Tranexamic acid reduces blood loss in primary total hip arthroplasty performed using the direct anterior approach: a one-center retrospective observational study

Guo-Chun Zha1†, Xian-Ren Zhu2†, Lei Wang3† and Hong-Wei Li1

Abstract

Background: It is still unknown whether tranexamic acid (TXA) is beneficial for the minimally invasive surgical approach to total hip arthroplasty (THA). The aim of this study is to investigate the efficacy and safety of intravenous TXA in primary THA via the direct anterior approach (DAA).

Materials and methods: We performed a retrospective analysis of prospectively collected data on 70 patients with nontraumatic avascular necrosis of the femoral head who underwent THA via the DAA between October 2017 and October 2018. Patients were divided into two groups: TXA group (39 patients received 1.5 g TXA intravenously) and control group (31 patients did not receive TXA). Patients were assessed by operative time, postoperative hemoglobin (HB) drop, transfusion rate, postoperative length of hospital stays (LHS), deep vein thrombosis (DVT), and Harris hip score (HHS).

Results: Total blood loss, hidden blood loss, and postoperative HB drop in the TXA group were significantly lower than in the control group ($p < 0.05$). There was no statistical difference between the two groups in terms of intraoperative blood loss, operative time, transfusion rate, postoperative LHS, HHS, or incidence of DVT ($p > 0.05$).

Conclusions: TXA may reduce perioperative blood loss without increasing complications in THA via the DAA.

Level of evidence: Level IV, therapeutic study.

Keywords: Total hip arthroplasty, Tranexamic acid, Blood loss, Direct anterior approach

Introduction

Total hip arthroplasty (THA) has been widely used for the treatment of end-stage hip disease, which can effectively relieve pain, restore function, and improve quality of life [1]. It has been reported that the total blood loss during the perioperative period of THA can be as high as 2000 mL, with a transfusion rate as high as 37% [2–4]. Massive transfusion not only increases the risk of surgery, but also causes transmission of viral diseases, hemolytic reactions, immune reactions, and other transfusion-related risks [5, 6].

With the popularization of the minimally invasive concept and the continuous improvement of prosthesis materials and design, there are a variety of THA surgical approaches available clinically, such as direct anterior approach (DAA), anterolateral approach, posterior approach, posterolateral approach, SuperPATH approach (SuperPATH approach, namely supercapsular percutaneously assisted approach, which is a direct superior portal-assisted approach for THA that utilizes the interval...
between the gluteus minimus and the piriformis to access the hip capsule), and lateral approach. Among them, DAA is a minimally invasive surgical approach through a natural intermuscular and internervous interval. This approach has the advantages of minimizing soft tissue disruption and reducing the incidence of dislocation [7–9]. Tranexamic acid (TXA) is a synthetic derivative of the amino acid lysine, which can reduce fibrinolysis through the reversible blockade of lysine-binding sites on plasminogen molecules [10]. As a synthetic antifibrinolytic agent, TXA has been shown to be effective in reducing blood loss and transfusion rate in THA [11, 12]. However, few studies have explored the efficacy of TXA in minimizing perioperative blood loss in primary THA with DAA [13–15]—in other words, it remains unclear whether TXA is beneficial for the minimally invasive surgical approach to THA.

Therefore, this study aimed to investigate the efficacy and safety of intravenous TXA in THA via the DAA. We hypothesized that the use of TXA would be associated with less blood loss, without increasing the rates of complications, when compared with the control in primary THA performed using the DAA.

**Materials and methods**

**Patient source**

We performed a retrospective analysis of prospectively collected data on 80 patients (90 hips) with nontraumatic avascular necrosis of the femoral head who underwent total hip arthroplasty (THA) via the direct anterior approach (DAA) between October 2017 and October 2018. Patients were excluded if they had the following: (1) bilateral THA (10 patients); (2) incomplete radiographic or clinical data (0 patients); (3) follow-up time less than 3 months (0 patients). After applying the exclusion criteria, 70 patients (70 hips) qualified for the study.

Patients were divided into two groups: TXA group (39 patients received 1.5 g TXA intravenously) and control group (31 patients did not receive TXA). This study was approved by the ethics committee of Affiliated Hospital of Xuzhou Medical University (no. 20170829). All methods were performed in accordance with the relevant guidelines and regulations, and all patients gave informed consent.

**Study setting**

All surgeries were performed by the senior author (Z.G.C) using cementless THA via DAA. All patients received general anesthetic and the same design of the femoral stem (CLS stem; Zimmer, Warsaw, USA) and acetabular cup (Trilogy; Zimmer, Warsaw, USA). We did not use a wound drainage after the procedure. In the TXA group, TXA was given as a 1.5 g intravenous infusion 10 min prior to incision; the control group did not receive TXA.

All patients were managed with a similar perioperative regimen, including intravenous prophylactic antibiotics, prophylaxis against venous thrombosis, and postoperative pain control.

Patients were transfused if their postoperative hemoglobin level was below 70 g/L or if the patient had a hemoglobin above 70 g/L and below 100 g/L but poor mental status, palpitation, or pale complexion. All patients underwent deep vein ultrasound of the lower limbs 1 week postoperatively to detect thrombosis.

**Data collection**

Data were collected on patient characteristics including sex, age, body mass index (BMI), preoperative hemoglobin (HB), preoperative hematocrit (HCT), and American Society of Anesthesiologists (ASA) classification. HB and HCT levels were also measured at each timepoint on postoperative days 1 and 3. Operative time, transfusion rate, postoperative HB drop, postoperative length of hospital stays (LHS), and Harris hip score (HHS) were recorded. Total blood loss and pulmonary blood volume (PBV) were calculated according to the Gross and Nadler equation [16, 17]. The discharge criteria for patients with THA in our hospital are as follows: (1) stable vital signs, (2) good mental and physical status, (3) no nausea/vomiting, (4) pain control, and (5) no redness, swelling, or exudate from the incision.

\[
\text{PBV} = k_1 \times \text{height}^2 + k_2 \times \text{weight} + k_3, \quad k_1 = 0.3669, \quad k_2 = 0.03219, \quad k_3 = 0.6041
\]

for men; and

\[
\text{PBV} = k_1 \times \text{height}^2 + k_2 \times \text{weight} + k_3, \quad k_1 = 0.3561, \quad k_2 = 0.03308, \quad k_3 = 0.1833
\]

for women.

Total red blood cell volume loss = PBV × (Hct\text{pre} – Hct\text{post}), Hct\text{pre} = initial preoperative Hct level, Hct\text{post} = Hct of third postoperative day.

Total blood loss = 1000 × total red blood cell volume loss/(average of Hct\text{pre} and Hct\text{post}).

Postoperative HB drop = HB\text{pre} – HB\text{post}, HB\text{pre} = initial preoperative HB level, HB\text{post} = HB of third postoperative day.

Obvious blood loss = intraoperative blood loss + postoperative blood loss.

Hidden blood loss = total blood loss − obvious blood loss.

**Statistical methods**

All the statistical analyses were performed using IBM SPSS version 19.0 (IBM, USA). Means are presented as mean ± standard deviation (SD), Student’s t-test was used to analyze the normally distributed numerical variable; Pearson chi-squared test or Fisher’s exact test was
used to analyze the qualitative variable. The significance level used for all tests was $p < 0.05$.

**Results**

**Patient characteristics**

All patients were followed up for 3 months. Detailed distribution of patient demographics and characteristics is presented in Table 1.

**Operative variable**

Operative time, intraoperative blood loss, hidden blood loss, total blood loss, preoperative HB level, HB level of the first postoperative day, HB level of the third postoperative day, postoperative HB drop, and transfusion rate are presented in Table 2. The total blood loss, hidden blood loss, and postoperative HB drop in the TXA group were significantly lower than in the control group ($p < 0.05$). There was no statistical difference in terms of operative time, intraoperative blood loss, or transfusion rate between the two groups ($p > 0.05$).

**Clinical results and complications**

All patients completed the operation successfully. All patients did not receive blood transfusion on the day of surgery. In the TXA group, 2.6% (1/39) required blood transfusion with 2 units (400 mL) of red blood cell suspension (RBCs) on the third postoperative day, whereas in the control group, 12.9% (4/31) required blood transfusion with 8 units (1600 mL) of RBCs (2 units per patient) (Table 2). There was no statistical difference in

| Table 1 | Demographics of both groups |
|---------|-----------------------------|
| Variable| TXA group ($n = 39$) | Control group ($n = 31$) |
|         | $n$ (%) or mean ± SD (range) | $n$ (%) or mean ± SD (range) | 95% CI (lower to upper) | $p$-Value |
| Age (years) | 54.4 ± 13.6 (24–83) | 53.7 ± 15.4 (25–83) | 50.1–58.6 | 48.3–59.1 | 0.841† |
| Years | Sex (%) | | | | | | |
| Male | 26 (66.7) | 20 (64.5) | | | | | |
| Female | 13 (33.3) | 11 (35.5) | | | | | |
| BMI (kg/m²) | 22.3 ± 2.6 (17.8–25.5) | 22.2 ± 2.8 (17.9–28.5) | 21.5–23.1 | 21.2–23.2 | 0.878† |
| ASA grade (%) | 33:6 | 27:4 | 0.768†† |
| I | 33 (84.6) | 27 (87.1) | | | | | |
| II | 6 (15.4) | 4 (12.9) | | | | |
| HBpre* (g/L) | 134.2 ± 12.0 (114–159) | 134.8 ± 10.1 (113–155) | 130.4–138.0 | 131.2–138.4 | 0.825† |

| Table 2 | Clinical outcomes of both groups |
|---------|-----------------------------|
| Variable| TXA group ($n = 39$) | Control group ($n = 31$) |
|         | $n$ (%) or mean ± SD (range) | $n$ (%) or mean ± SD (range) | 95% CI (lower to upper) | $p$-Value |
| Operative time (min) | 57.4 ± 12.8 (43–109) | 60.4 ± 11.7 (42–89) | 53.4–61.4 | 56.3–64.5 | 0.315† |
| Intraoperative blood loss (mL) | 106.5 ± 36.1 (78–200) | 122.0 ± 32.6 (75–207) | 95.5–117.5 | 110.0–133.0 | 0.067† |
| Hidden blood loss (mL) | 630.5 ± 98.6 (409–807) | 893.4 ± 140.3 (644–1175) | 599.5–661.5 | 844.4–942.4 | <0.001† |
| Total blood loss (mL) | 736.9 ± 102.2 (567–927) | 1015.4 ± 152.4 (773–1285) | 704.9–768.9 | 961.4–1069.4 | <0.001† |
| HBpost‑1* (g/L) | 108.9 ± 14.9 (65–140) | 99.2 ± 13.8 (80–132) | 104.2–113.6 | 94.3–104.1 | 0.007† |
| HBpost‑3* (g/L) | 87.4 ± 16.3 (63–128) | 79.8 ± 10.9 (56–110) | 82.3–92.5 | 76.0–83.6 | 0.029† |
| Postoperative HB drop (g/L) | 46.8 ± 10.8 (22–80) | 55.0 ± 13.7 (31–79) | 43.4–50.2 | 50.2–59.8 | 0.007† |
| Transfusion rate (%) | 2.6% (1/39) | 12.9% (4/31) | 0.279†† |
| Transfusion rate (%) | 4.3% (2/39) | 3.2% (1/31) | 0.279†† |
| Harris hip score (point) | 91.8 ± 4.9 (80–100) | 91.1 ± 6.1 (83–100) | 90.3–93.3 | 89.0–93.2 | 0.596† |

---

* $\text{HB}_{\text{pre}}$ = initial preoperative HB level
† Student’s t-test was used
†† Chi-squared test was used
terms of postoperative LHS, HHS, or incidence of DVT between the two groups ($p > 0.05$) (Table 2).

Two patients (one patient per group) developed intraoperative fractures of the calcar during seating of the stem, and the fractures were treated by cerclage wire fixation. Subsidence of the stem during loading was not observed after 3 months of follow-up. Two patients (one in each group) had asymptomatic DVT and did not receive any special treatment. No incisional infection occurred in either group. No patient died during the study period.

Discussion

There is growing evidence that TXA is effective in reducing blood loss and transfusion rates in the perioperative period of THA. Most studies have been performed using the posterolateral approach [12, 18] or the lateral approach [19] or the posterior approach [20, 21]. Although some studies [13, 14, 22–24] have reported the efficacy of TXA in DAA, few studies have compared the efficacy and safety of DAA-THA with and without TXA [13, 14]. This study aimed to explore whether TXA reduced perioperative blood loss and the rate of blood transfusion in patients undergoing THA via the DAA.

In the present study, 1.5 g of TXA was infused intravenously, and it was effective in reducing total blood loss, hidden blood loss, and the degree of Hb drop, but had no significant effect on intraoperative blood loss or transfusion rate during the perioperative period in DAA-THA. Fraval et al. [13] performed a single-center randomized, double-blind trial of 101 patients undergoing THA via DAA, 50 of whom received TXA during the perioperative period. The results found that TXA significantly reduced the blood loss (both intraoperative and calculated blood loss), but there was no statistical significance in transfusion rate between the two groups. Our results are consistent with those of Fraval et al. [13], except for the intraoperative blood loss. We speculate that the reason for this is that the patients in our study were younger and had a lower BMI and shorter operative time than those in the study by Fraval et al. [13], because these factors would theoretically reduce intraoperative blood loss (our patients: 106 mL; Fraval’s patients: 460 mL). In addition, our findings are identical to those of Free et al. [14], who found a postoperative transfusion rate of 1.2% for THA with DAA, which was significantly lower than the 11.1% transfusion rate in the control group. We speculate that the reason for this is that (1) our patients were younger and have better tolerance to blood loss, so there is no difference in blood transfusion rates between the two groups (TXA group versus control group), while Free’s patients were older and may have poor tolerance to blood loss, so the blood transfusion rates between the two groups (DAA without TXA versus DAA TXA) were different; (2) the sample size of these patients in our study was smaller than that of the patients in the study by Free et al. [14]. Whether TXA can reduce the transfusion rate for THA via DAA requires a larger sample size and more prospective studies to determine.

Few studies [13, 14] have found that the use of TXA during the perioperative period can reduce the LHS in THA. However, our study found that the use of TXA during the perioperative period of THA via DAA did not shorten the postoperative LHS. We speculate that this is because DAA is a minimally invasive procedure that shortens the LHS. Whether TXA shortens LHS for THA via DAA requires a larger sample size and more prospective studies to determine.

Many studies [12, 25, 26] have reported that the use of TXA did not increase the incidence of DVT in patients undergoing THA. However, Nishihara et al. [27] conducted a study to observe whether TXA increased the risk of DVT in lower limbs without routine chemical thromboprophylaxis, and found that the use of TXA increased the incidence of distal DVTs in the muscular veins. Our study found one case of DVT in the TXA group, and one case in the control group, with no statistically significant difference ($p = 1.000$).

There are several limitations to this study. The incidence of DVT in the lower extremities was assessed only in the short term. Our sample size was small, and the results may have been biased. A larger randomized prospective trial is required to further improve the relevant experiments to determine the efficacy and safety of TXA in the perioperative period of THA via DAA.

Conclusion

Single intravenous administration of 1.5 g of TXA 10 min prior to incision may effectively reduce the perioperative blood loss in primary THA through DAA, without increasing the incidence of DVT in lower extremities.

Abbreviations

TXA: Tranexamic acid; THA: Total hip arthroplasty; DAA: Direct anterior approach; HB: Hemoglobin; DVT: Deep vein thrombosis; LHS: Length of hospital stays; HHS: Harris hip score; BMI: Body mass index; HCT: Hematocrit; ASA: American Society of Anesthesiologists; PBV: Pulmonary blood volume.

Acknowledgements

The authors thank Shuo Feng and Zhi Yang from the Department of Orthopedic Surgery, Affiliated Hospital of Xuzhou Medical University for the Working Environment for valuable technical assistance and support.

Authors’ contributions

G.C.Z. designed the study, performed the surgery, acquired, analyzed, and interpreted the data, and drafted and revised the manuscript. X.R.Z. acquired, analyzed, and interpreted the data, and drafted and revised the manuscript. T.W., L.W., and H.W.L. analyzed and interpreted the data, and revised the manuscript. All authors read and approved the final manuscript.
**Funding**
This work was supported by the Jiangsu Provincial Medical Youth Talent (QNRC201800), the Foundation of Jiangsu Province commission of Health and Family Planning (H(2017)081), and the Special Scientific Research Fund for Introducing Talents in Yijishan Hospital.

**Availability of data and materials**
The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

**Declarations**

**Ethics approval and consent to participate**
This study has been approved by the ethics committee of the Affiliated Hospital of Xuzhou Medical University (no. 20170829).

**Competing interests**
No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article. The funding was used in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

**Author details**
1. Department of Orthopedic Surgery, The Affiliated Hospital of Xuzhou Medical University, No. 99 Huaihai West Road, Xuzhou 221002, Jiangsu, People’s Republic of China.
2. Department of Orthopedic Surgery, Mudan People’s Hospital of Heze City, No. 2111 Kangzhuang Road, Mudan District, Heze 274000, Shandong, People’s Republic of China.
3. Department of Orthopedics, The First Affiliated Hospital of Wannan Medical College, Wuhu 241001, Anhui, People’s Republic of China.

**Received:** 4 January 2022  **Accepted:** 27 February 2022  **Published online:** 07 March 2022

**References**
1. O’boyle CA, Mcgee H, Hickey A, O’malley K, Joyce CR (1992) Individual quality of life in patients undergoing hip replacement. Lancet 339(8801):1088–1091
2. Bierbaum BE, Callaghan JJ, Galante JO, Rubash HE, Tooms RE, Welch RB (1999) An analysis of blood management in patients having a total hip or knee arthroplasty. J Bone Joint Surg Am 81(12):2–10
3. Rosencher N, Kerkkamp HE, Macheras G, Munuera LM, Menichella G, Barton DM et al. (2003) Orthopedic Surgery Transfusion Hemoglobin European Overview (OSTHEO) study: blood management in elective knee and hip arthroplasty in Europe. Transfusion 43(4):459–469
4. Young SW, Marsh DJ, Akhavan MA, Walker CG, Skinner JA (2008) Attitudes to blood transfusion post arthroplasty surgery in the United Kingdom: a national survey. Int Orthop 32(3):325–329
5. Busch MP, Kleinman SH, Nemo GJ (2003) Current and emerging infectious risks of blood transfusions. JAMA 289(8):959–962
6. Vanvkaes EC, Blachman MA (2009) Transfusion-related mortality: the ongoing risks of allogeneic blood transfusion and the available strategies for their prevention. Blood 113(15):3406–3417
7. Kennon RE, Keggi JM, Wetmore RS, Zatorski LE, Hua MH, Keggi KJ (2003) Total hip arthroplasty through a minimally invasive anterior surgical approach. J Bone Joint Surg Am 85(Suppl 4):39–48
8. Berger RA, Jacobs JJ, Meneghini RM, Delta Valle C, Paprosky W, Rosenberg AG (2004) Rapid rehabilitation and recovery with minimally invasive total hip arthroplasty. Clin Orthop Relat Res 429:239–247
9. Bremer AK, Kalberer F, Pfirrmann CW, Dora C (2011) Soft-tissue changes in hip abductor muscles and tendons after total hip replacement: comparison between the direct anterior and the transgluteal approaches. J Bone Joint Surg Br 93(7):866–889
10. Dunn CJ, Goa KL (1999) Tranexamic acid: a review of its use in surgery and other indications. Drugs 57(6):1005–1032
11. Othman Y, Melebeck F, Daubresse F (2020) Tranexamic acid in joint replacement: a randomized trial comparing intravenous oral and topical routes. Acta Orthop Belg 86(3):397–404
12. Yi Z, Bin S, Jing Y, Zongke Z, Pengde K, Fuxing P (2016) Tranexamic acid administration in primary total hip arthroplasty: a randomized controlled trial of intravenous combined with topical versus single-dose intravenous administration. J Bone Joint Surg Am 98(12):983–991
13. Fraval A, Effeney P, Fiddelaers L, Smith B, Towell B, Tran P (2017) OBTAIN: A outcome benefits of tranexamic acid in hip arthroplasty a randomized double-blind controlled trial. J Arthroplasty 32(5):1516–1519
14. Free MD, Owen DH, Pascoe E, Allen P, Yang L, Harvie P (2019) Transfusion rates with intravenous tranexamic acid in total hip arthroplasty performed using the direct anterior approach. Hip Int 29(5):511–515
15. Zhao H, Xiang M, Xia Y, Shi X, Pei FX, Kang P (2018) Efficacy of oral tranexamic acid on blood loss in primary total hip arthroplasty using a direct anterior approach: a prospective randomized controlled trial. Int Orthop 42(11):2535–2542
16. Nadler SB, Hidalgo JH, Bloch T (1962) Prediction of blood volume in normal human adults. Surgery 51(2):224–232
17. Gross JB (1963) Estimating allowable blood loss: corrected for dilution. Anesthesiology 28(3):277–280
18. Yamasaki S, Masuhara K, Fuji T (2004) Tranexamic acid reduces blood loss after cementless total hip arthroplasty—prospective randomized study in 40 cases. Int Orthop 28(2):69–73
19. Benoni G, Fredin H, Knebel R, Nilsson P (2001) Blood conservation with tranexamic acid in total hip arthroplasty: a randomized, double-blind study in 40 primary operations. Acta Orthop Scand 72(5):442–448
20. Kayevo Y, Fillingham YA, Okrok P, Plummer DR, Moric M, Gerlinger TL et al. (2017) Oral and intravenous tranexamic acid are equivalent at reducing blood loss following total hip arthroplasty: a randomized controlled trial. J Bone Joint Surg Am 99(5):373–378
21. Lee QJ, Chang WY, Wong YC (2017) Blood-sparing efficacy of oral tranexamic acid in primary total hip arthroplasty. J Arthroplasty 32(11):139–142
22. Vles GF et al. (2021) Hidden blood loss in direct anterior total hip arthroplasty: a prospective, double blind, randomized controlled trial on topical versus intravenous tranexamic acid. Musculoskelelet Surg 105(3):267–273
23. Jungwirth-Weinberger A, Do HT, Krell EC, Valle AGD, Chalmers BP, Boetnner F (2021) Blood management in direct anterior versus posterior primary total hip arthroplasty using tranexamic acid: a matched cohort study. Arch Orthop Trauma Surg. https://doi.org/10.1007/s00402-021-03965-2 (Epub ahead of print)
24. Komons GA, Manrique J, Foltz C, Klement MR, Restrepo C, Parvizi J (2021) Transfusion rates in total hip arthroplasty are lower in patients with direct anterior approach. Arch Bone Jt Surg 9(6):659–664
25. Alshtyda S, Mason J, Sarda P, Nargol A, Cooke N, Ahmad H et al. (2013) Topical (intrarticular) tranexamic acid reduces blood loss and transfusion rates following total hip replacement: a randomized controlled trial (TRANX-H). J Bone Joint Surg Am 95(21):1969–1974
26. El Beheiry H, Lubbederk A, Clements N, Dhillon K, Sharma V (2018) Tranexamic acid administration to older patients undergoing primary total hip arthroplasty conserves hemoglobin and reduces blood loss. Can J Surg 61(3):177–184
27. Nishihara S, Hamada M (2015) Does tranexamic acid alter the risk of thromboembolism after total hip arthroplasty in the absence of routine chemical thromboprophylaxis? Bone Joint J 97-b(4):458–462

**Publisher’s Note**
Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.