Author's response to reviews

Title: Temporary clamping of drains combined with tranexamic acid reduce blood loss after total knee arthroplasty: A Prospective Randomized Controlled Trial.

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Temporary clamping of drains combined with tranexamic acid reduce blood loss after total knee arthroplasty: A Prospective Randomized Controlled Trial.

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Investigation performed at Department of Orthopedic Surgery, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand

Abstract

Background: Total knee arthroplasty is associated with a significant amount of blood loss. Several methods have been reported to reduce post-operative blood loss and avoid homologous blood transfusions. In this study, we investigated the efficacy of temporally clamping the drain with tranexamic acid to control bleeding.

Methods: This study was a prospective, randomized, and double-blind study. 240 patients with primary osteoarthritis scheduled to undergo a primary total knee arthroplasty were randomized into four groups. In Group A, the drain was not clamped and the patient received a placebo (control group); in Group B, the drain was not clamped and the patient received tranexamic acid; in Group C, the drain was clamped and the patient received a placebo; and in Group D, the drain was clamped and the patient received...
tranexamic acid. We measured the volume of drained blood 48 hours post-operatively, the levels of haemoglobin fall at 12 hours post-operatively and the number of patients

**Results:** The mean post-operative volumes of drained blood in the three study groups were significantly lower than those in the control group (p<0.05). There were no significant differences in the volumes of drained blood between group B and group C (p=0.37). Among the three study groups, the mean post-operative volumes of drained blood in group D were significantly lower than those in the other groups (p<0.05).

The amount of blood transfused in group B and group D were significantly lower than the control group (p<0.05). The amount of blood transfused in group C was lower than the control group, but this was not a significant difference (p=0.053). Among the three study groups, the amount of blood transfused in group B was significantly lower than group C (p<0.05), and the amount of blood transfused in group D was significantly lower than in either group B or group C (p<0.05).

**Conclusions:** Tranexamic acid and drain clamping significantly reduced post-operative blood loss after total knee replacement. In this study, we found that tranexamic acid combined with drain clamping resulted in a
significantly better haemostatic effect when compared with tranexamic acid alone or drain clamping alone.

**Trial registration:** ClinicalTrials.gov NCT01449552. It was approved by the Ethics Committee of Siriraj Hospital. All of the patients gave their written informed consent.
Background

Total knee arthroplasty is one of the options for the treatment of severe osteoarthritis of the knee. The goals of total knee arthroplasty are simple: to restore pain-free motion while maintaining stability, and to correct deformity of the knee. Total knee arthroplasty is widely acknowledged to be one of the most successful and cost-effective procedures in orthopedic practice and has become a very common procedure.

Total knee arthroplasty can be associated with considerable blood loss, and transfusion carries a substantial risk of both immunologic reaction and transmission of disease. Blood transfusion also involves additional cost, so a reduction in its use is important. Several methods have been reported to reduce post-operative blood loss, thus avoiding homologous blood transfusions. The methods shown to be effective include autologous blood transfusion, post-operative blood salvage, the use of a femoral intramedullary plug, hypotensive anaesthesia, cryotherapy and Jones blandage, use of fibrin tissue adhesive, drain clamping, and the administration of tranexamic acid. In this study, we investigated the efficacy of temporally clamping the drain and the administration of tranexamic acid for the control of bleeding after total knee arthroplasty.
Most total knee arthroplasty is performed with the use of a tourniquet and most blood loss occurs after surgery. Jou et al. 34 reported that most blood loss occurs during the first few post-operative hours (37% in two hours and 55% in four hours). Sakihara et al. 11 reported a method for reducing post-operative bleeding after total knee arthroplasty where 50 ml of saline containing antibiotic was infused into the knee joint through the drain tube before releasing the tourniquet. The drain was then clamped for one hour after the tourniquet was released. Ryu et al. 12 reported that drain-clamping for 20 hours with saline infusion significantly reduced post-operative bleeding after total knee arthroplasty, and the hemostatic effect was even greater when epinephrine was added to the saline than that of saline alone. Yamada et al. 13 compared 1-hour and 24-hour drain clamping after total knee arthroplasty. They concluded that the haemostatic effects were similar for each, but that there were significantly more complications after 24-hour clamping. They recommended clamping for one hour to minimize complications. Some studies have reported that clamping drains have no benefit in routine knee arthroplasty. For example, Kiely et al. 19 reported that no significant differences were found between the 2-hour clamping group and the non-clamping group in terms of the volume of drained blood, transfusion requirements, knee motion, and wound status.
In 2005, Shen et al.\textsuperscript{15} reported that clamping the drainage within the first four post-operative hours reduced post-operative blood loss compared to non-clamping drainage and did not cause excess morbidity after total knee arthroplasty. In 2006, Tsumara et al.\textsuperscript{16} reported that drain clamping for 30 minutes with intra-articular injection of saline with adrenaline is more effective than post-operative blood salvage in reducing blood loss during total knee arthroplasty. In 2005, Prasad et al.\textsuperscript{17} compared two methods of drain clamping; group 1 had the drain clamped for one hour and group 2 had the drain clamped and released for 10 minutes every two hours for 24 hours. They concluded that 2-hour clamping of the drain and release for 10 minutes significantly reduced post-operative blood loss without any added increase in complication after total knee arthroplasty. In 2006, Roy et al.\textsuperscript{18} reported that drain clamping for one hour significantly reduced blood loss and transfusion requirement following total knee arthroplasty. In 2007, Raleigh et al.\textsuperscript{14} reported a method of drain clamping and release for five minutes every two hours for 24 hours. They concluded that clamping drains intermittently and resulted in significantly less external blood loss than observed in the non-clamping group with no change in morbidity, mortality, or in the requirement for transfusion between the two groups.
Tranexamic acid is a synthetic anti-fibrinolytic drug used to prevent bleeding. Fibrinolysis is stimulated by surgical trauma, and is further augmented by the use of a tourniquet. This increased fibrinolytic activity may increase blood loss after total knee arthroplasty, at least during the first few post-operative hours. Tranexamic acid produces anti-fibrinolytic effects by competitively inhibiting the activation of plasminogen to plasmin.

Tranexamic acid blocks the lysine binding sites of plasminogen to fibrin, displacing plasminogen from the fibrin surface, which results in inhibition of fibrinolysis.

Several studies have reported that tranexamic acid reduced both blood loss and the amount of blood needed for transfusions (Benoni et al. 1996, Hippala et al. 1997, Jansen et al. 1999, Good et al. 2003, Camarasa et al. 2006). Some studies reported that tranexamic acid significantly decreased blood loss, but did not significantly alter transfusion requirements (Veien et al. 2002, Orpen et al. 2006). In 2003, Hynes et al. reported that the administration of tranexamic acid is an effective method for reducing the haemoglobin decrease following knee arthroplasty. In 2001, Engel et al. reported that tranexamic acid did not cause a significant modulation of fibrinolysis variables or a significant reduction of post-operative bleeding and transfusion requirements. In 2001, Tanaka et
al.\textsuperscript{29} compared the timing of the administration of tranexamic acid for maximum reduction in blood loss in arthroplasty of the knee and they concluded that two injections of tranexamic acid, one given pre-operatively and one upon deflation of the tourniquet, significantly reduced blood loss without increasing the risk of thromboembolic complications. In 2003, Ho et al.\textsuperscript{30} reported on a meta-analysis of 12 studies and they concluded that intravenous tranexamic acid appears effective and safe in reducing allogenic blood transfusion and blood loss in both total hip and total knee arthroplasty without increasing the risk of thromboembolic complications. In 2005, Cid et al.\textsuperscript{31} reported on a meta-analysis of randomized controlled trials and nine studies met the criteria for meta-analysis. They concluded that the use of tranexamic acid for patients undergoing total knee arthroplasty is effective in reducing the requirement of allogenic blood transfusion.

More recent studies in 2007 by Molloy et al.\textsuperscript{32} compared the efficacy of topical fibrin spray and tranexamic acid on blood loss after total knee arthroplasty. They concluded that there was a significant reduction in the total calculated blood loss for those in the topical fibrin spray group and tranexamic acid group compared with the control group. The reduction in blood loss in the fibrin spray group was not significantly different from that achieved in the tranexamic acid group.
To our knowledge, no study has compared the efficacy of drain clamping with the administration of tranexamic acid in the control of bleeding following total knee arthroplasty. The purpose of this study was to evaluate the efficacy of drain clamping when compared with the administration of tranexamic acid and the combined effect of these two modalities in the control of bleeding following total knee arthroplasty.

Materials and Methods

This study was designed to be a prospective, randomized, and double-blind study.

Between June 2008 and November 2008, 240 patients scheduled to undergo a primary total knee arthroplasty were enrolled in the study. The inclusion criteria were patients aged younger than 85 years with primary osteoarthritis that were awaiting total knee arthroplasty. The exclusion criteria were secondary osteoarthritis (such as rheumatoid arthritis, post-traumatic arthritis, gouty arthritis, post-septic arthritis), patients who have high risk medical co-morbidity, simultaneous bilateral total knee arthroplasties, history of thromboembolic disease, patients with a bleeding disorder, known allergy to tranexamic acid, and patients who received anti-coagulant drugs.
All of the 240 patients were randomized using a block-design technique with permutated blocks of 12. Randomization into blocks of 12 was done by an independent second year resident who was not otherwise engaged in the study. Six ampoules, each containing 5 ml of either tranexamic acid (Transamin 250mg/5ml; OLIC Thailand Limited) combined with 30 capsules of tranexamic acid (Transamin 250mg/capsule) or a placebo (equivalent volume of physiologic saline combined with a starch capsule) were numbered and packed into envelopes that were opened by the anaesthetist or the nurse at the ward before administration. These envelopes could only be identified by their number, and the randomization code was known only to an independent pharmacologist. The code was not broken until all data had been corrected and included in the database.

All patients were randomized into four groups.

Group A: the drain was not clamped and the patient received a placebo (saline 10 minutes before surgery and three hours post-operative, and then an oral form of placebo 2X3 capsules for five days).

Group B: the drain was not clamped and the patient received tranexamic acid 10mg/kg intravenous 10 minutes before inflating the tourniquet and 10mg/kg intravenous three hours post-operative, and then tranexamic acid 250mg/capsule 2X3 orally for five days.
Group C: the drain was clamped for three hours, released for three hours, then clamped for another three hours, and then released free for 48 hours. The patient received placebo (saline 10 minutes before surgery and three hours post-operative, and then an oral form of placebo 2X3 capsules for five days).

Group D: the drain was clamped for three hours, released for three hours, then clamped for another three hours, and then released free for 48 hours. The patient received tranexamic acid 10mg/kg intravenous 10 minutes before inflating the tournique and 10mg/kg intravenous three hours post-operative, and then tranexamic acid 250mg/capsule 2X3 orally for five days.

The pre-operative data included patient age at the time of operation, the ratio of men to women, and pre-operative haemoglobin levels were shown in Table 1. The haemoglobin levels were measured before surgery, 12 hours post-operative, six hours after blood transfusion, and 48 hours post-operative. One unit of allogenic pack red cells was transfused if the haemoglobin level fell below 10 g/dl and two units of pack red cell was transfused if the haemoglobin level fell below 8 g/dl.

All patients received spinal anaesthesia. A dose of cefazolin (2 g) was given intravenously shortly before the operation. Patients allergic to
penicillin were given clindamycin instead. A tourniquet was placed around the upper thigh and inflated to a pressure of 350 mmHg after exsanguination with an Esmarch bandage. The tourniquet was not released before skin closure. One surgeon with experience in total knee replacement performed or supervised all the operations. An anteromedial skin incision from the upper border of the patellar to the tibial tubercle and Quad-sparing approach were used in all cases. An intramedullary alignment jig was used for the femur with an extramedullary device for the tibia in the case of bony resections. All the patients received a posterior stabilized cemented total knee arthroplasty (Nexgen LPS, Zimmer) without patellar resurfacing. Palacos cement without antibiotics was used for fixation of the cemented arthroplasties. The hole created for the intramedullary guide rod was occluded with bone before implantation of the femoral component.

One intra-articular drain (10 gauge) was used and connected to a high vacuum drain bottle in each knee. All patients’ knees were placed in a compressive bandage and slap. All of the compressive bandage and slap and the Foley’s catheter were removed on the first day after operation. Physiotherapy was started on the first day after operation and all drains were removed at 48 hours post-operatively. The total volume of drained blood at 48 hours post-operatively and haemoglobin fall at 12 hours post-operatively
were recorded. Blood transfusions were recorded as the number of units of pack red cell. Thromboembolic complications such as clinical deep vein thrombosis, pulmonary emboli, and other complications such as wound complications were noted during the hospital stay. All of the patients were discharged from the hospital on the fifth day after the operation.

We used a one-way analysis of variance (ANOVA) for statistical appraisal of the data using SPSS version 11.5. All 240 randomized patients were included in the data analysis with a level of significance set at $p \leq 0.05$.

**Results**

Over a six-month period, we prospectively studied 240 patients who underwent unilateral primary total knee arthroplasty at Siriraj hospital. The patients ranged from 53-84 (69.75±6.82) years-old. There were 205 women and 35 men. Each group consisted of 60 patients. The four groups were comparable in age, gender, and pre-operative haemoglobin. The pre-operative data included patient age at the time of operation, the ratio of men to women, and pre-operative haemoglobin level were shown in Table 1. There were no significant differences between them in regards to the data presented.
Blood loss (Table 2). The mean post-operative volumes of
drained blood between the four groups were comparable, with 1181.83±411
ml in group A (control group), 723.50±246 ml in group B, 820.83±337 ml in
group C, and 525.75±222 ml in group D. The mean post-operative volumes
of drained blood in the three study groups were significantly lower than
those in the control group (p<0.05). There were no significant differences in
the volumes of drained blood between group B (TNA group) and group C
(drain-clamping group) (p=0.37). Among the three study groups, the mean
post-operative volumes of drained blood in group D (TNA and drain-
clamping group) were significantly lower than those in the other groups
(p<0.05).
Haemoglobin fall at 12 hours post-operatively (Table 2). The mean haemoglobin fall at 12 hours post-operatively was 3.29±0.85 g/dl in group A (control group), 2.14±0.64 g/dl in group B, 2.78±0.84 g/dl in group C, and 1.79±0.69 g/dl in group D. The mean level of haemoglobin fall at 12 hours post-operatively in the three study groups were significantly lower than those in the control group (p<0.05). Among the three study groups, the mean level of haemoglobin fall in group B (TNA group) was significantly lower than group C (drain-clamping group) (p<0.05). The mean level of haemoglobin fall in group D (TNA and drain-clamping group) was significantly lower than group C (p<0.05) but there were no significant differences between group D and group B (p=0.68).

Transfusion requirements (Table 2). The parameters of the transfusion requirements between the four groups were comparable. The mean red cell units were 1.77 units in group A, 0.72 units in group B, 1.32 units in group C, and 0.40 units in group D. The amount of blood transfused in group B and group D were significantly lower than the control group (p<0.05). The amount of blood transfused in group C was lower than the control group (1.32 compared to 1.77 units) but this was not a significant difference (p=0.053). Among the three study groups, the amount of blood
transfused in group B was significantly lower than group C (p<0.05) and the amount of blood transfused in group D was significantly lower than group B and group C (p<0.05), respectively. The number of patients requiring transfusion was 53 patients (88.3%) in group A, 34 patients (56.7%) in group B, 49 patients (81.7%) in group C, and 23 patients (38.3%) in group D. The number of patients that required a blood transfusion in group D was significantly lower than the other groups, which had an odds ratio of 12.18 (95% CI= 4.736-31.322) in group A, 2.10 (95% CI=1.015-4.361) in group B, and 7.17 (95% CI=3.107-16.529) in group C (Fig 3).

Complication: There were no differences in the incidence of adverse events among the four groups. No patients had clinical signs of deep vein thrombosis or pulmonary embolism. Three patients (in groups A, B, D,) developed an ecchymosis around the knee which no further treatment. No other wound complications or infection were found.

Discussion
Total knee arthroplasty is associated with a significant amount of blood loss and patients undergoing total knee arthroplasty may require a blood transfusion. Significant complications after allogenic blood transfusions have been well-reported in the literature. Several methods have been reported to reduce post-operative blood loss and help avoid allogenic blood transfusions. The methods shown to be effective include autologous blood transfusion, post-operative blood salvage, the use of a femoral intramedullary plug, hypotensive anaesthesia, cryotherapy and Jones blandage, use of fibrin tissue adhesive, drain clamping, and the administration of tranexamic acid. However, the best method of reducing the need for transfusion and blood loss after total knee replacement remains contentious. This study has re-examined the potential benefits of drain clamping compared with tranexamic acid in the control of bleeding after unilateral total knee replacement.

The drain-clamping method after total knee replacement has been previously evaluated. Several studies have verified the effectiveness of drain clamping in controlling blood loss and precluding the need for allogenic blood transfusion. However, some technical issues still remained with the drain clamping method. In previous studies, the optimal clamping time, the volume of saline used, and the concentration of adrenaline were
different. The reported duration of such drain clamping varies from 30 minutes to 24 hours, with or without the adjuvant infusion of saline or saline with adrenaline. These reports indicated that the optimal drain-clamping method is still arbitrary.

Jou et al. reported that most blood loss occurred within the first few post-operative hours (37% in two hours and 55% in four hours). Based off their recent study, they recommended that clamping the drainage within the first four post-operative hours reduced post-operative blood loss compared with non-clamping drainage without causing excess morbidity. Ryu et al. reported that drain-clamping for 20 hours with saline infusion significantly reduced post-operative bleeding after total knee arthroplasty. Moreover, the hemostatic effect was even greater than saline alone when epinephrine was added to the saline. Yamada et al. showed that 1-hour clamping was preferable to 24 hour clamping for minimizing complications. Kiely et al. concluded that a 2-hour clamping drain was of no benefit in routine knee arthroplasty.

The volume of saline in the previous reports varied from 0-50 ml. Ryu et al. and Yamada et al. used saline containing 1:200,000 adrenaline when drain clamping. Olszewski et al. reported the effective use of 1:1,000,000 adrenaline saline irrigation during routine arthroscopic knee
surgery for the control of bleeding. Tsumara et al.\textsuperscript{16} used saline containing 1:500,000 adrenaline with drain clamping. In our study, we proposed a method of drain clamping where the drain was clamped for three hours, released for three hours, then clamped for another three hours, and then released free for 48 hours without infusion of saline. This method of drain clamping significantly reduced blood loss from 1181.83 ml to 820.83 ml (p<0.05) without causing excess morbidity. The amount of blood transfused in the drain clamping groups were lower than the control group (1.32 compared to 1.77 units), but this was a not significant difference (p=0.053).

There are four methods of administering tranexamic acid in order to reduce blood loss in total knee arthroplasty: intramuscular, oral, intravenous, and intra-articular\textsuperscript{29}. The time taken for maximum plasma levels of tranexamic acid to be reached has been reported to be 30 minutes for intramuscular, two hours for oral, and 5-15 minutes for intravenous administration\textsuperscript{44,45}. Several clinical studies have shown the efficacy of tranexamic acid when given before surgery\textsuperscript{22,46}. Some clinical studies show the efficacy of tranexamic acid when given upon deflation of the tourniquet with a repeated dose post-operatively\textsuperscript{20,21,23-32}. Hynes et al.\textsuperscript{27} recommended two doses of tranexamic acid; once upon induction and another dose shortly before the release of the tourniquet. Orpen et al.\textsuperscript{26} recommended a dose of 15
mg/kg of tranexamic acid at the time of cementing of the prosthesis. Alvarez et al.\textsuperscript{47} recommended the dose of 10 mg/kg bolus dose followed by 1 mg per kg per hour. Tanaka et al.\textsuperscript{29} concluded that the haemostatic effect was best when tranexamic acid was given once every 10 minutes before surgery and once upon deflation of the tourniquet and they also recommended that the haemostatic was better when tranexamic acid was administered before the operation rather than upon deflation of the tourniquet. Tanaka et al.\textsuperscript{29} also suggested that the suppression of fibrinolysis from the beginning of the operation may be more effective than later at the time of the peak of hyperfibrinolysis. Pharmacokinetic studies\textsuperscript{44-45,48-49} indicated that a dose of 20 mg/kg of tranexamic acid is suitable for total knee replacement since therapeutic levels can be maintained for approximately 8 hours after the operation, which covers the period of hyperfibrinolysis in cases of increased blood loss. Prasad et al.\textsuperscript{17} have shown that 65\% of the drainage volume occurs in the first eight hours post-operatively. In our study, we used a dose of 10 mg/kg every 10 minutes before inflation of the tourniquet and another dose of 10 mg/kg every three hours post-operatively in order to maintain the therapeutic level for approximately 8 hours after the operation and followed by tranexamic given in an oral form for five days. Several studies have reported that tranexamic acid reduced blood loss about 30-50\% when used in
total knee replacements\textsuperscript{20-25,29}. We found a 40\% reduction of blood loss in our prospective study, and tranexamic acid also significantly reduced the amount of blood transfused from 1.77 to 0.72 units when compared to the control group (p<0.05). These comparisons in the reduction of blood transfusion are difficult because the indicators for blood transfusions were different.

Some studies have compared the efficacy of two modalities in reducing blood loss after total knee replacement. Molloy et al.\textsuperscript{32} compared the efficacy of topical fibrin spay and tranexamic acid and they concluded that topical fibrin spay and tranexamic acid significantly reduced blood loss when compared with the control group. However, the haemostatic effects between the two modalities were not significantly different. Tsumara et al.\textsuperscript{16} concluded that drain clamping with intra-articular injection of saline with adrenaline is more effective than post-operative blood salvage in reducing blood loss after total knee replacement.

In our study, we compared the efficacy of drain clamping and tranexamic acid in the control of bleeding after total knee replacement. We found a significant reduction in the volume of drained blood of 40\% between the control group and the tranexamic acid group (p<0.05) and of 30\% between the control group and the drain-clamping group (p<0.05). We
also found a significant reduction in the level of haemoglobin fall and the number of patients that required a transfusion between the control group and the tranexamic acid group (p<0.05). In the drain-clamping group, the level of haemoglobin fall and the volume of drained blood was significantly different when compared to the control group (p<0.05). The difference in the amount of blood transfused and the number of patients requiring an allogenic blood transfusion between the control group and the drain-clamping group was not significant.

The haemostatic effects of the tranexamic acid group were significantly better than the drain-clamping group with regards to the level of haemoglobin fall, amount of blood transfused, and the number of patients that required a blood transfusion. The volume of drained blood between these two group was not significantly different (p=0.37). These findings confirm that some blood might remain around the knee joint, leak through the wound, or diffuse into the soft tissue, especially when the drain is clamped\(^{13,33,50}\). This study, therefore, also verified the efficacy of the administration of tranexamic acid combined with the drain-clamping method (group D), which significantly reduced the volume of drained blood up to 55% compared with the tranexamic acid group (group B) 40%, and the drain-clamping group 30%. When tranexamic acid administration was
combined with drain clamping, the amount of blood transfused was significantly reduced to 0.40 units when compared to the tranexamic acid group, which had 0.72 units and the drain-clamping group had 1.32 units. The number of patients that required an allogenic blood transfusion was reduced to 38.3% when compared to the tranexamic acid group (56.7%) and the drain-clamping group (81.7%).

In conclusion, our study confirmed the findings of previous studies that showed that tranexamic acid and drain clamping significantly reduced post-operative blood loss after total knee replacement. In this study, we also found that when tranexamic acid administration is combined with drain clamping, the haemostatic effect was significantly better than with tranexamic acid alone or drain clamping alone.

**Competing interests**

The authors declare that they have no competing interests.

**Authors’ contributions**

Author is Associate Prof. Keerati Charoencholvanich who has made substantial contributions to conception and design, acquisition of data, analysis, interpretation of data and has given final approval of the version to be published. Dr. Pichet Siriwattanasakul is author who has made substantial contributions to conception and design, acquisition of data,
analysis, interpretation of data and has been involved in drafting the manuscript or revising it critically for important intellectual content.

Authors’ information

Associate Prof. Keerati Charoencholvanich and Dr. Dr. Pichet Siriwattanasakul are instructor at Department of Orthopedic Surgery, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand.

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Authors contributed towards the study by making substantial contributions to conception, design, acquisition of data, analysis and interpretation of data, involving in drafting the manuscript or revising it critically for important intellectual content.

Table 1. Pre-operative data

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<tr>
<td>Mean age</td>
<td>69.80±6.25</td>
<td>69.43±6.28</td>
<td>68.87±7.45</td>
<td>70.09±7.22</td>
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<td>Male:Female</td>
<td>8:52</td>
<td>9:51</td>
<td>10:50</td>
<td>8:52</td>
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<tr>
<td>Pre-op Hb</td>
<td>12.47±1.06</td>
<td>12.38±1.14</td>
<td>12.40±1.09</td>
<td>12.64±0.95</td>
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Table 2 Mean blood loss and transfusion requirements

<table>
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<tr>
<td>Volume of drained blood (ml)</td>
<td>1181.83±411 (420-2260)</td>
<td>723.50±246 (230-1330)</td>
<td>820.83±337 (230-2020)</td>
<td>525.75±222 (180-960)</td>
<td>p&lt;0.05</td>
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<td>Hb fall at 12 hours (g/dl)</td>
<td>3.29±0.85 (1.30-5.30)</td>
<td>2.14±0.64 (0.90-3.80)</td>
<td>2.78±0.84 (0.90-4.40)</td>
<td>1.79±0.69 (0.40-3.60)</td>
<td>p&lt;0.05</td>
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<td>Blood transfusion (PRC unit)</td>
<td>1.77±0.99 (0-4)</td>
<td>0.72±0.72 (0-2)</td>
<td>1.32±0.85 (0-3)</td>
<td>0.40±0.53 (0-2)</td>
<td>p&lt;0.05</td>
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<td>Blood transfusion (Number of patients)</td>
<td>53 88.3%</td>
<td>34 56.7%</td>
<td>49 81.7%</td>
<td>23 38.3%</td>
<td>p&lt;0.05</td>
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