

Prognostic Factors of Perioperative Hemorrhage, Blood Transfusion and Tranexamic Acid Infusion in Bilateral Total Knee Replacement: A Prospective Comparative Study

Kumar SV* and Lakhwani OP

Department of Orthopedics, ESI-PGIMS Model Hospital, Basaidarapur, New Delhi, India

*Corresponding author: Kumar SV, Department of Orthopedics, ESI-PGIMS Model Hospital, Basaidarapur, New Delhi, India, E-mail: mailvenkatesh91@gmail.com

Received date: August 17, 2020; Accepted date: August 31, 2020; Published date: September 07, 2020

Citation: Kumar SV, Lakhwani OP (2020) Prognostic Factors of Perioperative Hemorrhage, Blood Transfusion and Tranexamic Acid Infusion in Bilateral Total Knee Replacement: A Prospective Comparative Study. Trauma Acute Care Vol.5 No.3: 84. DOI: 10.36648/2476-2105.5.3.84

Abstract

Background: Perioperative hemodynamic control is considered critical for intra-operative and post-operative outcomes in bilateral Total Knee Replacement (TKR). We carried out a prospective study to determine the factors affecting the perioperative blood loss, blood transfusion, and tranexamic acid requirement in bilateral total knee replacement. The factors analyzed were gender, blood pressure, and body mass index (BMI).

Methods: Selected primary osteoarthritis knee patient's gender and comorbidities such as hypertension, obesity, diabetic mellitus, thyroid disorders, etc., were recorded. We prospectively recorded total blood loss, blood transfusions and tranexamic acid infusion in 21 patients who have undergone staged bilateral TKR and 20 patients who have undergone simultaneous bilateral TKR randomly.

Results: Male patients among bilateral TKR have significantly more average total blood loss compared to female patients ($p < 0.001$). Hypertensive and obese patients among bilateral TKR have significantly more average total blood loss compared to non-hypertensive and non-obese patients respectively ($p < 0.001$). Male patients more blood transfusion prevalence rate compared to female patients, but this difference is not of statistical significance ($p = 0.08$). Hypertensive and obese patients have more but not significant blood transfusion prevalence rate compared to non-hypertensive ($p = 0.09$) and non-obese ($p = 0.08$) patients respectively. Male patients more intravenous tranexamic acid infusion rates compared to female patients, but this difference is not of statistical significance ($p = 0.79$). Hypertensive and obese patients have more but not significant tranexamic acid infusion rates compared to non-hypertensive ($p = 0.50$) and non-obese ($p = 0.70$) patients respectively.

Conclusion: Male gender, patients with hypertensive and obesity has significantly higher average blood loss, higher blood transfusion rate and higher tranexamic acid infusion rate. Hence staged bilateral procedure is preferred in the male gender, comorbidities like hypertension and obesity instead of simultaneous procedure in those patients.

Keywords: Bilateral TKR; Gender differences; Hypertension; Obesity; Total blood loss; Blood transfusion rate; Tranexamic acid infusion rates

Introduction

Osteoarthritis of the knee is a chronic disabling and painful degenerative joint disease most commonly affecting older people, which often involve both the knees. Advanced stages of osteoarthritis require bilateral total knee replacement to reduce pain, improve range of motion [1]. Bilateral Total Knee Replacement can be scheduled as a simultaneous procedure or as a staged procedure [2]. Among the patients of osteoarthritis hypertension, obesity, diabetes, coronary artery disease, hyper and hypothyroidism, etc., are common co-morbidities [3,4].

We carried out a prospective comparative study to analyze various factors affecting the blood loss in a primary bilateral total knee replacement and to compare the blood loss and blood transfusion prevalence rate and tranexamic acid infusion rate in our series with some of the published series. The independent factors analyzed were gender, blood pressure and body mass index.

Materials and Methods

A total of 41 patients were enrolled prospectively with a diagnosis of primary bilateral Osteoarthritic knee having Kellgren and Lawrence grade 3 or more having less than 30 degrees of varus and flexion deformity with or without comorbidities like hypertension, obesity, diabetes, etc., out of which 20 patients undergone simultaneous bilateral TKR procedure, where both the arthritic knees are replaced under same anesthetic exposure by one orthopedic team and 21 patients undergone staged bilateral TKR procedure with a gap of at least six weeks. Exclusion criteria were patients with more than 30 degrees of flexion or varus deformity, previous complex knee surgery within 6 months, retained metal hardware at the hip and Knee, revision knee surgery, hinge prostheses, on anti-coagulants/HRT and patients with coagulation disorders. The patients meeting inclusion criteria were enrolled for study after taking prior consent in the orthopedics department by the investigator and

were randomly assigned to staged and simultaneous bilateral TKR surgeries. All routine pre-anesthetic blood and radiological investigations were done including standard antero-posterior and lateral and Merchant's view to assess the patellar tilt and the comorbidities such as hypertension with BP>140/90 [5] in at least three reading at different occasions, obesity with BMI \geq 25 kg/m² [6], thyroid disorders were recorded by one physician. As multiple comorbidities are common among patients of TKR, the charlson comorbidity index was calculated in all the patients. On total, three surgical teams were involved in these bilateral TKR surgeries. The day before the elective surgery blood pressure and BMI were recorded again. The preoperative Hb was optimized to more than 10 g/dL in all the patients. The patients received regional anesthesia and were given routine preoperative intravenous antibiotics. All the procedures were performed under pneumatic tourniquet control using conventional medial para-patellar approach and all patients received posterior stabilized TKR and prosthesis was fixed with cement. No local infiltration techniques or other measures were used for the reduction of blood loss. Intra-operative complications like tachycardia, bradycardia, hypertension, hypotension, fall in SpO₂ were recorded meticulously.

Intraoperative blood transfusion was done at the discretion of the anesthesiologist and surgeon based on the amount of blood lost, hemogram, signs of inadequate perfusion and oxygenation of vital organs. Intra-operative blood loss estimation was done by measuring irrigation fluid and by gauze visual analog. The intravenous tranexamic acid infusion was done at the discretion of the surgeon during high intra-operative blood loss, fall in hemogram and high postoperative blood loss in the drain.

In the postoperative period, the amount of blood in the drain at 48 hours was recorded, a fall in hemoglobin compared to the pre-op level was recorded on day 1 and day 5 and the number of units of blood transfused was recorded. Blood transfusion was performed if patients in whom drain output more than 500 mL (D1+D2), those patients in which drop in Hemoglobin was found to be <8 g/dL and patients whose hemoglobin was above 8.5 g/dL but who had symptoms related to anemia develop, such as tachycardia and tachypnea.

All the patients received Deep Vein Thrombosis (DVT) prophylaxis in the form Low Molecular Weight Heparin (LMWH), calf pumps in the post-operative period, mobilization along with quadriceps and hamstring exercises and in-bed knee ROM exercises.

Results

Following points are drawn from our study.

The staged group on average takes 80.83 minutes as Operative time, whereas the simultaneous group on average takes 161.785 minutes.

Among the staged group, 8 out of 21 are males (38%) and 13 out of 21 are females (62%) and among the simultaneous group, 6 out of 20 are males (30%) and 14 out of 20 are females (70%).

Hypertension (BP>140/90) is more prevalent comorbidity with 9 out of 21 patients (57.1%) among the staged group and 8 out

of 20 patients (60%) among the simultaneous group patients and obesity (BMI>25 kg/m²) is the second most prevalent comorbidity among both the groups with 4 out of 21 patients (19%) among the staged group and 4 out of 20 patients (20%) among the simultaneous group patients.

Male patients in the staged and simultaneous groups have an average total blood loss of 499.69 ml and 1025 ml respectively, which is more compared to the average total blood loss of female patients in their respective groups (staged group-324.42 ml; simultaneous groups-628 ml) and is of statistical significance (p value<0.001) (**Tables 1 and 2**).

Male patients in the staged and simultaneous group have a blood transfusion prevalence rate of 50% and 83% respectively which is more compared to the female patients in their respective groups (staged group-33%; simultaneous groups-64%), but this difference is not of statistical significance (p value=0.08) (**Tables 1 and 2**).

Table 1: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|---------|-------------------------------|----------------------------------|------------------------------------|
| Male | 499.69 | 50 | 33 |
| Female | 324.42 | 33 | 27 |
| p value | 0.001 | 0.08 | 0.79 |

Table 2: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|---------|-------------------------------|----------------------------------|------------------------------------|
| Male | 1025 | 83 | 35 |
| Female | 628 | 64 | 30 |
| p value | 0.001 | 0.08 | 0.79 |

Hypertensive patients (BP>140/90) in the staged and simultaneous group have an average total blood loss of 507 ml and 986 ml respectively, which is more compared to the average total blood loss of non-hypertensive patients in their respective groups (staged group-308 ml; simultaneous group-560 ml) and is of statistical significance (p<0.001) (**Tables 3 and 4**).

Hypertensive patients in the staged and simultaneous group have a blood transfusion prevalence rate of 33% and 75% respectively which is more compared to the blood transfusion prevalence rate of non-hypertensive patients in their respective groups (staged group-28%; simultaneous group-71%) but this difference is not of statistical significance (p value=0.09).

On comparison of prevalence of intravenous tranexamic acid, hypertensive patients in the staged and simultaneous group have a blood transfusion prevalence rate of 37% and 40% respectively, which is more compared to the non-hypertensive patients in their respective groups (staged group-30%;

simultaneous groups-31%), but this difference is not of statistical significance (p value=0.5).

Table 3: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|-----------------------|-------------------------------|----------------------------------|------------------------------------|
| Hypertensive patients | 507 | 33 | 37 |
| Normotensive patients | 308 | 28 | 30 |
| p value | 0.001 | 0.09 | 0.5 |

Table 4: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|-----------------------|-------------------------------|----------------------------------|------------------------------------|
| Hypertensive patients | 986 | 75 | 40 |
| Normotensive patients | 560 | 71 | 31 |
| p value | 0.001 | 0.09 | 0.5 |

Obese patients (BMI>25 kg/m²) in the staged and simultaneous group have an average total blood loss of 533 ml and 1042 ml respectively, which is more compared to the average total blood loss of non-obese patients in their respective groups (staged group-355 ml; simultaneous group-666 ml) and is of statistical significance (p value<0.001) (Tables 5 and 6).

Table 5: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|--------------------|-------------------------------|----------------------------------|------------------------------------|
| Obese patients | 533 | 37.5 | 38 |
| Non-obese patients | 355 | 30 | 34 |
| p value | 0.001 | 0.08 | 0.7 |

Obese patients in the staged and simultaneous group have a blood transfusion prevalence rate of 37.5% and 100% which is more compared to the blood transfusion prevalence rate of non-obese patients in their respective groups (staged group-30%; simultaneous group-62%) but this difference is not of statistical significance (p value=0.08) (Tables 5 and 6).

On comparison of prevalence of intravenous tranexamic acid, obese patients in the staged and simultaneous group have a

blood transfusion prevalence rate of 38% and 45% respectively which is more compared to the non-obese patients in their respective groups (staged group-34%; simultaneous groups-37%), but this difference is not of statistical significance (p value=0.7) (Tables 5 and 6).

Table 6: Comparison of Average total blood loss, blood transfusion prevalence and Inj Tranexamic acid prevalence in male and female patients of staged BTKR.

| | Average total blood loss (ml) | Blood Transfusion prevalence (%) | Inj Tranexamic acid prevalence (%) |
|--------------------|-------------------------------|----------------------------------|------------------------------------|
| Obese patients | 1042 | 100 | 45 |
| Non-obese patients | 666 | 62 | 37 |
| p value | 0.001 | 0.08 | 0.7 |

Discussion

Total Knee Replacement has become widely accepted treatment in orthopedic surgery to relieve pain and to restore functions to an arthritic knee. Simultaneous bilateral TKR is the operative procedure where both the arthritic knees are replaced under the same anesthetic exposure by either one or two orthopedic teams. Whereas Staged bilateral TKR is a two separate operative procedure, one for each arthritic knee under separate anesthesia with an optimal time interval between the two procedures is shown that an interval of as little as one week is safe and effective [7,8].

Among the staged group, 8 out of 21 are males (38%) and 13 out of 21 are females (62%) and among the simultaneous group, 6 out of 20 are males (30%) and 14 out of 20 are females (70%). Brian Parsley [9] reported 61% of female patients and 39% of male patients have undergone the surgery and Kim [13] also stated that the total knee replacement rate in women was much higher than that in men. Women tend to use the kneeling and squatting posture more often than men in daily activities, such as for the toilet and house chores and since kneeling and squatting are strong risk factors for knee OA and this might account for the higher prevalence of knee osteoarthritis in females [10].

In our study, among both the staged group and simultaneous group, hypertension (BP>140/90) is more prevalent comorbidity with 9 out of 21 patients (57.1%) among staged group and 8 out of 20 patients (60%) among simultaneous group patients. Following hypertension, obesity (BMI>25 kg/m²) is the second most prevalent comorbidity among both groups with 4 out of 21 patients (19%) among staged groups and 4 out of 21 patients (20%) among simultaneous group patients. Memtsoudis [3] states from his study that hypertension is the most common comorbidity among patients undergoing TKR, which is in concordance with our study, but diabetes is second most common comorbidity followed by obesity and CAD according to his study, whereas Kandemir [4] states that among the patients 20.4% were obese, 20.4% had coronary artery disease, 70% had hypertension, 25% had diabetes, 15% had chronic pulmonary

disease. In a total of 41 patients, 20 patients undergone simultaneous TKR and 21 patients undergone staged TKR.

Intra-operative hemodynamic control is considered an important prognostic factor for surgical outcomes. Poor hemodynamic control has been reported in the cardiovascular literature to be associated with death, stroke, cognitive and renal dysfunction, perioperative myocardial infarction, and increased mortality [11]. Total blood loss is calculated by the sum of intraoperative blood loss and postoperative drain amount [12]. The male patients in staged and simultaneous groups have an average total Blood loss of 499.69 ml and 1025 ml respectively, which is more compared to the average total blood loss of female patients in their respective groups (staged group-324.42 ml; simultaneous groups-628 ml) and is of statistical significance (p value<0.001) (Figure 1).

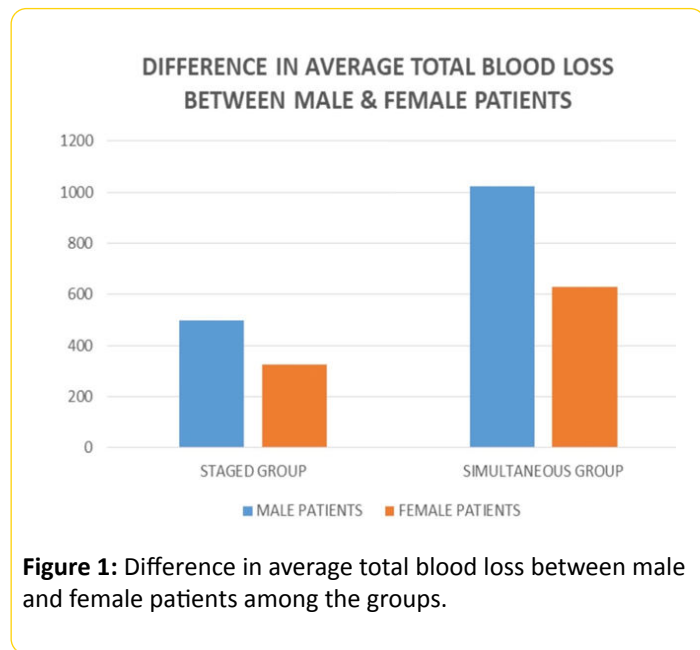


Figure 1: Difference in average total blood loss between male and female patients among the groups.

Durasek [13] states that male patients have a larger mean blood loss volume compared to female patients which is in concordance with our study. Prasad N [12] states that significantly more perioperative blood loss is seen in male patients than in females. Nwachukwu [14] stated that women had a moderately increased risk of poor hemodynamic control compared to men (RR 1.7; 0.7-3.9), but this finding was not statistically significant.

The staged group has an average total blood loss of 391.19 ml, whereas the simultaneous group has an average total blood loss of 747.5 ml. Hypertensive patients (BP>140/90) in the staged group and simultaneous group have average total blood loss of 507 ml and 986 ml respectively which is more compared to average total blood loss of non-hypertensive patients in their respective groups (staged group-308 ml; simultaneous group-560 ml) and is of statistical significance (p value<0.001) (Figure 2). Durasek [13] states that hypertensive patients had a statistically greater perioperative blood loss, both of the studies are in concordance with our study. Nwachukwu (2013) [14] stated from his retrospective study that patients with controlled hypertension had a risk of poor hemodynamic control comparable to patients without any hypertension (RR 1.3; 95%

CI 0.3-5.0). The highest intraoperative systolic blood pressure was significantly higher in hypertensive patients compared to normotensive patients (P<0.01) and the difference between the highest and the lowest intraoperative systolic blood pressure was significantly greater in hypertensive patients compared to normotensive patients (P<0.05) [18]. The poor intra-operative blood pressure control is attributed to the increased risk of hemodynamic complications in hypertensive patients undergoing knee replacements [14].

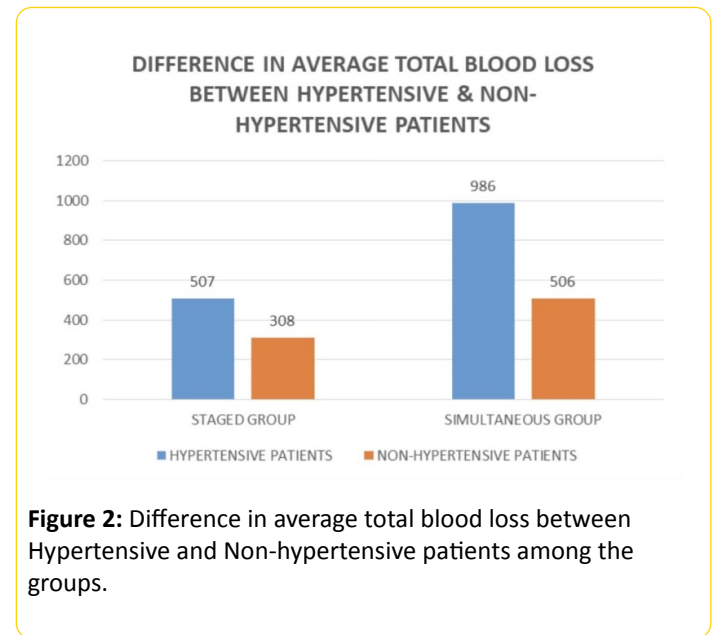


Figure 2: Difference in average total blood loss between Hypertensive and Non-hypertensive patients among the groups.

Obese patients in the staged and simultaneous group have average total blood loss of 533 ml and 1042 ml respectively, which is more compared to average total blood loss of non-obese patients in their respective groups (staged group-355 ml; simultaneous group-666 ml) and is of statistical significance (p value<0.001) (Figure 3).

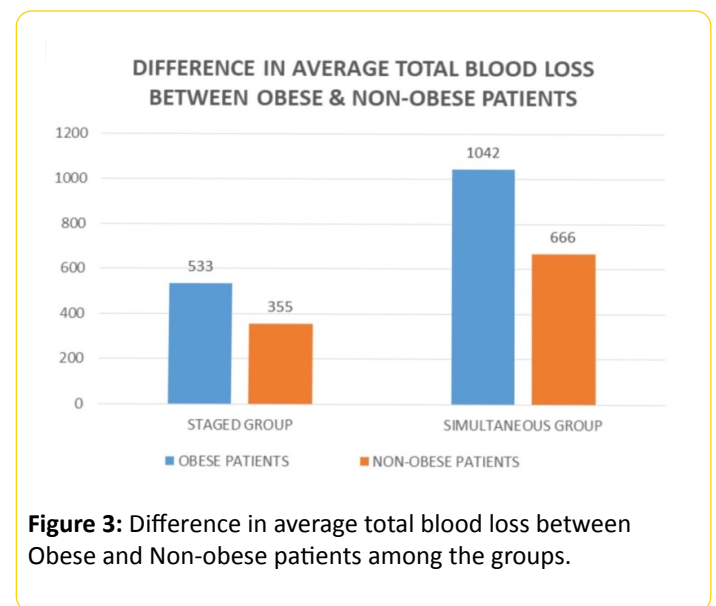


Figure 3: Difference in average total blood loss between Obese and Non-obese patients among the groups.

So hypertensive and obese patients in simultaneous group have more total blood loss, nearly twice as much of similar comorbid patients in staged group and this difference is of

statistical significance, in both hypertensive and obese patients. Meng [16] states that obesity can result in increased blood loss and there is not much of gender difference among blood loss in obese patients. Nwachukwu [14] found that being overweight/obese was independently associated with an increased risk for poor hemodynamic control. Autonomic dysfunction in these obese patients could be a possible cause for high blood loss during the perioperative period [17].

Male patients in staged and simultaneous group have a blood transfusion prevalence rate of 50% and 83% respectively which is more compared to female patients in their respective groups (staged group-33%; simultaneous groups-64%), but this difference is not of statistical significance (p value=0.08) (Figure 4). Prasad [14] states that there is a higher average blood transfusion requirement seen in male patients than in females but the difference is not statistically significant (p=0.05). Bong [18] states that male patients are associated with an increased need for transfusion. Given the increased blood loss seen in male gender compared to female patients, increased need for blood transfusion in male patients is well understood.

DIFFERENCE IN BLOOD TRANSFUSION PREVALENCE RATE BETWEEN MALE & FEMALE PATIENTS

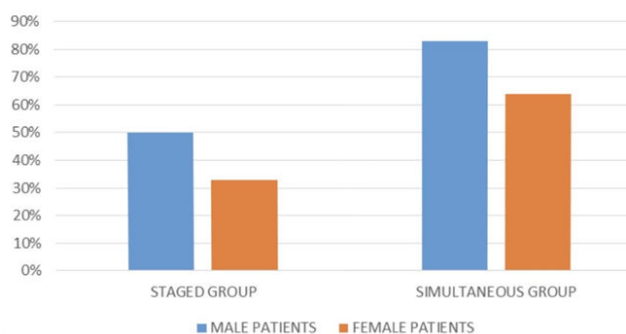


Figure 4: Difference in average blood transfusion prevalence rate between male and female patients among the groups.

Hypertensive patients in staged and simultaneous group have a blood transfusion prevalence rate of 33% and 75% respectively which is more compared to blood transfusion prevalence rate of non-hypertensive patients in their respective groups (Staged group-28%; Simultaneous group-70%). Therefore, among hypertensive patients, the average blood transfusion prevalence rate in the simultaneous group is more compared to the staged group and is not of statistical significance (Figure 5).

DIFFERENCE IN BLOOD TRANSFUSION PREVALENCE RATE BETWEEN HYPERTENSIVE & NON-HYPERTENSIVE PATIENTS

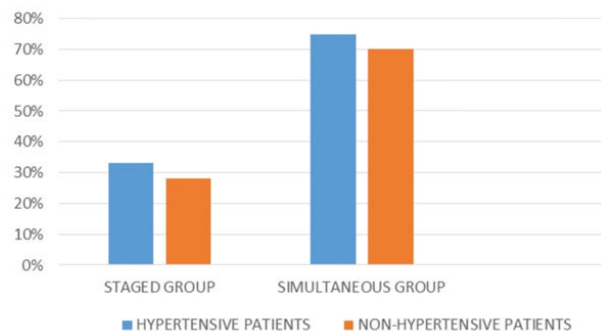


Figure 5: Difference in average blood transfusion prevalence rate between Hypertensive and Non-hypertensive patients among the groups.

Durasek [13] studied the factors affecting major blood loss in patients undergoing total knee arthroplasty, requirements for blood transfusion will be greater in patients with hypertension. Hafez [19] stated that patients with hypertension have a greater need for transfusion.

DIFFERENCE IN BLOOD TRANSFUSION PREVALENCE RATE BETWEEN OBESE & NON-OBESE PATIENTS

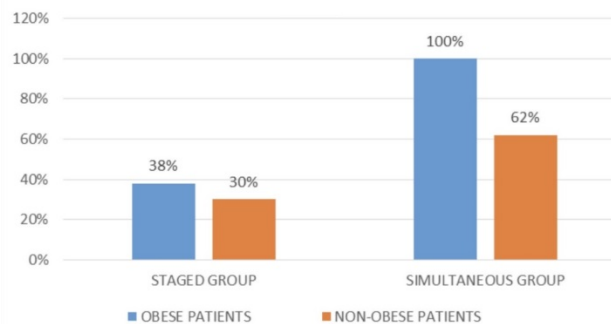


Figure 6: Average Blood transfusion prevalence rate between Obese and Non-obese patients among the groups.

Among patients with obesity, patients in the staged and simultaneous group have a blood transfusion prevalence rate of 37.5% and 100% which is more compared to the blood transfusion prevalence rate of non-obese patients in their respective groups (Staged group-30%; Simultaneous group-62%). Therefore, among obese patients, the blood transfusion prevalence rate in the simultaneous group is more compared to the staged group and is not of statistical significance (p<0.08) (Figure 6). Madsen [20] evaluated the perioperative complications of 2-team simultaneous bilateral TKA in the morbidly obese states that simultaneous group has an increased percentage of blood transfusion-64% compared to

staged group 11%. Hafez [19] stated that patients with obesity have a greater need for transfusion.

Increased bleeding after total knee arthroplasty may necessitate blood transfusion and result in knee joint swelling, knee motion restriction, and delayed recovery. Surgical trauma and the use of a pneumatic tourniquet activate the fibrinolytic system in the first few postoperative hours. Ischemia increases fibrinolysis owing to the proteolytic action of plasmin and this increases postoperative blood loss and thus the need for blood transfusion [21,22]. Tranexamic acid (TXA) is a synthetic amino acid that inhibits fibrinolysis by saturating the lysine binding sites of plasminogen, thereby competitively inhibiting plasminogen from binding to fibrin and thus intravenous administration of TXA reduces blood loss and thus the need for blood transfusion after TKR [23]. The male patients in staged and simultaneous group have an intravenous tranexamic acid prevalence rate of 33% and 35% respectively which is more compared to the female patients in their respective groups (staged group-27%; simultaneous groups-30%), but this difference is not of statistical significance (p value=0.79) (Figure 7).

DIFFERENCE IN INJECTION TRANEXAMIC ACID PREVALENCE BETWEEN MALE & FEMALE PATIENTS

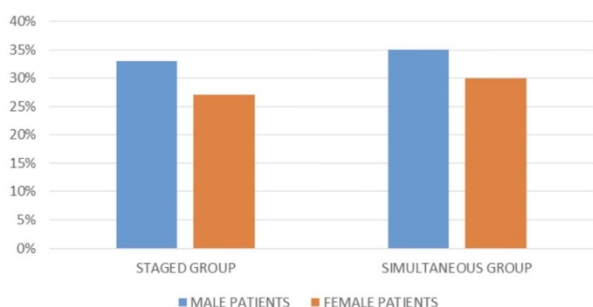


Figure 7: Difference in intravenous tranexamic acid prevalence between male and female patients among the groups.

Hypertensive patients in the staged and simultaneous group have an intravenous tranexamic acid prevalence rate of 37% and 40% respectively which is more compared to the normotensive patients in their respective groups (staged group-30%; simultaneous groups-31%), but this difference is not of statistical significance (p value=0.50) (Figure 8).

DIFFERENCE IN INJECTION TRANEXAMIC ACID PREVALENCE BETWEEN HYPERTENSIVE & NORMOTENSIVE PATIENTS

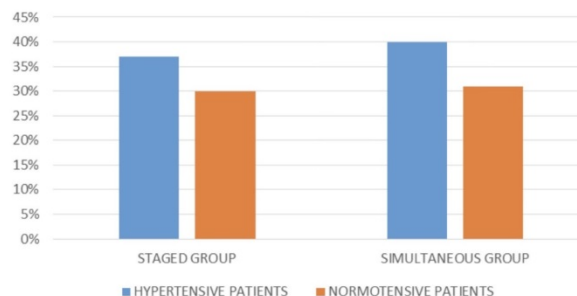


Figure 8: Difference in intravenous tranexamic acid prevalence between Hypertensive and Non-hypertensive patients among the groups.

Obese patients in staged and simultaneous group have an intravenous tranexamic acid prevalence rate of 38% and 45% respectively which is more compared to non-obese patients in their respective groups (staged group-34%; simultaneous groups-37%), but this difference is not of statistical significance (p value=0.70) (Figure 9). There is no report of venous thromboembolism in our cases. Tranexamic acid infusions are given only to indicated patients and not only based on total blood loss, so the difference will be noted between the average blood loss and the prevalence of blood transfusions since there is high total blood loss in male, hypertensive and obese patients compared to female, normotensive and non-obese patients still, this needs further research on the difference in usage based on gender difference and comorbidities to consolidate the findings of our study as literature is lacking on this topic.

DIFFERENCE IN INJECTION TRANEXAMIC ACID PREVALENCE BETWEEN OBESE & NON-OBESE PATIENTS



Figure 9: Difference in intravenous tranexamic acid prevalence between obese and Non-obese patients among the groups.

A potential limitation of this study is that the small sample size which precludes unstable perioperative and postoperative systemic complications from poor hemodynamic control. Only controlled hypertensive and diabetes patients were included

and also some patients had associated comorbidities like diabetes, coronary artery disease in this study whose prevalence is insignificant. Another potential limitation of this study pertains to the variability in pre-operative blood pressure readings due to the limited number of pressure recording as per the methodology and perioperative and postoperative weight loss in patients with obesity, especially in the staged group.

Complications such as deaths and cardiac and other systemic morbidities due to poor hemodynamic control are not reported in our patients. Allergies to blood transfusion are seen in two patients where we opted to adjuvant therapy.

Conclusion

We conclude that male gender, hypertension and obesity status play a significant role in perioperative blood loss and the incidence of blood transfusion and tranexamic acid infusion is high amongst male gender, hypertensive and obese patients during bilateral knee arthroplasty surgeries, but the percentile is higher in the simultaneous group of patients than the staged group.

So we emphasize the importance of hemodynamic control in the planning of bilateral knee replacement surgeries and that the staged bilateral total knee replacement procedure is preferred in patients who are prone to increased blood loss and requirement of blood transfusion and its related complications like in patients with comorbidities like hypertension and obesity and simultaneous procedure is preferred in selected patients without hypertension and obesity.

Conflict of Interest

Regarding this article, I announce no conflict of interest.

References

1. Ferket BS, Feldman Z, Zhou J, Oei EH, Bierma-Zeinstra SM, et al. (2017) Impact of total knee replacement practice: cost effectiveness analysis of data from the osteoarthritis initiative. *BMJ* 356: 1131.
2. Hutchinson JR, Parish EN, Cross MJ (2006) A comparison of bilateral uncemented total knee arthroplasty: simultaneous or staged? *J Bone Joint Surg Br* 88: 40-43.
3. Memtsoudis SG, Besculides MC, Reid S, Gaber-Baylis LK, Valle AGD (2009) Trends in Bilateral Total knee arthroplasties: 153,259 discharges between 1990 and 2004. *Clin Orthop Relat Res* 467: 1568-1576.
4. Kandemir T, Muslu S, Kalayci D, Kandemir E (2015) Effects of Systemic Disorders on Postoperative Complications After Simultaneous Bilateral Total Knee Replacement. *Turk J Anaesthesiol Reanim* 43: 169-173.
5. Angeli F, Reboldi G, Verdecchia P (2015) The 2014 hypertension guidelines: implications for patients and practitioners in Asia-Heart Asia 7: 21-25.
6. Mahajan K, Batra A (2018) Obesity in adult asian indians-the ideal BMI cut-off. *Indian Heart J.* 70: 195.
7. Gabr A, Withers D, Pope J, Santini A (2011) Functional outcome of staged bilateral knee replacements. *Ann R Coll Surg Engl.* 93: 537541.
8. Forster MC, Bauze AJ, Bailie AG, Falworth MS, Oakeshott RD (2006) A retrospective comparative study of bilateral total knee replacement staged at a one week interval. *J Bone Joint Surg Br* 88: 1006-10.
9. Parsley BS, Bertolusso R, Harrington M, Brekke A, Philip C (2010) Noble-influence of gender on age of treatment with TKA and functional outcome. *Clin Orthop Relat Res* 468: 1759-1764.
10. Kim HA, Kim S, Seo YI, Choi HJ, Seong SC, et al. (2008) The epidemiology of total knee replacement in South Korea: national registry data. *Rheumatology* 47: 88-91.
11. Charlson ME, MacKenzie CR, Gold JP, Ales KL, Topkins M, et al. (1990) Intraoperative blood pressure. What patterns identify patients at risk for postoperative complications? *Ann Surg* 212: 567-580.
12. Prasad N, Padmanabhan V, Mullaji A (2007) Blood loss in total knee arthroplasty: an analysis of risk factors. *Int Orthop.* 31: 39-44.
13. Durasek J, Dovzak-Bajs I, Sarić V (2010) Factors affecting blood loss in total knee arthroplasty patients. *Acta Med Croatica.* 64: 209-14.
14. Nwachukwu BU, Collins JE, Nelson EP, Concepcion M, Thornhill TS, et al. (2013) Obesity and hypertension are determinants of poor hemodynamic control during total joint arthroplasty: A retrospective review. *BMC Musculoskelet Disord* 14: 20.
15. Kordić K, Sakić K, Oberhofer D (2012) Analysis of blood pressure changes in patients undergoing total hip or knee replacement in spinal and general anesthesia. *Acta Clin Croat* 51: 17-23.
16. Meng Y, Li Z, Gong K, An X, Dong J, et al. (2018) Tranexamic acid reduces intraoperative occult blood loss and tourniquet time in obese knee osteoarthritis patients undergoing total knee arthroplasty: a prospective cohort study. *Ther Clin Risk Manag* 14: 675-683.
17. Kurukulasuriya LR, Stas S, Lastra G, Manrique C, Sowers JR (2011) Hypertension in obesity. *Med Clin North Am* Sep 95: 903-17.
18. Bong MR, Patel V, Chang E, Issack PS, Hebert R, et al. (2004) Risks associated with blood transfusion after total knee arthroplasty. *J Arthroplasty* 19: 281-7.
19. Hafez MA, Ghazal I (2016) Rate of Blood Transfusion in Patients Undergoing Bilateral Simultaneous Total Knee Arthroplasty using Patient-Specific Templates and Conventional Techniques: A Comparative Study. *Remed Open Access* 1: 1028.
20. Madsen AA, Taylor BC, Dimitris C, Hansen DC, Steensen RA, et al. (2014) Safety of bilateral total knee arthroplasty in morbidly obese patients. *Orthopedics* 37: e252-9.
21. Petäjä J, Myllynen P, Myllyla G, Vahtera E (1987) Fibrinolysis after application of a pneumatic tourniquet. *Acta Chir Scand* 153: 647-51.
22. Benoni G, Fredin H (1996) Fibrinolytic inhibition with tranexamic acid reduces blood loss and blood transfusion after knee arthroplasty: a prospective, randomised, double-blind study of 86 patients. *J Bone Joint Surg Br* 78: 434-40.
23. Eubanks JD (2010) Antifibrinolytics in major orthopaedic surgery. *J Am Acad Orthop Surg* 18: 132-8.