

**Yang Z-G, Chen W-P, Wu L-D. Effectiveness and Safety of Tranexamic Acid in Reducing Blood Loss in Total Knee Arthroplasty: A Meta-Analysis. JBJS Am 2012;94:1153-9.**

Design: Meta-analysis of randomized clinical trials

Purpose of study : To estimate the effectiveness of tranexamic acid (TXA) in the setting of total knee arthroplasty (TKA) for the prevention of blood loss

PICOS:

- Patient population: adults undergoing TKA in which a pneumatic tourniquet was used intraoperatively
- Intervention: TXA
- Comparison intervention: placebo
- Outcomes: intraoperative blood loss, postoperative blood loss, number of transfusion units used, postoperative prothrombin time (PT) or partial thromboplastin time (PTT), number of patients with pulmonary embolus (PE) or deep vein thrombosis (DVT)
- Study types: randomized clinical trials only

Study selection:

- Databases were PubMed, MEDLINE, and EMBASE, as well as bibliographies of selected studies through May 2011
- Two authors independently selected articles for inclusion and rated the study quality using the Jadad Scale
  - o Jadad scale awards 2 points for adequate randomization, 2 points for blinding of investigators and patients, and 1 point for accounting for patients at the end of the study, including description of dropouts
- Outcomes such as blood loss and number of transfusion units were analyzed in terms of means and standard deviations, while PE, DVT, and need for transfusion were analyzed in terms of odds ratios

Results:

- 15 randomized trials with 837 patients of TXA for TKA were retrieved, including 608 women and 229 men, with mean ages ranging from 62 to 78 years
- NSAIDs were discontinued 2 weeks before surgery in one study, 1 week before surgery in 6 studies, 24 hours before surgery in 2 studies, and 12 hours before surgery in 1 study, with 5 studies not reporting this variable
- 14 studies administered low dose TXA (10 to 50 mg/kg), and 1 involved a high dose of 150 mg/kg

- In 7 studies, the mean duration of surgery was less than 100 minutes; 4 studies had a duration of surgery greater than 100 minutes, and 4 studies did not report duration of surgery
- Amount of blood loss was available in 14 studies, and was measured in various ways, either by the intraoperative blood loss (suction volume plus blood lost in sponges), postoperatively (from drain reservoirs in the first few postop days), or on the basis of losses of hemoglobin between preop and postop measurements
  - o In none of the 14 studies did TXA have greater blood loss than placebo
  - o The pooled difference in blood loss from the 14 studies was 504.9 ml (95% confidence interval from 388.9 to 620.9)
- The number of blood transfusions per patient was available in 6 studies, and the number of transfusions for TXA was 1.43 units fewer than for placebo (95% CI from 1.17 to 1.69 units)
- The odds ratio of needing a transfusion was estimated from 14 studies, and the odds of having a transfusion was lower with TXA than with placebo OR was 0.16 with 95% CI from 0.10 to 0.25
- The rate of DVT was available in 13 studies; the TXA rate was 10 of 361 patients and the rate for placebo was 13 of 361 patients; this was a non-significant difference in favor of TXA, meaning that the risk of DVT was substantially the same
- PE was reported in 6 studies, occurring in 2 of 174 TXA patients and in 4 of 175 placebo patients, a non-significant difference between groups
- TXA and placebo did not differ with respect to changes in PT (4 studies) or PTT (5 studies)

Authors' conclusions:

- TXA in the setting of TKA is safe and effective for reduction of blood loss, number of transfusion units, and the risk of needing a transfusion
- TXA does not increase the risk of PE or DVT and does not change PT or PTT compared to placebo
- The IV administration of 10 to 20 mg/kg of TXA 30 minutes before deflating the tourniquet, followed by additional administration in the 24 to 72 hours after surgery, appears to be a safe and effective method, but intra-articular injection once postoperatively is also feasible

Comments:

- The authors furnish a data supplement giving their Jadad scores for the included study, but this table supplies no details about the timing, dose, or route of administration of TKA
- The Jadad scale is somewhat dated, and does not include allocation concealment as a quality criterion

- The odds ratio in Figure 3 for the risk of having a transfusion probably inflates the effect size of TXA, since the outcome of having a transfusion was fairly common in the studies, and this tends to inflate the odds ratio as an estimate of the risk ratio
  - o The odds ratio (0.16, 95% CI 0.10 to 0.25) in Figure 3 is 0.43 (95% CI 0.35 to 0.53) when calculated as a risk ratio
  - o Also, the heterogeneity of the studies as estimated by  $I^2$  is greater when the data are pooled as a risk ratio, rising from 3% for an odds ratio to 57% as a risk ratio
- There was great heterogeneity of amount of blood loss in Figure 1; the value of  $I^2$  was 93%
  - o Even though all studies showed less blood loss with TXA than with placebo, the amount of that difference ranged from 66 ml to 820 ml
  - o Without more detailed information on the characteristics of the patients and the administration of TXA, this heterogeneity remains unexplained
- Even though some details of TXA administration remain to be filled in, the included studies are unbiased enough and the consistency of the results is great enough to warrant strong evidence that TXA reduces blood loss in the setting of TKA

Assessment: Adequate meta-analysis with strong evidence that tranexamic acid in the setting of total knee arthroplasty reduces blood loss, reduces the risk of transfusion, and reduces the number of units transfused, without increasing the risk of pulmonary embolus or deep vein thrombosis