Has Tranexamic Acid in Total Knee Arthroplasty Made Tourniquet Use Obsolete?

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Abstract The application of tranexamic acid (TXA) in total joint arthroplasty has dramatically improved peri-operative blood management. In light of these benefits, a study by Huang et al., “Intravenous and Topical Tranexamic Acid Alone Are Superior to Tourniquet Use for Primary Total Knee Arthroplasty,” evaluates the need for continued use of the intra-operative tourniquet, which remains a routine practice with documented benefits and adverse effects. This review evaluates the study’s design and critically interprets its findings for clinical practice. Through a prospective, randomized trial, Huang et al. demonstrated that among selected patients undergoing primary total knee arthroplasty, the use of a tourniquet results in no reduction in blood loss beyond that provided by TXA alone. Moreover, the use of TXA without a tourniquet led to improved early clinical outcomes such as reduced post-operative swelling, improved knee range of motion at discharge, and enhanced patient satisfaction. As medicine is practiced in an increasingly value-driven environment, this study provides a useful method for evaluating the utility of commonly used interventions. Its findings highlight the need for future investigations into the optimal administration of TXA in total knee arthroplasty.

Keywords blood loss · tourniquet · tranexamic acid · primary total knee arthroplasty

Introduction

By 2021, it is projected that more than 1.3 million primary total knee replacements will be performed annually in the USA [7]. Total knee arthroplasty (TKA) is highly effective in ameliorating pain, preserving function, and improving quality of life for patients with severe knee arthritis [3]. Despite its increasing prevalence, the procedure is associated with potential risks and complications, including infection, implant failure, venous thromboembolism, and acute blood loss [12].

Multiple blood management strategies have been developed to reduce peri-operative blood loss and the subsequent need for blood transfusion. Intra-operative tourniquet use has long been employed for this purpose, as well as for improving surgical exposure and optimizing cement fixation. The adverse effects of tourniquet use include increased post-operative limb swelling, superficial wound complications, and increased early post-operative pain [17, 19]. More recently, peri-operative administration of tranexamic acid (TXA) has gained in popularity as a pharmacologic adjuvant to reduce blood loss in various surgical procedures, including total joint arthroplasty [1, 4, 13, 15]. TXA inhibits the formation of plasmin from its precursor molecule, thereby inhibiting fibrinolysis and stabilizing blood clots [6]. With multiple modes of administration, including intravenous, oral, and intra-articular, TXA has revolutionized peri-operative blood management and may be partly responsible for a trend toward decreased blood transfusions in TKA [10].

The article reviewed here was published in the *Journal of Bone and Joint Surgery* by Huang et al. It re-examines the utility of tourniquets in the TXA era of primary TKA. The authors apply results from a prospective, randomized trial to argue that the use of TXA without a tourniquet provides equivalent, if not improved, outcomes for patients undergoing primary TKA compared to both TXA and a tourniquet. The current review aims to (1) evaluate the study’s design, results, and author interpretations and (2) consider the impact of these findings on present and future clinical practice.

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The Article

Intravenous and Topical Tranexamic Acid Alone Are Superior to Tourniquet Use for Primary Total Knee Arthroplasty: A Prospective, Randomized Controlled Trial

Huang Z, Xie X, Li L, Huang Q, Ma J, Shen B, Kraus VB, Pei F. *J Bone Joint Surg Am.* 2017;99(24):2053–2061.

Huang et al. asked the following research question: in primary TKA, does tourniquet use provide clinical benefit beyond that seen with TXA alone? To address this question, the authors conducted a prospective, randomized controlled trial that divided 150 patients undergoing primary TKA into three equal groups. In the first arm, patients received both TXA and a thigh tourniquet for the duration of the procedure. In the second arm, patients received TXA only. In the third arm, patients received a tourniquet only. TXA was delivered peri-operatively via a series of five, weight-adjusted intravenous doses, with a dose of topical TXA administered after component implantation. Participants were recruited over a 6-month period and shared similar baseline characteristics including age, body mass index, pre-operative hemoglobin and hematocrit levels, range of motion measurements, and pain scores.

Duration of surgery was similar among patients receiving both TXA and tourniquet and those receiving TXA only (51.8 ± 4.6 min vs. 52.2 ± 6.2 min, $p = 0.332$). No significant differences were identified in total blood loss (734.5 ± 274.2 mL vs. 627.7 ± 198.1 mL, $p = 0.086$) or intra-operative blood loss (144.8 ± 80.1 mL vs. 150.6 ± 86.0 mL, $p = 0.698$). Patients in the TXA-only group had less knee pain through post-operative day 5, less swelling through post-operative day 3, and higher satisfaction scores at discharge. All three advantages abated when measured at subsequent time points.

Commentary

With approximately one million primary TKAs performed annually in the USA [7], Huang et al. investigated a clinically relevant question, with findings that can readily be implemented into practice. The distinct benefits demonstrated in patient cohorts receiving TXA adds to a growing literature supporting its clinical impact in diverse surgical settings [1, 4].

Several strengths in study design substantiate the validity of the reported findings. By conducting a prospective, randomized trial, the authors controlled for a number of potential confounding variables, as evidenced by similar baseline characteristics across patient cohorts such as age, body mass index, pre-operative knee range of motion, and pain scores. Cohort size was determined a priori to ensure appropriate power to detect meaningful differences in peri-operative blood loss. This is especially important as the primary study outcome demonstrated non-inferiority of the TXA-only group. By ensuring the study was adequately powered, the authors reduced the risk of type II error or of failing to identify a significant difference between groups when one exists [14].

Huang et al. documented a rigorous study protocol that ensured patients from all cohorts received nearly identical pre- and post-operative care. Moreover, by restricting recruitment to a 6-month period, the authors reduced the risk that developments in hospital practices, implant technologies, or surgical techniques would be confounding variables. A similar study carried out over a 5- or 10-year period could be subject to such bias.

The study has several limitations. First, it excluded revision procedures, bilateral procedures, and patients with flexion deformity of 30° or more or varus-valgus deformity of 30° or more. Restricting patients with these conditions improves homogeneity of study groups but also limits the generalizability of results. Second, the calculation of blood loss is inherently challenging. To calculate total blood loss, the authors relied on the modified Gross formula [8], which is based on a fractional change in hematocrit. Blood loss calculations that rely on hematocrit levels presume that a patient's volume status is similar at both times measured. This is frequently not the case in the immediate post-operative period, when many patients have received either too much or too little intravenous fluids [16]. Moreover, among the many formulae created to calculate blood loss, there is no consensus of a gold standard. In analyzing results from a randomized trial comparing blood loss between two cohorts of patients, Lopez-Picado et al. demonstrated that calculated total blood loss varied according to the formula used and that the methods produced a low level of agreement [9]. Together, these factors highlight sources of potential inaccuracy in peri-operative blood loss calculations.

Despite efforts to reduce bias, the potential for such bias remains. Surgeons were blinded to participants' randomized treatment arm until the morning of the study; however, it is not specified whether these surgeons also were responsible for measuring post-operative outcomes such as range of motion, wound drainage, and thigh circumference. If so, these metrics were collected after the surgeons had been informed of the patient's study arm. In addition, the study reports no venous thromboembolism across all cohorts after Doppler ultrasound evaluation at four post-operative assessments. As the authors mention, however, the study groups are underpowered to evaluate differences in this and other treatment complications.

As effectively as the study demonstrates non-inferiority of a TXA-only protocol in reducing peri-operative blood loss, there is less evidence that the use of a tourniquet leads to clinically meaningful worse outcomes. Whereas the authors suggest tourniquet use may be "ill-advised," their data demonstrate equivalent outcomes between a "TXA plus tourniquet" approach and a "TXA-only" approach for length of stay, Hospital for Special Surgery (HSS) score at 6 months' follow-up, and patient satisfaction at 1-month follow-up. Furthermore, the advantages of early knee range of motion among TXA-only participants have been found to be below a clinically meaningful threshold [2]. In addition, the authors mention another limitation that they did not seek to evaluate implant stability, prosthetic fixation, or survival outcomes between groups. While prior evidence suggests that the use of a tourniquet did not affect cemented

component migration at 2-year follow-up [11], Huang et al. do not address this important concern about discarding the tourniquet. Huang et al. have contributed compelling new evidence to the long-debated use of a tourniquet. With increasing use of TXA, further studies are needed to definitively refine the utility and indications for tourniquet use.

Although not the study's primary focus, the findings demonstrate significant clinical benefits of TXA. The patients receiving a tourniquet only had significantly increased perioperative and total blood loss, as well as inferior short-term clinical outcomes. Benefits of TXA administration were demonstrated despite the lack of an evidence-based protocol for its optimal timing and mode of administration. Recent studies have attempted to evaluate these various strategies. In a 2018 prospective, randomized trial, George et al. reported that patients receiving topical TXA had similar changes in hemoglobin as those receiving intravenous TXA [5]. Wang et al.'s meta-analysis demonstrated that combined intra-articular and intravenous TXA was associated with less blood loss and fewer blood transfusions than intravenous TXA alone [18]. Further study is necessary to elucidate these details and maximize clinical outcomes with its use.

In conclusion, Huang et al. offer meaningful findings on the clinical benefit of TXA and encourage readers to reconsider the use of a tourniquet in patients undergoing uncomplicated primary TKA.

Compliance with Ethical Standards

Conflict of Interest: Christopher M. Brusalis, MD, and Shawn S. Richardson, MD, declare that they have no conflicts of interest. Mathias P.G. Bostrom, MD, reports being a paid consultant for Smith and Nephew, outside the submitted work.

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