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# Predictors of Hemoglobin Drop in Patients Undergoing Primary Cemented Total Knee Arthroplasty (TKA): A Prognostic Study for Identification of Risk Factors

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**Abstract:**

***Objectives***

*Knee pain secondary to osteoarthritis had become a prevailing presenting complain to orthopedic surgeons, after exhausting conservative modalities for managing such disabling pain, Total Knee Arthroplasty (TKA) is considered the gold standard for surgical treatment. However, the surgery isn't free of complications including but not limited to blood loss intraoperatively. Blood loss with eventual post-operative anemia can be a potential cause of decline in the functional status of the patient with even delay to rehabilitation phase after surgery.*

***Methods***

*In our study, we performed a retrospective analysis of 171 patients who underwent primary cemented Total Knee Arthroplasty for advanced osteoarthritis looking for potential causes, risk factors for post-operative hemoglobin drop. We linked the hemoglobin drop against many other variables to find possible correlation.*

***Results***

*In our study there was a positive correlation between duration of surgery, intra-operative blood loss and hemoglobin drop. Since we are a teaching hospital, we performed a comparison analysis between surgeries done by consultants and ones done by residents, no major differences were recorded.*

***Conclusion***

*There was a statistically significant link between duration of surgery, estimated intra-operative blood loss, and the resultant hemoglobin drop thereafter.*

**Key Words:** *Total Knee Arthroplasty (TKA), Hemoglobin Drop, Blood Loss, Cemented Knee Arthroplasty.*

**Level of Evidence:** *Level 4, Cross sectional Descriptive Prognostic Study*

## 1. INTRODUCTION

Knee pain secondary to osteoarthritis is becoming a public health concern due to increasing numbers of aging populations, and it is estimated that it affects one third of persons older than 65 years [1]. Evidence based medicine has formulated a combined approach for management of this prevailing conditions using a pharmacological conservative approach and a non-pharmacological approach. The

conservative approach is essentially based on life style modifications, weight reduction, physical therapy, and judicious use of analgesics.

In patients with advanced knee osteoarthritis, in whom conservative management is proven to be ineffective, knee arthroplasty is a considered the mainstay of surgical treatment. Total knee arthroplasty (TKA) is a major orthopedic surgery which may result in significant blood loss both intra- and post-operatively [2]. Blood loss can adversely affect patients' clinical status and functional activity. Moreover, significant blood loss may necessitate blood transfusion, which also has its own complications [3,4].

The estimated amount of blood loss and the need for transfusion is variable in the current available literature [5-9]. In this retrospective study, we present our results after investigating potential factors or predictors of post-operative blood loss and hemoglobin drop in patients undergoing primary cemented TKA. Multiple variables were studied, including age, gender, presence of comorbid conditions especially Rheumatoid Arthritis (RA), and body mass index.

## 2. Patients and Methods

This retrospective study was conducted over a 6-months period starting from Jan 2021 to Jun 2021. Our study was approved by the Institutional Review Board (IRB) at our hospital, with IRB Number 10/2021/339. It involved all patients who underwent primary cemented TKA for knee osteoarthritis. Inclusion criteria were, all patients underwent primary cemented TKA during the assigned study period. Exclusion criteria were, patients underwent revision TKA, or cases requiring long stems or other complex prosthesis designs. A total of 171 patients were considered eligible in our study. Data were extracted from the health records at our institution.

Patients' age, height, weight, and body mass index (BMI) were all recorded. Other included variables were, duration of surgery, intra-operative blood loss, use of tranexamic acid, and blood pressure variations during surgery.

Prophylactic anticoagulation was held 12 hours before surgery, and resumed 12 hours after surgery. 3 patients were on Clopidogrel before surgery and it was held 5 days pre-operatively. The procedure was performed under spinal anesthesia, with the application and of tourniquet inflated to 150 mmHg above systolic blood pressure in all patients. It was deflated after wound closure and compressive dressings for better hemostasis control. A Redivac suction drain was used in 40 patients (23%). Recording intra-operative blood loss was done via calculating the amount of blood in the suction container after subtracting the amount used for irrigation intra-operatively. Measuring blood loss was double checked both from the surgical operative notes and the anesthesia sheet.

We recorded hemoglobin (Hb) and packed cell volume (PCV) levels pre-operatively and post-operatively for all patients and measured the difference between the pre-operative and the lowest post-operative value.

Patients were allowed full weight bearing as tolerated in the post-operative day one, with initiation of full range of motion exercises. The cut-off point for blood transfusion was a hemoglobin (Hb) level below 8.0 along with symptoms of hypovolemia. Only 5 patients (3%) received blood transfusions during the study period.

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) version 23. A comparison was made between the hemoglobin differences between pre-op and post-op values against wide range of different variables including but not limited to age, BMI, duration of surgery, and ASA score. A regression analysis and student t test were used. All values were calculated as mean ± standard deviation. P value less than 0.05 was considered significant. Attempts were made to find out whether factors such as BMI, gender and diagnosis have any relation to total blood loss.

## 3. Results

171 patients met the inclusion criteria and were included in the study. 86.5% (148 patients)

were female. Around (51.5%) underwent right total knee arthroplasty, and 48.5% underwent for left total knee arthroplasty. All prostheses were cemented and without patellar resurfacing. The mean age of participants was 65.9 ± 7.2 years, the mean Body Mass Index (BMI) was 31.8 ± 5.3**.[Table 1]** Tranexamic acid was used in nearly half of the patients (50.3%). They were given 1 gram of tranexamic acid before skin incision and 1 gram at closure. About two thirds of our included patients were American Society of Anesthesiologists (ASA) II. In 40 patients (23.4%), a Redivac drain was used for better hemostasis due to concerns of bloody surgery.

**Table 1.** *Patient's demographics information*

| Parameter | Differences with percentage | | | | | |
|---|---|---|---|---|---|---|
| Gender n (%) * | Male | 23 | 13.5% | Females | 148 | 86.5% |
| Smoking n (%) | Smoker | 14 | 8.2% | Non-smoker | 157 | 91.8% |
| Site of surgery n (%) | Left | 83 | 48.5 | Right | 88 | 51.5% |
| Comorbidities (DM, HTN) n (%) | Present | 118 | 69 % | Not-present | 53 | 31% |
| **Variables expressed in mean + Standard deviation** | | | | | | |
| Age (years) | Mean | 65.9 | SD | | 7.2 | |
| Height (cm) | Mean | 163.1 | SD | | 12.2 | |
| Weight (kg) | Mean | 84.4 | SD | | 7.0 | |
| BMI | Mean | 31.8 | SD | | 5.3 | |
| * Numbers are presented as Number (Percent), DM: Diabetes Mellitus, HTN: Hypertension, BMI: Body Mass Index kg/m$^2$ | | | | | | |

In terms of use of anticoagulants, 52 patients (30.4%) were on Aspirin 100 mg which wasn't stopped perioperatively, 3 patients were on Clopidogrel 75 mg, which was held 5 days before surgery. All included patients received prophylactic dose of Enoxaparin 40 mg SC 12 hours before the time of surgery, and then resumed 12 hours after the surgery. Regarding complications of post-operative bleeding, 5 patients (2.9%) received blood transfusion, 4 patients developed wound complications from persistent oozing (2.3%) at the site of surgery [Table 2].

**Table 2.** *Summary of peri-operative complications*

| Parameter | Description (No. of patients combined with percentage) | |
|---|---|---|
| VTE (Thromboembolic events) | 9 | 5.3 % |
| Cardiovascular | 5 | 2.9 % |
| Wound (oozing) | 4 | 2.3 % |
| ICU admissions | 4 | 2.3 % |
| Blood transfusion (post-op) | 5 | 2.9 % |
| VTE: Venous thromboembolism, ICU: Intensive Care Unit | | |

To assess post-operative hemoglobin drop, we subtracted the lowest hemoglobin value post-operatively from the pre-operative value to create a variable for comparison with other variables. The mean duration of surgery was 115.4 ± 26.5 minutes, the mean intra-operative blood loss was 201.3 ± 113.8 ml, and the mean hemoglobin drop was 1.8 ±1.03 mg/dl [Table 3]. Using Pearson correlation and two tailed p-value for association, we found a positive correlation between Hemoglobin drop and patient's age (r=0.034; *P*= 0.66), and the duration of surgery (r=0.176; *P* = 0.021). Another positive correlation was evident between the amount of intra-operative blood loss in milliliters and the duration of surgery (r=0.225; *P* = 0.003) [Table 4].

**Table 3.** *Summary of peri-operative variables related to hemoglobin drop*

| Parameter | Mean * | SD |
|---|---|---|
| Duration of Surgery (min.) | 115.4 | 26.5 |
| Tourniquet time (min.) | 128 | 26.3 |
| Blood loss (ml) | 201.3 | 113.8 |
| Max. systolic BP intra-op. (mm Hg) | 152 | 23.8 |

| | | |
|---|---|---|
| Length of stays (days) | 5 | 3 |
| * Numbers are presented as Mean ± Standard Deviation | | |

**Table4.** *Pearson correlation of variables related to blood loss*

| Correlations | | | | | |
|---|---|---|---|---|---|
| | | Age | BMI | Duration of Surgery (min) | Intra-op Blood Loss |
| Hemoglobin Drop | Pearson Correlation | 0.034 | -0.027 | 0.176 | -0.035 |
| | Sig. (2-tailed) | 0.660 | 0.728 | 0.021 | 0.650 |
| | | **Age** | **BMI** | **Hemoglobin Drop** | **Intra-op Blood Loss** |
| **Duration of Surgery (min)** | Pearson Correlation | 0.009 | 0.090 | 0.176* | 0.225 |
| | Sig. (2-tailed) | 0.909 | 0.239 | 0.021 | 0.003 |
| | | Age | BMI | Hemoglobin Drop | Duration of Surgery (min) |
| Intra-op Blood Loss | Pearson Correlation | 0.016 | -0.093 | -0.035 | 0.225 |
| | Sig. (2-tailed) | 0.837 | 0.227 | 0.650 | 0.003 |

The mean length of hospital stay was 5.2 ± 3.0 days. Upon investigating predictors of the duration of hospital stay, we found positive Pearson's correlation with the duration of surgery (r= 0.31; $P < 0.001$) and the estimated blood loss (r= 0.27; $P < 0.001$).

Overall, 14 patients had perioperative complications, of which 8 (57.1%) did not receive tranexamic acid, while 6 (42.9%) received it ($P = 0.561$), accounting to a complication rate of 9.4% and 7% respectively among the two groups. However, no significant difference was found between the aforementioned groups in terms of ICU admissions ($P = 0.621$). Notably, a drain was used in 30 (35.3%) of the patients who did not receive tranexamic acid, compared to only 10 (11.6%) among those who received it ($P < 0.001$). No significant differences were found between the two groups in the duration of surgery ($P = 0.635$), intraoperative blood loss ($P = 0.99$), hemoglobin level difference ($P = 0.141$), and the length of hospital stay ($P = 0.44$).

We compared surgeries performed by orthopedic consultants and those done by senior orthopedic residents. Although no significant differences were found between them in terms of the duration of surgery ($P = 0.205$), surgeries performed by orthopedic residents had increased mean intra-operative blood loss (229.4 ± 93.6 ml versus 190.4 ± 119.4 ml; $P = 0.013$); however, without significant differences between hemoglobin drop (1.7 ± 0.8 mg/dl vs 1.9 ± 1.1 mg/dl; $P = 0.163$). On the other hand, the mean length of hospital stays for both groups were nearly the same (5.3 ± 3.4 days for consultants versus 5.1 ± 1.5 days for residents; $P = 0.591$), with no significant difference between them in perioperative complications ($P = 0.965$) **[Table 5].**

**Table5.** *Differences between overall complications including bleeding complications with resulting post-operative hemoglobin drop between surgeries done by the consultant versus residents*

| Variable | Surgeon | | Total (n=171) | p-value |
|---|---|---|---|---|
| | Consultant (n=123) | Resident (n=48) | | |
| VTE | 7 (5.7) | 2 (4.2) | 9 (5.3) | 1 |
| CVS | 3 (2.4) | 2 (4.2) | 5 (2.9) | 0.621 |
| Wound | 4 (3.3) | 0 (0) | 4 (2.3) | 0.578 |
| Use of drain | 32 (26.0) | 8 (16.7) | 40 (23.4) | 0.194 |
| Duration of surgery (minutes) | 116.8 ± 26.8 | 111.9 ± 25.9 | 115.40 ± 26.6 | 0.205 |
| Estimated blood loss (mL) | 190.4 ± 119.4 | 229.4 ± 93.6 | 201.3 ± 113.9 | 0.013 |
| Time of tourniquet (minutes) | 129.8 ± 26.3 | 124.2 ± 26.3 | 128.2 ± 26.4 | 0.169 |
| Length of stay (days) | 5.3 ± 3.4 | 5.1 ± 1.5 | 5.2 ± 3.0 | 0.591 |
| Hb difference (g/dL) | 1.9 ± 1.1 | 1.7 ± 0.8 | 1.8 ± 1.0 | 0.163 |

Data are presented as: Number (percentage), VTE: Venous thromboembolic events, CVS: Cardiovascular events. Wound complications mainly represent recurrent oozing. Hb: Hemoglobin differences.

## 4. DISCUSSION

Total Knee Arthroplasty (TKA) is considered a major surgery with ensuing blood loss. The missing blood can be either revealed or apparent during surgery, or, it could be hidden in the form of soft tissue hematoma. Both forms can contribute to post-operative hemoglobin drop. Post-operative anemia in these patients confer negative functional outcome in terms of rehabilitation [10-13]. Therefore, identification of potential risk factors and predictors of this condition is of paramount importance for better functional and rehabilitative outcome.

In the present study, patients' demographics were: mean age of 66 years, mean BMI 31.8, and preponderance of patients being females (86.5%). Consistently other scholars reported approximate numbers. Boutsiadis et al in their study to predict blood transfusion need in TKA reported mean age of 69.5 years, mean BMI of 28.5, and female gender percentage of (61.3%)[14]. Kalairajah et al in their study of blood loss in computer assisted TKA reported a mean age of 66 years, with more female participants 63.3% [15]. Cao et al. reported in their work a mean age of 66.8 years, a female predominant participants (69%), however, lower BMI compared to our study (mean 26.4)[16]. Of note in our patient sample is that the majority of patients were non-smokers (91.8%), this variable was not usually mentioned in the previous literature.

In our study, we found that the average amount of blood loss was 200 ml which is much lower than what is reported in the literature. Narayana et al, in their prospective study of 66 patients underwent primary cemented total knee arthroplasty reported blood loss of 220 ml [17]. Hatzidakis et al, in their retrospective study for patients undergoing total knee arthroplasty reported a blood loss of 310 ml[18]. However, in studies were tourniquet was not used, there was much higher blood loss as reported by Aglietti et al[19], Vandenbussche et al[20], and Fukuda et al[21], with blood loss of 482 ml, 1557 ml, and 1089 ml respectively. We believe that this lower blood loss is probably due to routine use of tourniquet and keeping it inflated until the application of compressive dressing after wound closure.

Most previous literature focused on quantitative measurement of blood loss and then using it to establish a cut off point for transfusion requirements. Quantifying hemoglobin drop sheds light on the effect of post-operative anemia on the post-operative patient-related parameters like functional and quality of life issues, length of hospital stays, and transfusion requirements [22-24]. However, in our study we preferred to concentrate more on another parameter and to use a different approach by not only measuring the blood loss, but also quantifying degree of hemoglobin drop post-operatively. In our study, the mean hemoglobin drop post-operatively was 1.8 mg/dL. Influential risk factors deemed culprit were by far the intra-operative blood loss and duration of surgery. Unlike results presented by Prasad et al., there was no influence of either tourniquet time or gender[25]. Other potential suspected factors didn't seem to contribute much to hemoglobin drop.

As a teaching institute, we focus on high quality resident training and building a high profile of surgical skills for residents. In this study we compared results of Total Knee Arthroplasty (TKA) performed by residents and those done by consultants in terms of general perioperative complications, duration of surgery, and intra-operative blood loss. As depicted in Table 5, there was no statistically significant differences in hemoglobin drop ($p = 0.1$) between surgeries performed by residents and those performed by consultants [Table 5]. The same case was evident also in peri-operative complications (cardiovascular complications $p= 0.6$, wound complications $p= 0.5$, and duration of surgery $p=0.2$). According to the authors' best knowledge and current available literature, no previous study focused on this issue, so, we believe that the blood loss and hemoglobin drop is unlikely to be related to person who performs surgery provided having a standard quality of surgical training.

As evident in table 6 which compares male and female participants, there was no significant differences between the two groups in term of estimated blood loss, length of hospital stays or hemoglobin drop, however, difference was noted in duration of surgery, and tourniquet time in favor to females, which mean surgery for male patients tends to have more blood loss mostly due to using larger prosthesis and much surface area for surgery [Table 6].

**Table6.** *Differences between males and females*

| Variable | Gender | | Total (n=171) | p- value |
|---|---|---|---|---|
| | male (n=23) | Female (n=148) | | |
| Use of drain | 5 (21.7) | 35 (23.6) | 40 (23.4) | 0.84 |
| Duration of surgery (minutes) | 127.6 ± 28.6 | 113.5 ± 25.8 | 115.40 ± 26.6 | 0.026 |
| Estimated blood loss (mL) | 207.0 ± 153.0 | 200.5 ± 107.2 | 201.3 ± 113.9 | 0.689 |
| Time of tourniquet (minutes) | 138.3 ± 27.2 | 126.6 ± 26.0 | 128.2 ± 26.4 | 0.036 |
| Length of stay (days) | 6.9 ± 7.0 | 5.0 ± 1.6 | 5.2 ± 3.0 | 0.057 |
| Hemoglobin difference | 2.1 ± 1.0 | 1.8 ± 1.0 | 1.8 ± 1.0 | 0.178 |

There are some limitations to this study typical of non-comparative observational studies, our analysis was retrospective, and most of the sample were females and non-smokers which reduces the accuracy of measuring the effect of male gender and smoking on blood loss. Moreover, measurement of post-operative hemoglobin was done mostly on postoperative day 1 and 2, raising the probability of missing delayed post-operative blood loss as noticed in previous studies [26]. As a summary, there was a statistically significant association between duration of surgery, intra-operative blood loss and eventual hemoglobin drop post-operatively.

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