± 8.1 mm Hg vs. 42.0 ± 8.08 mm Hg, $P = .127$), the mean ΔP (20.9 ± 10.5 mm Hg vs. 21.8 ± 8.5 mm Hg, $P = .845$), or the number of times a change in pump pressure was required (1.7 ± 0.9 vs. 1.7 ± 0.8, $P = .915$). Overall arthroscopic visualization was not significantly different between the TXA group and the control group (7.2 ± 1.8 vs. 7.4 ± 1.6, $P = .464$). No significant difference existed between the TXA and control groups regarding postoperative pain scores assessed by VAS pain scale (4.1 ± 2.0 vs. 4.3 ± 1.9, $P = .519$) at 24 hours after surgery.

Conclusion: The use of IV TXA demonstrated no measurable improvement in surgeon ability to maintain a lower pump pressure during arthroscopic rotator cuff repair. Additionally, there was no measurable improvement in arthroscopic visualization or early pain scores.

Thomas Jefferson University Institutional Review Board approved this study (protocol no. 18D.610).

*Reprint requests: Surena Namdari, MD, MSc, Shoulder & Elbow Surgery, Rothman Orthopaedic Institute at Thomas Jefferson University, 925 Chestnut St 5th floor, Philadelphia, PA 19107, USA.
E-mail address: Surena.namdari@rothmanortho.com (S. Namdari).

https://doi.org/10.1016/j.jse.2022.06.027

Level of evidence: Level II; Randomized Controlled Trial; Treatment Study

Keywords: Tranexamic acid; rotator cuff repair; pump pressure; arthroscopy; visualization; shoulder

Arthroscopic visualization is contingent on several factors including arthroscopic pump pressure, hemostasis, and mean arterial pressure (MAP).[1,11,25] Increases to pump pressure can effectively decrease bleeding but come with a risk of greater soft tissue swelling. Decreasing MAP can also decrease bleeding, but risks cerebral hypoperfusion.[3,10,12,13,21,23] As a result, methods to reduce bleeding while maintaining appropriate pump pressure and MAP can have value. For example, several studies have found that the use of dilute epinephrine saline irrigation improves surgeon visualization,[2,7,16,22] decreases operative time, and reduces the total amount of irrigation fluid used.[22]

Tranexamic acid (TXA) is a synthetic lysine analog antifibrinolytic that competitively inhibits the conversion of plasminogen to plasmin, resulting in its antifibrinolytic activity.[5,6,15,17] It is commonly used to reduce blood loss in surgery and is an inexpensive medication that is now widely used in orthopedic surgeries.[12,17-19] One study has shown decreased intraoperative bleeding and improved visual clarity with use of intravenous (IV) TXA in arthroscopic rotator cuff surgery.[4,18] The aim of this study was to determine the effect of IV TXA on change in pump pressure (ΔP) and visualization during shoulder arthroscopy. We hypothesized that patients in the IV TXA group would have lower ΔP and better visualization scores.

Methods

This was a prospective, randomized, double-anonymized controlled trial, undertaken by 3 shoulder and elbow–trained subspecialty attending surgeons between June 2019 and November 2020.

Inclusion criteria included patients aged 18-80 years old with an American Society of Anesthesiologists (ASA) score between 1 and 3 and with a surgical indication of full-thickness small to massive rotator cuff tear. Exclusion criteria consisted of patients with an allergy to TXA, active thromboembolic disease, seizure disorder, prior cerebrovascular accident, cardiac stents or a history of thromboembolic disease, full-thickness subscapularis tear (>50%), or irreparable rotator cuff tears.

Enrolled patients were randomized into 2 groups via a random number generator. The control group underwent rotator cuff repair without TXA, and the intervention group was given 1000 mg of IV TXA in the preoperative holding area, approximately 30 minutes prior to induction of anesthesia. The operating surgeon remained anonymized to treatment. The anesthesia team was non-anonymized and administered TXA to the intervention group. All patients underwent a preoperative interscalene brachial plexus nerve block.

Both groups used the same intraoperative pump fluid. Normal saline with 3 mL epinephrine was injected into the first 1000-mL saline bag, and all subsequent saline irrigation was without epinephrine.

All cases were performed in the beach chair position. The arthroscopic fluid pump was initially set to 20 mm Hg and was increased at the discretion of the surgeon. Outcome variables including total operative time, final pump pressure, number of increases in pump pressure and reason for change in pump pressure, total amount of irrigation fluid utilized, MAP, blood pressure and anesthesia medical interventions for blood pressure were recorded. Anterior-posterior dimension of the tear (AP tear), medial-lateral dimension of the tear (ML tear), and presence or absence of subscapularis involvement was recorded. Additionally, satisfaction with visualization during the procedure was measured using a 10-point visualization scale, with 0 categorized as ''poor'' and 10 categorized as ''good.'' This was completed by the operative surgeon at the end of the case. Patient postoperative visual analog scale pain scores were obtained via telephone 24 hours after surgery.

Chi-square tests with their respected P values were conducted to test the independence between categorical variables. Fisher exact tests with their respected P values were conducted to test the independence between categorical variables with cell counts lower than 5. Categorical variables are presented as cell count (percentage of total count). Independent t tests were used to calculate P values for continuous parametric data presented by mean (standard deviation). Mann-Whitney test was used to calculate P values for continuous nonparametric data but is presented as mean (standard deviation). Significance was represented with a P value of $<.05$, indicating that the null was rejected and that a difference is very likely to exist. The primary aim of this study was to investigate the effect that IV TXA has on ΔP during shoulder arthroscopy, with a ΔP of 15 mm Hg set as a threshold for clinical significance. With the expectation of TXA to have a substantial effect, we wanted to be slightly conservative in the power/sample size estimate, so we used an effect size just less than medium in size. There were no prior studies in the literature that could be used as a guide for the number of patients to enroll and as such our power analysis provides numbers to detect small changes in the pump pressures. We originally aimed at enrolling 100 cases per group for a total of 200 cases (power of 0.8, with a beta of 0.2, and an effect size of 0.4). At interim analysis, a neutral effect was present and it became increasingly unlikely that a positive, clinically relevant effect would be demonstrated by the end of the trial. As a result, the study was terminated early.

Results

From June 2019 to November 2020, a total of 105 patients were consented for study participation. Five patients were

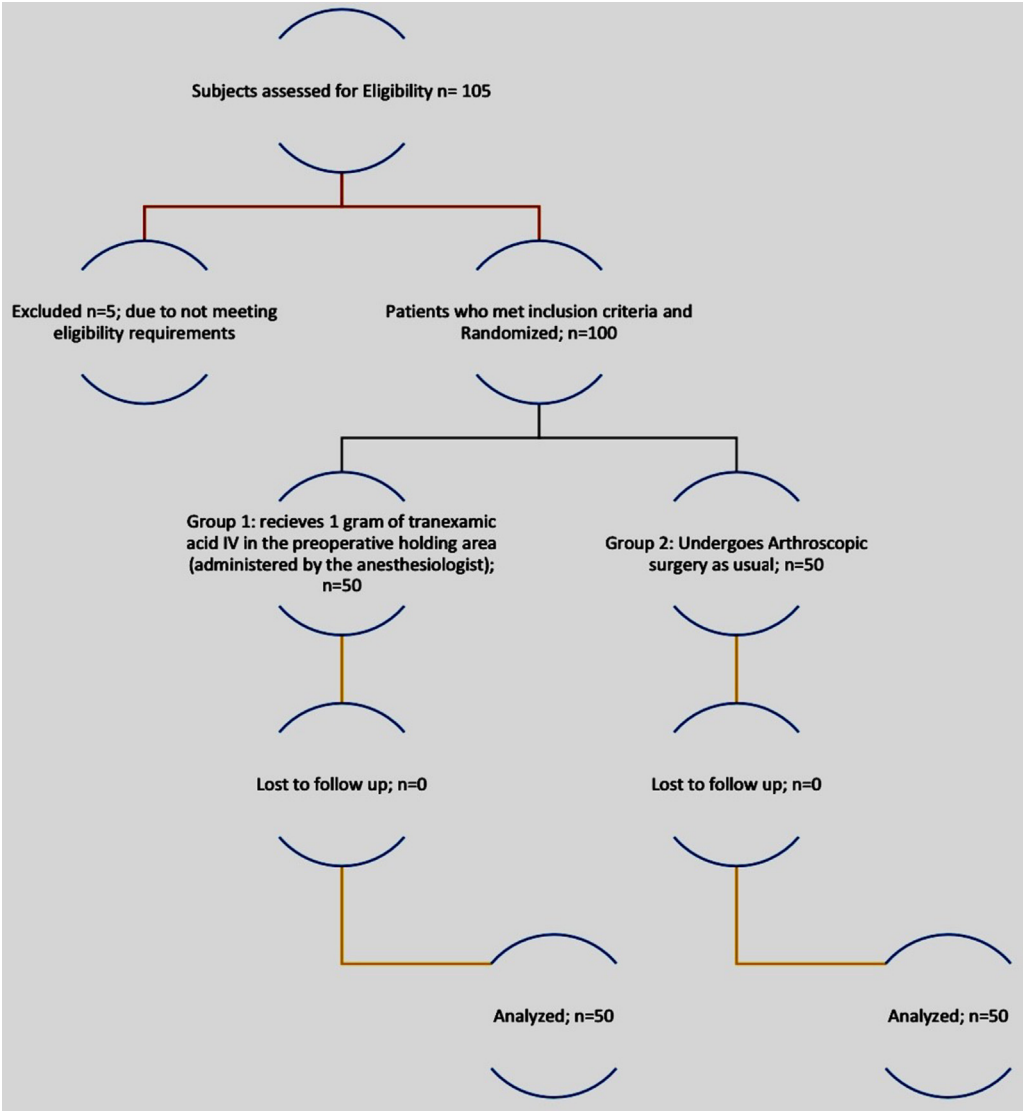

Figure 1 Flow diagram of enrolled patients.

excluded from participation for not meeting inclusion criteria [Fig. 1]. The final cohort consisted of 100 patients; 50 patients randomized to the control group (no TXA) and 50 patients in the TXA group. There was no significant difference between the 2 study groups with regard to age, gender, body mass index, or comorbidities (Table I). There was no difference between the TXA group and the control group with regard to AP tear (17 vs. 18 mm, $P = .591$), ML tear (17 vs. 21 mm, $P = .187$), or subscapularis involvement (10 vs. 14, $P = .482$) between groups.

There was no difference between the control group and the TXA group with regard to the ΔP (20.9 ± 10.5 mm Hg vs. 21.8 ± 8.50 mm Hg, $P = .845$) or the overall surgeon visualization (7.2 ± 1.8 vs. 7.4 ± 1.6, $P = .464$), respectively (Table II). There was also no significant difference between the TXA group and the control group in the ending pump pressure (44.5 ± 8.10 mm Hg vs. 42.0 ± 8.08 mm Hg, $P = .127$). There was no difference between the control group and the TXA group in other factors such as the number of times the pump pressure was adjusted during surgery (1.7 ± 0.9 vs. 1.7 ± 0.8, $P = .915$), total irrigation fluid used throughout the surgery (9577 ± 5166 vs. 10750 ± 6550, $P = .572$), and MAP (80.9 ± 10.0 mm Hg vs. 82.1 ± 9.58 mm Hg, $P = .549$). Pump pressure was increased to a maximum of 60 mm Hg in 4 cases in the TXA group and to a maximum of 60 mm Hg in 2 cases in the control group. In all cases, pump pressure was increased for insufflation reasons. In 34 (68%)

Table I Patient demographics

	Control group: No TXA (n = 50)		TXA group (n = 50)		*P* value
	n	Mean ± SD	n	Mean ± SD	
Age, yr		59.2 ± 7.2		59.7 ± 11.3	.428
Sex					
Male	29		39		
Female	21		11		
BMI		30.3 ± 4.9		29.2 ± 4.9	.292
ASA grade		1.2		1.2	

BMI, body mass index; *ASA*, American Society of Anesthesiologists; *TXA*, tranexamic acid; *SD*, standard deviation.

Table II Operative variables

Procedure: RCR	Control group: No TXA	TXA group	*P* value
Operative time, min	93.0 ± 12.1	75.6 ± 24.6	.966
Total irrigation fluid used, mL	10,750 ± 6550	9577 ± 5166	.572
Starting pump pressure	20.2 ± 1.41	23.6 ± 9.85	.027
Ending pump pressure	42.0 ± 8.08	44.5 ± 8.10	.127
Δ Pump pressure	21.8 ± 8.50	20.9 ± 10.5	.845
Number of times pump pressure was adjusted	1.74 ± 0.78	1.68 ± 0.89	.915
MAP, mm Hg	82.1 ± 9.58	80.9 ± 10.0	.549
Minimum MAP	66.7 ± 8.85	69.1 ± 9.40	.205
Maximum MAP	99.3 ± 13.7	99.9 ± 13.5	.824
Overall surgeon visual clarity rating (VAS)	7.42 ± 1.57	7.19 ± 1.84	.464

RCR, rotator cuff repair; *MAP*, mean arterial pressure; *VAS*, visual analog scale; *TXA*, tranexamic acid.
Values are mean ± standard deviation.

cases in the TXA group and 32 (64%) cases in the control group, pump pressure was increased for bleeding ($P = .833$).

There was no significant difference in total operative time between the TXA group and control group (75.6 ± 24.6 vs. 93.0 ± 12.1 minutes, $P = .966$). There was also no significant difference in patients' postoperative day 1 pain visual analog scale score between the TXA and control groups (4.1 ± 2.0 vs. 4.3 ± 1.9, $P = .519$). Blood pressure required adjustment in 12 of 50 (24%) of the TXA patients and 8 of 50 (16%) of the control group patients ($P = .439$). There was a weak positive correlation between tear size and operative time (AP tear, $r = 0.399$; ML tear, $r = 0.465$) but not between tear size and visualization score (AP tear, $r = 0.020$; ML tear, $r = -0.034$).

Discussion

In this randomized controlled trial, we sought to investigate the effect of TXA on change in pump pressure and arthroscopic visualization during rotator cuff repair surgery. Use of IV TXA demonstrated no measurable improvement in surgeon ability to maintain a lower pump pressure during arthroscopic rotator cuff repair. Additionally, there was no measurable improvement in arthroscopic visualization.

Increasing pump pressure during arthroscopic rotator cuff repair can improve insufflation of the joint and decrease bleeding.[8,9,14,24,26] We demonstrated no difference in ΔP, number of times the pump pressure was changed, end pump pressure, or total volume of fluid utilized. Liu et al[18] also performed a randomized controlled trial IV administration of TXA utilization before arthroscopic rotator cuff repair. They used the same TXA dosage and administration protocol as our study. Dissimilar to our study, cases were performed in the lateral decubitus position, did not use any epinephrine in the irrigation, and started the pump pressure at 60 mm Hg. They did not specifically evaluate the ΔP but noted no difference in the number of times the pump pressure was increased. Although using somewhat different irrigation and pump pressure protocols, neither study appears to

demonstrate an advantage to use of IV TXA for reducing pump pressure parameters.

With regard to visual clarity, we did not observe any difference between the control group and the TXA group. This is dissimilar to the findings of Liu et al,[18] who showed that visual clarity was significantly better in the TXA group. The authors used a 3-point numeric rating scale where grade 1 clarity showed active bleeding leading to poor visibility, grade 2 clarity showed a moderate amount of blood mixed with the irrigation fluid, and grade 3 clarity showed little or no bleeding. They reported a greater percentage of grade 3 vision clarity (53.7% ± 18.9% vs. 40.5% ± 22.1%, $P = .036$) in the TXA group and a better average visual clarity score in the TSA group (2.5 ± 0.2 vs. 2.3 ± 0.3, $P = .048$). These differences may be explained by the variability in the 2 studies with regard to use of epinephrine in the irrigation, the starting pump pressure, and/or the scale used to assess visibility. Additionally, the differences noted by Liu et al,[18] although statistically significant, are small and may lack clinical significance and be prone to data fragility given the small sample size and nearly nonsignificant P values.[20] The use of epinephrine in the first bag of irrigation may have masked the impact of TXA on bleeding; however, given the standard use of epinephrine at our institution, we did not eliminate it during the study period. Further study is necessary by multiple investigators in order to resolve the discrepancies seen between our study and that of Liu et al.[18] Our study is limited in that it was a single-institution study with 3 surgeons judging visual clarity and deciding on changes in pump pressure. We did not validate the visualization scale, and a better approach may have been to have surgeons review arthroscopic videos from their colleagues to determine interobserver and intraobserver reliability of the visualization scale. This limits the study's generalizability to other centers and underscores the benefit of multicenter investigation. Additionally, we did not determine whether the administration of IV TXA decreased postoperative opioid consumption. Our assessment of visual grading was both subjective and used a visual analog scale that has not been previously validated. Notably, the dosage of TXA was not adjusted based on body weight. Finally, based on an interim analysis of our data, we chose to stop the study without reaching the goal of 100 cases per group. This was decided because it became increasingly unlikely that a positive, clinically relevant effect would be demonstrated by the end of the trial. Because of this, negative statistical results may be a result of lack of power.

Conclusions

Intravenous administration of TXA prior to arthroscopic rotator cuff repair did not influence pump pressure parameters or improve arthroscopic visual clarity in this randomized controlled trial. Further study with a greater number of surgeons and institutions is needed to confirm these findings.

Disclaimers:

Funding: This study did not receive any support from grants, equipment, or other items.
Conflicts of interest: The authors, their immediate families, and any research foundations with which they are affiliated have not received any financial payments or other benefits from any commercial entity related to the subject of this article.

Acknowledgments

The authors thank Manan Patel, MD, Arjun Singh, and Christopher Hadley for their technical assistance.

References

1. Aleem AW, Brophy RH. Outcomes of rotator cuff surgery: what does the evidence tell us? Clin Sports Med 2021;31:665-74. https://doi.org/10.1016/j.csm.20212.07.004
2. Avery DM 3rd, Gibson BW, Carolan GF. Surgeon-rated visualization in shoulder arthroscopy: a randomized blinded controlled trial comparing irrigation fluid with and without epinephrine. Arthroscopy 2015;31:12-8. https://doi.org/10.1016/j.arthro.2014.08.010
3. Bahl V, Goyal A, Jain V, Joshi D, Chaudhary D. Effect of haemarthrosis on the rehabilitation of anterior cruciate ligament reconstruction–single bundle versus double bundle. J Orthop Surg Res 2013;8:5. https://doi.org/10.1186/1749-799X-8-5
4. Bayram E, Yildirim C, Erturk AK, Yilmaz M, Atlihan D. Comparison of the efficacy of irrigation with epinephrine or tranexamic acid on visual clarity during arthroscopic rotator cuff repair: a double blind randomized controlled study. Jt Dis Relat Surg 2021;32:115-21. https://doi.org/10.5606/ehc.2021.78393
5. Belk JW, McCarty EC, Houck DA, Dragoo JL, Savoie FH, Thon SG. Tranexamic acid use in knee and shoulder arthroscopy leads to improved outcomes and fewer hemarthrosis-related complications: a systematic review of level I and II studies. Arthroscopy 2021;37:1323-33. https://doi.org/10.1016/j.arthro.202011.051
6. Bolam SM, O'Regan-Brown A, Paul Monk A, Musson DS, Cornish J, Munro JT. Toxicity of tranexamic acid (TXA) to intra-articular tissue in orthopaedic surgery: a scoping review. Knee Surg Sports Traumatol Arthrosc 2021;29:1862-71. https://doi.org/10.1007/s00167-020-06219-7
7. Chierchini A, Frassanito L, Vergari A, Santoprete S, Chiarotti F, Saccomanno MF, et al. The effect of norepinephrine versus epinephrine in irrigation fluid on the incidence of hypotensive/bradycardic events during arthroscopic rotator cuff repair with interscalene block in the sitting opposition. Arthroscopy 2015;31:800-6. https://doi.org/10.1016/j.arthro.2015.02.030
8. Fígar A, Mc Loughlin S, Slullitel PA, Scordo W, Buttaro MA. Influence of single-dose intravenous tranexamic acid on total hip replacement: a study on transfusions, collateral complications, and readmissions. Orthopade 2017;46:359-65. https://doi.org/10.1007/s00132-016-3352-8

9. Fillingham YA, Darrith B, Calkins TE, Abdel MP, Malkani AL, Schwarzkopf R, et al., Hip Society Research Group. 2019 Mark Coventry Award: A multicentre randomized clinical trial of tranexamic acid in revision total knee arthroplasty: does the dosing regimen matter? Bone Joint J 2019;101-B(7_Supple_C):10-6. https://doi.org/10.1302/0301-620X.101B7.BJJ-2018-1451.R1
10. Gicquel-Schlemmer B, Beller JP, Mchalwat A, Gicquel P. Fatal Takotsubo cardiomyopathy due to epinephrine in shoulder arthroscopy. Orthop Traumatol Surg Res 2015;101:981-2. https://doi.org/10.1016/j.otsr.2015.09.026
11. Gillespie R, Shishani Y, Joseph S, Streit JJ, Gobezie R. Neer Award 2015: A randomized prospective evaluation on the effectiveness of tranexamic acid in reducing blood loss after total shoulder arthroplasty. J Shoulder Elbow Surg 2015;24:1679-84. https://doi.org/10.1016/j.jse.2015.07.029
12. Grzelecki D, Dudek P, Okoń T, Marczak D, Kordasiewicz B, Sibiński M, et al. Efficacy of intravenous tranexamic acid administration in revision hip arthroplasty. Orthopade 2021;50:464-70. https://doi.org/10.1007/s00132-020-03959-9
13. Gürpınar T, Polat B, Tekin SB, Esin Polat A, Çarkçı E, Öztürkmen Y. Comparison of early clinical results and re-tear rates of transosseous-equivalent rotator cuff repairs with or without medial knots. Eklem Hastalik Cerrahisi 2019;30:193-200. https://doi.org/10.5606/ehc.2019.70137
14. Hines JT, Hernandez NM, Amundson AW, Pagnano MW, Sierra RJ, Abdel MP. Intravenous tranexamic acid safely and effectively reduces transfusion rates in revision total hip arthroplasty. Bone Joint J 2019;101-B(6_Supple_B):104-9. https://doi.org/10.1302/0301-620X.101B6.BJJ-2018-1376.R1
15. Ishida K, Tsumura N, Kitagawa A, Hamamura S, Fukuda K, Dogaki Y, et al. Intra-articular injection of tranexamic acid reduces not only blood loss but also knee joint swelling after total knee arthroplasty. Int Orthop 2011;35:1639-45. https://doi.org/10.1007/s00264-010-1205-3
16. Jensen KH, Werther K, Stryger V, Schultz K, Falkenberg B. Arthroscopic shoulder surgery with epinephrine saline irrigation. Arthroscopy 2001;17:578-81.
17. Kirsch JM, Bedi A, Horner N, Waiter JM, Pauzenberger L, Koueiter DM, et al. Tranexamic acid in shoulder arthroplasty: a systematic review and meta-analysis. JBJS Rev 2017;5:e3. https://doi.org/10.2106/JBJS.RVW.17.00021
18. Liu YF, Hong CK, Hsu KL, Kuan FC, Chen Y, Yeh ML, et al. Intravenous administration of tranexamic acid significantly improved clarity of the visual field in arthroscopic shoulder surgery. A prospective, double blind and randomized controlled trial. Arthroscopy 2020;36:640-7. https://doi.org/10.1016/j.arthro.2019.10.020
19. Ng W, Jerath A, Wsowicz M. Tranexamic acid: a clinical review. Anaesthesiol Intensive Ther 2015;47:339-50. https://doi.org/10.5603/AIT.a2015.0011
20. Parisien RL, Dashe J, Cronin PK, Bhandari M, Tornetta P 3rd. Statistical significance in trauma research: too unstable to trust? J Orthop Trauma 2019;33:e466-70. https://doi.org/10.1097/BOT.0000000000001595
21. Speer DP. Early pathogenesis of hemophilic arthropathy. Evolution of the subchondral cyst. Clin Orthop Relat Res 1984;185:250-65.
22. Van Montfoort DO, Van Kampen PM, Huijsmans PE. Epinephrine diluted saline-irrigation fluid in arthroscopic shoulder surgery: a significant improvement of clarity of visual field and shortening of operation time. A randomized controlled trial. Arthroscopy 2016;32:436-44. https://doi.org/10.1016/j.arthro.2015.08.027
23. Weber SC, Abrams JS, Nottage WM. Complications associated with arthroscopic shoulder surgery. Arthroscopy 2002;18(2 Suppl 1):88-95. https://doi.org/10.1053/jars.2002.31801
24. Xie J, Hu Q, Huang Q, Ma J, Lei Y, Pei F. Comparison of intravenous versus topical tranexamic acid in primary total hip and knee arthroplasty: an updated meta-analysis. Thromb Res 2017;153:28-36. https://doi.org/10.1016/j.thromres.2017.03.009
25. Yoo JS, Ahn J, Karmarkar SS, Lamoutte EH, Singh K. The use of tranexamic acid in spine surgery. Ann Transl Med 2019;7(Suppl 5):S172. https://doi.org/10.21037/atm.2019.05.36
26. Zhang Y, Zhang L, Ma X, Jia Y, Wang H, Zhu Y, et al. What is the optimal approach for tranexamic acid application in patients with unilateral total hip arthroplasty? Orthopade 2016;45:616-21. https://doi.org/10.1007/s00132-016-3252-y