**ABSTRACT**

**Purpose.** To compare the outcome after simultaneous bilateral total knee arthroplasty (TKA) with or without an intra-articular tranexamic acid (TXA) wash in terms of blood loss, haemoglobin change, and transfusion requirement.

**Methods.** 35 women and 10 men (mean age, 67.5 years) who underwent primary simultaneous bilateral TKA by a single senior surgeon were compared with 45 matched controls. In the TXA group, 1500 mg of TXA diluted in 100 ml of 0.9% sodium chloride was administered as a wash after cementing of implant and before closure of the retinaculum. At least 5 minutes of contact time was allowed before wound closure and tourniquet deflation. No drain was used.

**Results.** No patients had thromboembolic complication. Compared with controls, the TXA group had lower perioperative blood loss (920 vs. 657 ml, p=0.001), total blood loss (997 vs. 679 ml, p<0.001), blood transfusion rate (60% vs. 37.8%, p=0.035), percentage of patients requiring more than one blood unit (24.4% vs. 8.9%, p=0.048), and length of hospitalisation (6 vs. 4 days, p<0.001). Nonetheless, the 2 groups were comparable in blood units and volume transfused.

**Conclusion.** An intra-articular TXA wash during simultaneous bilateral TXA reduced total blood loss and resulted in a difference of 22.2% in blood transfusion rate and a 2-day reduction in the length of hospital stay.

**Key words:** arthroplasty, replacement, knee; blood loss, surgical; blood transfusion; tranexamic acid

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**INTRODUCTION**

Among patients undergoing simultaneous bilateral total knee arthroplasty (TKA), 29.8% to 95.1% require allogeneic blood transfusion.¹⁻³ This may cause complications such as viral infection, haemolytic transfusion reaction, and transfusion-associated sepsis,⁴ as well as infectious complications secondary to cell-mediated immune suppression.⁵ Various methods to reduce blood loss have their own risks.⁶
Tranexamic acid (TXA) is a synthetic antifibrinolytic agent that inhibits the activation of plasminogen to plasmin, an enzyme that degrades fibrin clots, fibrinogen, and pro-coagulant factors V and VIII. At a higher concentration, TXA acts directly to inhibit plasmin activity. Both intra-articular and intravenous TXA have been used to reduce blood loss and transfusion requirement for TKA.\textsuperscript{7,12-13} Intra-articular application of TXA results in less systemic side-effects such as thrombosis, yet provides comparable effects in reducing blood loss and transfusion requirement.\textsuperscript{14,15} This study compared the outcome after simultaneous bilateral TKA with or without intra-articular TXA wash in terms of blood loss, haemoglobin change, and transfusion requirement.

MATERIALS AND METHODS

This study was approved by the institutional review board of SingHealth (CIRB: 2014-458/D) and in accordance with the Declaration of Helsinki. 35 women and 10 men (mean age, 67.5; interquartile range, 61–72) years who underwent primary simultaneous bilateral TKA by a single senior surgeon between April 2011 and December 2013 were compared with 45 controls matched for sex, anaesthesia type,\textsuperscript{16,17} age, body mass index, the presence of diabetes mellitus,\textsuperscript{18} hypertension,\textsuperscript{19} and preoperative serum haemoglobin concentration.\textsuperscript{20} Patients with high-risk medical comorbidities (chronic renal or liver impairment) were excluded, as were those with a history of thromboembolic diseases (deep vein thrombosis, pulmonary embolism, stroke, and myocardial infarction) or bleeding disorder, and those prescribed anticoagulant drug treatment.

All patients underwent simultaneous bilateral TKA under tourniquet control through the standard medial parapatellar quadriceps splitting approach with patella eversion.\textsuperscript{21} In the TXA group, 1500 mg of TXA (Cyklokapron, Pfizer, New York, USA) diluted in 100 ml of 0.9% sodium chloride was administered as a wash after cementing of implants and before closure of the retinaculum. At least 5 minutes of contact time was allowed before wound closure followed by tourniquet deflation. No drain was used. In the control group, no TXA was given.

Postoperatively, pneumatic calf pumps were applied immediately until ambulation. Subcutaneous enoxaparin 40 mg once daily was given on day 1 and continued until discharge from hospital. Physiotherapy was standardised and aimed at early mobilisation. Only symptomatic patients were evaluated using ultrasonography (for the lower limb deep veins) and computed tomography (for the chest). Patients were discharged when able to flex the knee to 90\degree, perform an unassisted straight-leg raise, walk independently with or without aids, and climb stairs.

<table>
<thead>
<tr>
<th>Table</th>
<th>Patients undergoing simultaneous bilateral total knee arthroplasty with or without an intra-articular tranexamic acid (TXA) wash*</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of male:female</td>
<td>TXA group (n=45)</td>
</tr>
<tr>
<td>10:35</td>
<td>10:35</td>
</tr>
<tr>
<td>Age (years)</td>
<td>67.5 (61–72)</td>
</tr>
<tr>
<td>Body mass index (kg/m(^2))</td>
<td>27.0 (24.1–29.2)</td>
</tr>
<tr>
<td>Patients with general anaesthesia</td>
<td>19 (42.2)</td>
</tr>
<tr>
<td>Patients with hypertension</td>
<td>35 (77.8)</td>
</tr>
<tr>
<td>Patients with diabetes mellitus</td>
<td>7 (15.6)</td>
</tr>
<tr>
<td>Preoperative haemoglobin level (g/dl)</td>
<td>13.4 (12.35–14.35)</td>
</tr>
<tr>
<td>Perioperative drop in haemoglobin level (g/dl)</td>
<td>2.2 (1.25–2.70)</td>
</tr>
<tr>
<td>Total drop in haemoglobin level (g/dl)</td>
<td>2.2 (1.55–2.75)</td>
</tr>
<tr>
<td>Perioperative blood loss (ml)</td>
<td>657 (524–838)</td>
</tr>
<tr>
<td>Total blood loss (ml)</td>
<td>679 (543–850)</td>
</tr>
<tr>
<td>Patients transfused</td>
<td>17 (37.8)</td>
</tr>
<tr>
<td>Blood units transfused (units)</td>
<td>1 (1–2)</td>
</tr>
<tr>
<td>Blood volume transfused (ml)</td>
<td>354 (299–518)</td>
</tr>
<tr>
<td>Patients requiring 1 blood unit</td>
<td>13 (28.9)</td>
</tr>
<tr>
<td>Patients requiring &gt;1 blood unit</td>
<td>4 (8.9)</td>
</tr>
<tr>
<td>Operating time (minutes)</td>
<td>125 (110–150)</td>
</tr>
<tr>
<td>Length of hospitalisation (days)</td>
<td>4 (4–6)</td>
</tr>
</tbody>
</table>

* Data are presented as no. (%) or mean (interquartile range)
Blood loss was calculated using the haemoglobin balance method: total blood volume (TBV) [ml] is equal to \(0.0003669 \times \text{height}^3\) (cm) + [32.19 \times \text{body weight (kg)} + 604] for males, and \(0.0003561 \times \text{height}^3\) (cm) + [33.08 \times \text{body weight (kg)} + 183] for females. Blood loss (ml) is equal to TBV (ml) \(\times \frac{\text{Hb}_i - \text{Hb}_e}{\text{Hb}_i} + \text{sum of blood products transfusion (ml)}\), where \(\text{Hb}_i\) and \(\text{Hb}_e\) (g/dl) are pre- and post-operative serum haemoglobin concentration, respectively. In our hospital, a serum haemoglobin concentration of <8.0 g/dl is the transfusion trigger. In patients with hypoxia such as tachycardia, dyspnoea, or syncope, the transfusion trigger is <9.0 g/dl.

The 2 groups were compared using the Mann-Whitney U test (for continuous variables) or Pearson Chi squared test (for categorical variables). A p value of <0.05 was considered statistically significant.

RESULTS

No patients had thromboembolic complication. Compared with controls, the TXA group had lower perioperative blood loss (920 vs. 657 ml, p=0.001), total blood loss (997 vs. 679 ml, p<0.001), blood transfusion rate (60% vs. 37.8%, p=0.035, odds ratio=0.405, 95% confidence interval: 0.173, 0.945), percentage of patients requiring more than one blood unit (24.4% vs. 8.9%, p=0.048), and length of hospitalisation (6 vs. 4 days, p<0.001). Nonetheless, the 2 groups were comparable in blood units and volume transfused.

DISCUSSION

Patients who underwent bilateral TKA without TXA had significantly more blood loss than those given 2 doses of 15 mg/kg or 10 mg/kg of intravenous TXA (918 vs. 462 vs. 678 ml), but this did not translate into a reduction of allogeneic blood transfusion in the TXA groups, possibly due to autologous blood collection and reinfusion. Patients who received 2 doses of 10 mg/kg intravenous TXA had a lower postoperative drain output (275 vs. 810 ml) and requirement for allogeneic blood units (0.80 vs. 3.17 units) than those without TXA. The TXA group had a smaller decrease in haemoglobin level (1.29 vs. 1.46 g/dl), less blood loss in the drain (402 vs. 569 ml), and required fewer allogeneic blood transfusion units (0.07 vs. 0.3 units) than those without TXA.

Intravenous TXA, intra-articular TXA injection after wound closure, and an intra-articular TXA wash after cementing of implants and before closure of the retinaculum are comparably effective. The intra-articular TXA wash can directly target the site of bleeding within a contained joint cavity; it reduces the marked increase in local fibrinolysis after release of the tourniquet, and increases microvascular haemostasis. In addition, a drain is not used due to the rapid washout of the TXA. Neither intravenous nor intra-articular TXA result in an increased risk of thromboembolic complications.

The haemoglobin balance method takes into consideration the amount of hidden blood loss that cannot be directly measured by the drain output. Intra-operative blood loss can also be estimated by: (1) subtracting the total amount of wash given from the total suction volume intra-operatively, or (2) subtracting the weight of used swabs from their original weight (1 g=1 ml). Surgical blood loss is underestimated by 64% when suction bottles and blood-soaked swabs are used. The haemoglobin balance method is less likely to underestimate the total blood loss, and thus the blood loss is generally greater than that reported in other studies.

Measuring the blood units or blood volume required reflects more accurately the blood transfusion requirement. In our study, patients with or without the intra-articular TXA wash were comparable in blood units or blood volume required, but more patients without TXA required more than one blood unit.

One limitation of this study was its retrospective nature, but potential confounders have been matched with controls. In addition, haemostasis status such as prothrombin time and partial thromboplastin time was inadequately monitored, although substantial outliers were excluded.

CONCLUSION

An intra-articular TXA wash during simultaneous bilateral TXA reduced total blood loss and resulted in a difference of 22.2% in blood transfusion rate and a 2-day reduction in the length of hospital stay.

DISCLOSURE

No conflicts of interest were declared by the authors.
REFERENCES


