Effects of the ratios of marrow cavity diameter to intramedullary nail diameter from different layers on blood loss during perioperative period for femoral intertrochanteric fractures

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Abstract
The study aimed to investigate the effect of ratios of marrow cavity diameter to intramedullary nail diameter from different layers on hidden blood loss (HBL), overt blood loss (OBL) and total blood loss (TBL) during using proximal femoral nail antitrotation-Asian version (PFNA)-II for femoral intertrochanteric fractures.

We retrospectively studied 70 patients treated in our hospital recently. We recorded postoperative hematocrit (Hct) and OBL during operation. TBL and HBL were calculated using CROSS equation. The ratios of marrow cavity diameter to intramedullary nail diameter from different layers, including start of funnel, end of funnel and femoral ishthmus, were measured. The mean of the ratio from frontal and lateral X-ray were designated as R. We classified all included participants into a high and a low matching group according to z-score of R within each layer. TBL, HBL, and OBL were compared between the 2 groups. We applied multiple linear regression analysis between the HBL as a dependent variable and gender, age, body mass index, fracture type, and R as independent variables.

The present study indicated a significant reduction in the HBL and TBL in the high matching group compared to low matching group on three layers, whereas it showed no significant difference in OBL between the 2 groups on three layers. It showed that R values from start of funnel and end of funnel were significantly associated with HBL.

Matching rate of PFNA II at the funnel might be an important factor for HBL and TBL postoperatively.

Abbreviations: APTT = activated partial thromboplastin time, BMI = body mass index, CT = computed tomography, HBL = hidden blood loss, Hct = hematocrit, IBL = intraoperative blood loss, LOS = length of hospital stay, OBL = overt blood loss, PFNA = proximal femoral nail antitrotation-Asian version, PT = prothrombin time, TBL = total blood loss.

Keywords: femoral intertrochanteric fracture, hidden blood loss, matching rate, perioperative period, PFNA

1. Introduction
Intertrochanteric fractures are mostly common in the elderly population[1] and have become increasingly common due to the increase in the elderly population.[2,3] In addition, 35% to 40% of these fractures are classified as unstable (AO/OTA classification: 31-A2/31-A3) and thus are related to high disability rate.[4] According to previous studies, types of intertrochanteric fracture[5] and treatment[5] might affect functional outcomes and mortality in patients. It remains controversial for the optimal implant for repairing of intertrochanteric fractures. Present treatments include extramedullary and intramedullary fixation. Gamma nail placement and proximal femoral nail antitrotation (PFNA) were included in methods of intramedullary fixation. PFNA-II is specially designed for the Asian population, and accommodates the anatomic characteristics of Asian.[1,7,8] Some clinical trials demonstrated that intramedullary fixation is beneficial to patients with unstable peritrochanteric fractures, which might be associated with less blood loss and fewer complications compared to Dynamic hip screw (DHS) fixation.[7,8] However, according to previous studies, hidden blood loss (HBL) often occurs after intramedullary nailing of intertrochanteric fractures. Foss[8] reported that intramedullary nailing of hip fractures contributed to more HBL than did other methods of fixation. However, surgeons often ignore the HBL in patients treated with intramedullary fixations, because of a relatively simple surgical procedure, short operative time and less overt blood loss (OBL). Consequently, critical patients are not
dealt timely or occurred other complications. Patients with underlying anemia have a greater risk of dying in the perioperative period than others.\textsuperscript{[8,9]} Thus, HBL should be minimized during surgery for intertrochanteric fracture. Heterogeneity among individuals in HBL according to our clinical observation showed that there might be some potential factors affecting the amount of HBL. Previous studies have explored the influence of age, gender, body mass index (BMI), and fracture type on HBL.\textsuperscript{[10,11]} Until now, no study explored the effect of matching degree of intramedullary nail to marrow cavity on HBL. The present aimed to explore the effect of the ratios of marrow cavity diameter to intramedullary nail diameter from different layers on HBL, OBL, and total blood loss (TBL) in the perioperative period during using PFNA-II for femoral intertrochanteric fracture.

2. Materials and methods

2.1. Patients

The present study was a retrospective study including patients managed operatively in Department of Orthopedics, Suzhou Municipal Hospital between January 2015 and November 2018. Finally, the study included 70 patients treated with PFNA-II for femoral intertrochanteric fracture. Mean age of patients was 79.9 years (ranged from 45–98 years old), 46% male gender. Time interval from injury to operation was 2 to 6 days. Fractures were classified on the basis of the AO classification, 31. A1-A3. We reviewed all patients’ electronic medical records retrospectively. We recorded variables such as age, gender, height, weight, BMI, preoperative and postoperative hematocrit (Hct) levels, intraoperative blood loss (IBL), operation time, length of hospital stay (LOS), and fracture classification. Written informed consents were obtained from all the participants, and this study was reviewed all patients’ electronic medical records retrospectively. We recorded variables such as age, gender, height, weight, BMI, preoperative and postoperative hematocrit (Hct) levels, intraoperative blood loss (IBL), operation time, length of hospital stay (LOS), and fracture classification. Written informed consents were obtained from all the participants, and this study was reviewed all patients’ electronic medical records retrospectively. Written informed consents were obtained from all the participants, and this study was reviewed all patients’ electronic medical records retrospectively.

2.2. Inclusion criteria and exclusion criteria

All included patients meet the criteria, which included:

1. patients with a confirmed diagnosis of unilaterally acute and closed intertrochanteric fracture and fracture classified according to AO type on X-ray or computed tomography (CT);
2. the following data were provided: height, weight, blood routine results at the third day preoperatively and postoperatively;
3. fracture was treated with closed reduction and PFNA-II fixation;
4. the amount of rehydration did not exceed 2000ml;
5. the prothrombin time (PT) and activated partial thromboplastin time (APTT) were in the normal range;
6. no serious liver or kidney and no history of digestive tract bleeding.

The exclusion criteria include patients without postoperative images and non-standard placement of implant, with lower extremity arteriosclerosis obliterans, receiving anti-coagulation therapy (e.g. low molecular weight heparin or NOACs) or hemostatic therapy pre- or before a blood routine test obtained on the second or third postoperative day and failure of internal fixation.

2.3. Management of blood loss

A team of senior surgeons performed all the operations following a standard surgical technique recommended by the manufacturer (PFNA-II, Sunan Temed, China). IBL was evaluated by the measured suction loss and blood loss in swabs, and recorded by the anesthetists. No patients obtained wound drainage. Thus, the OBL was equal to IBL. Additionally, a blood routine test, including Hct levels, was obtained preoperatively and on the second or third postoperative day for calculation of blood loss.

2.4. Calculation of HBL

According to methods provided by Gross et al.\textsuperscript{[12]} the TBL was calculated on the basis of the Hct level and the patient’s blood volume (PBV), as follows:

\[
\text{TBL (ml)} = \frac{\text{PBV} \times (\text{Hct}_{\text{pre}} - \text{Hct}_{\text{post}})}{\text{Hct}_{\text{ave}}} \times 1000;
\]

\[
\text{Hct}_{\text{ave}} = \frac{\text{Hct}_{\text{pre}} + \text{Hct}_{\text{post}}}{2}.
\]

\[
\text{PBV} = k_1 \times \text{height}^3 + k_2 \times \text{weight}^2 + k_3;
\]

k1=0.3669, k2=0.03219 and k3=0.6041 for males, and k1=0.3561, k2=0.03308 and k3=0.1833 for females.

In addition, on the basis of methods provided by Sehat et al.\textsuperscript{[13]} HBL was calculated by using the following formula:

\[
\text{HBL (ml)} = \text{TBL (ml)} - \text{IBL (ml)}.
\]

2.5. Calculation of R

According to postoperative X-ray results, the ratios of marrow cavity diameter to intramedullary nail diameter from different layers, including start of funnel, end of funnel and femoral isthmus, were measured. The mean of the ratio from frontal and lateral X-ray were designated as R. We classified the all included participants into a high matching group and a low matching group according to z-score of R within each layer. All individuals reporting a z-score < 0 were considered as belonging to a high matching group. Conversely, individuals with a z-score ≥ 0 were considered as belonging to a low matching group. In addition, TBL, HBL, and OBL were compared between the 2 groups. We applied multiple linear regression analysis between the HBL as a dependent variable and age, fracture type and R as independent variables. Figure 1 showed the start of funnel, end of funnel, and femoral isthmus in frontal and lateral X-ray.

2.6. Statistical analysis

The statistical analyses were implemented with SPSS 21.0 software. Statistical threshold was set at a \( P < .05 \). Ratio statistics were applied to calculate the ratio of HBL to TBL in different groups. Normal distribution for continuous data
...was assessed by the Kolmogorow–Smirnoff test. For continuous
data with a normal distribution we used an independent-samples \( t \)
test for independent samples; the Mann–Whitney test was used
when normality was rejected. Independent-samples \( t \) test and Chi-
Squared test were performed to compare the demographic data,
TBL, HBL, and OBL between low matching group and high
matching group. A step-wise multivariate linear regression analysis
was performed to relate several independent factors, including age,
gender, BMI, fracture type, \( R \) in different layers, to HBL.

3. Results

According to the \( z \)-scores of \( R \) of start of funnel, included
individuals were divided into the 2 groups: low matching group
(\( n = 31 \)) and high matching group (\( n = 39 \)). Ratio statistics
indicated that HBL accounted for approximately 80% of TBL
(84.7% in low-matching group and 78.0% in high-matching
group, respectively). Table 1 showed demographic data, TBL,
HBL, and OBL between the 2 groups. Figure 2 showed TBL,
HBL, and OBL comparisons between the 2 groups. Independent-

Table 1

|                      | Low matching group (\( n = 31 \)) | High matching group (\( n = 39 \)) | \( t \) or \( \chi^2 \) | \( P \) |
|----------------------|----------------------------------|-----------------------------------|------------------------|-------|
| Age                  | 79.87 (10.14)                    | 79.92 (9.22)                      | \(-0.022\)             | \( .982^* \) |
| Gender (male/female) | 17/14                            | 15/24                             | \( 1.867 \)            | \( .172^\dagger \) |
| BMI (kg/m\(^2\))     | 21.33 (2.80)                     | 22.70 (4.39)                      | \(-1.576 \)            | \( .120^* \) |
| AO type (I/II/III)   | 14/11/6                          | 16/22/1                           | \( 4.543 \)            | \( .053^* \) |
| TBL (ml)             | 1061.2 (389.7)                   | 771.1 (333.6)                     | \( 3.354 \)            | \( .001^\dagger \) |
| OBL (ml)             | 142.9 (61.1)                     | 132.8 (53.4)                      | \( 0.625 \)            | \( .534^* \) |
| HBL (ml)             | 918.3 (393.7)                    | 638.3 (336.0)                     | \( 3.209 \)            | \( .002^* \) |

Data are presented as mean ± standard deviation (SD).

\( ^* \) \( P \) values were obtained by Independent-samples \( t \) test.

\( ^\dagger \) \( P \) value was obtained by Chi-Squared test.

\(^\dagger\dagger \) Significant differences were found in between the 2 groups.

BMI = body mass index, HBL = hidden blood loss, OBL = overt blood loss, TBL = total blood loss.
samples $t$ tests indicated no significant difference in age and BMI between the 2 groups. A Chi-Squared test indicated no significant difference in gender and fracture AO types between 2 groups. Independent-samples $t$ tests showed decreased TBL and HBL in low-matching group, compared to high-matching group, whereas it showed no significant difference in OBL between the 2 groups. On the basis of the z-scores of $R$ of end of funnel, we classified included individuals into the 2 groups: low matching group ($n=29$) and high matching group ($n=41$). Ratio statistics showed that HBL accounted for approximately 80% of TBL (87.3% in low-matching group and 76.5% in high-matching group, respectively). Table 2 showed demographic data, TBL, HBL, and OBL between the 2 groups. Figure 3 showed TBL, HBL, and OBL comparisons between the 2 groups. Independent-samples $t$ tests showed no significant difference in age and BMI between the 2 groups. A Chi-Squared test indicated no significant difference in gender and fracture AO types between the 2 groups. Independent-samples $t$ tests showed decreased TBL and HBL in low-matching group, compared to high-matching group, whereas it showed no significant difference in OBL between the 2 groups. According to the z-scores of $R$ of femoral isthmus, we divided included patients into the 2 groups: low matching group ($n=32$) and high matching group ($n=38$). Ratio statistics indicated that HBL accounted for approximately 80% of TBL (84.5% in low-matching group and 77.9% in high-matching group, respectively).

4. Discussion

The present study indicated that the ratios of marrow cavity diameter to intramedullary nail diameter measured in start of funnel, end of funnel layers were significantly associated with HBL, whereas age, gender, BMI, and fracture type were not significantly correlated to HBL.

The concept of HBL was firstly proposed by Sehat et al.

Evidence suggested that TBL during hip fracture surgery may be much greater than OBL. One study reported that TBL was 1473 ml greater than OBL in patients undergoing hip surgery.

Table 2 showed demographic data, TBL, HBL, and OBL between the 2 groups. Figure 4 showed TBL, HBL, and OBL comparisons between the 2 groups. Independent-samples $t$ tests indicated no significant difference in age and BMI between the 2 groups. A Chi-Squared test indicated no significant difference in gender and fracture AO types between the 2 groups. Independent-samples $t$ tests showed decreased TBL and HBL in low-matching group, compared to high-matching group, whereas it showed no significant difference in OBL between the 2 groups.

Multivariate linear regression analysis indicated that the ratios of marrow cavity diameter to intramedullary nail diameter measured in start of funnel, end of funnel layers were significantly associated with HBL, whereas age, gender, BMI, and fracture type were not significantly correlated to HBL (Table 4).

### Table 2

| Demographic data and blood loss for included patients, who were grouped according to z-score of $R$ (the ratios of marrow cavity diameter to intramedullary nail diameter) from end of funnel. |
|-----------------|-----------------|-----------------|
| **Age**  | 80.45 (8.15) | 79.51 (10.54) |
| **Gender (male/female)** | 15/14 | 17/24 |
| **BMI (kg/m²)** | 22.84 (3.89) | 21.57 (3.70) |
| **AO type (I/II/III)** | 12/13/4 | 18/20/3 |
| **TBL (ml)** | 1099.5 (335.6) | 758.2 (357.2) |
| **OBL (ml)** | 128.3 (45.2) | 143.7 (78.5) |
| **HBL (ml)** | 971.2 (325.0) | 614.5 (300.0) |

Data are presented as mean ± standard deviation (SD).

$^*$ $P$ values were obtained by Independent-samples $t$ test.

$^+$ $P$ value was obtained by Chi-Squared test.

Significant differences were found in between the 2 groups.

BMI = body mass index, HBL = hidden blood loss, OBL = overt blood loss, TBL = total blood loss.
Another study[16] showed $277.2 \pm 7.6$ ml HBL in patients undergoing PFNA for intertrochanteric fractures. These results were corresponding to our result that HBL accounted for approximately 80% of TBL. Until now, the causes and mechanism of HBL are not yet clear. Intertrochanteric fracture belongs to fractures of the metaphysis with rich blood supply. The process of expanding the medullary cavity could lead to internal bleeding after the intramedullary needle was fixed. Additionally, the intramuscular gaps and intramedullary cavities could also provide storage cavities for HBL. Smith[17] indicated that the main reason for HBL is that perioperative blood pours into the tissue compartments that are not involved in the systemic circulation. In addition, an abnormal capillary bed opening caused by free fatty acids, intraoperative intramedullary fat, bone cement and bone debris entering the blood circulation results in further reduction of hemoglobin levels. Millar et al[18] suspected intramedullary penetration might contribute to HBL. Foss et al[19] speculated that HBL might originate from the initial trauma, postoperative hemorrhage, and the gastrointestinal tract. However, up to now, there is not yet fully evidence to support these ideas. It is essential that we should focus on the calculation of HBL, individualized estimation of TBL and perioperative monitoring, including changes in vital signs and urine, changes of blood glucose and blood pressure, supplementation of blood levels, and prevention of deep-vein thrombosis.

Notably, the present study indicated that the ratios of marrow cavity diameter to intramedullary nail diameter measured in start of funnel, end from medullary cavity of total femoral, preventing perioperative blood pouring into the tissue compartments and free fatty acids entering the blood circulation.

#### Table 3: Demographic data and blood loss for included patients, who were grouped according to z-score of R (the ratios of marrow cavity diameter to intramedullary nail diameter) from femoral isthmus.

|                | Low-matched group (n = 32) | High-matched group (n = 38) | t or χ² | P   |
|----------------|----------------------------|-----------------------------|---------|-----|
| Age            | 82.06 (6.870)              | 78.08 (11.12)               | 1.832   | .072|
| Gender (male/female) | 14/18                   | 18/20                       | 0.092   | .762|
| BMI (kg/m²)    | 22.76 (4.760)             | 21.53 (2.700)               | 1.304   | .199|
| AO type (I/II/III) | 15/12/5                  | 15/21/2                     | 3.250   | .197|
| TBL (ml)       | 996.9 (367.7)             | 817.6 (385.2)               | 1.881   | .046|
| OBL (ml)       | 128.8 (45.40)             | 144.5 (80.40)               | 0.981   | .330|
| HBL (ml)       | 868.2 (364.6)             | 673.1 (386.0)               | 2.160   | .034|

Data are presented as mean ± standard deviation (SD).

* P values were obtained by Independent-samples t test.

† P value was obtained by Chi-Squared test.

‡ Significant differences were found in between the 2 groups.

BMI = body mass index, HBL = hidden blood loss, OBL = overt blood loss, TBL = total blood loss.

#### Table 4: Multiple linear regression analysis on influential factors of HBL in each group.

|                | Beta | t     | P value |
|----------------|------|-------|---------|
| Constant       | –    | –2.500| .015∗   |
| Age            | –0.067| –0.701| .486    |
| Gender         | –0.165| –1.660| .101    |
| BMI            | 0.202 | 2.000 | .050    |
| Fracture type  | 0.053 | 0.573 | .568    |
| R1             | 0.271 | 2.110 | .039†   |
| R2             | 0.478 | 3.060 | .003∗   |
| R3             | –0.069| –0.518| .606    |

† Significant associations.

BMI = body mass index, R1 = the ratios of marrow cavity diameter to intramedullary nail diameter) from start of funnel, R2 = the ratios of marrow cavity diameter to intramedullary nail diameter) from end of funnel, R3 = the ratios of marrow cavity diameter to intramedullary nail diameter from femoral isthmus.

The process of expanding the medullary cavity could lead to internal bleeding after the intramedullary needle was fixed.

The present study provided evidence to support that the ratios of marrow cavity diameter to intramedullary nail diameter might be an important factor for HBL in the perioperative period during PFNA-II stabilization for femoral intertrochanteric fracture.
However, the present study showed that age, gender, BMI, and fracture type were not significantly correlated with HBL. The results were consistent with 2 recent studies, which revealed that HBL was not associated with age, gender, BMI, percentage of height loss, percentage of height restoration, fracture type, or operation time with multivariate linear regression analysis. However, another study indicated that several readily available preoperative factors in the form of non-drainage, BMI<23 kg/m², admission specific gravity of urine <1.020, fracture type, and admission albumin <30g/L were associated with a greater likelihood of larger HBL.

The study explored the effect of the ratios of narrow cavity diameter to intramedullary nail diameter on blood loss during perioperative period regarding different layers, including start of funnel, end of funnel, and femoral isthmus. Due to the different proximal femur shape, the matching levels of different layers are not necessarily the same in themselves. This study tried to find out which layer is most closely related to blood loss. According to our result, the HBL was obviously associated with the ratios of narrow cavity diameter to intramedullary nail diameter obtained from end of funnel, which revealed that the indices could work as important evaluation indices for intramedullary nail. We could select the appropriate intramedullary nail with high matching degree from end of funnel with the help of software simulation or imaging template.

The limitations of this study include that our sample size was small, and the results may be biased as a consequence.

5. Conclusion

In conclusion, matching rate of PFNA II at the funnel might be an important factor for HBL and TBL postoperatively. It is essential that the appropriate intramedullary nail should be timely adjusted according to the matching degree during the operation. In addition, the study provided evidence for the improvement of the intramedullary nail in the future.

Author contributions

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