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ORIGINAL RESEARCH

# Perioperative Bleeding Risk and Associated Factors in End-Stage Kidney Disease Patients Undergoing Intertrochanteric Fracture Surgery: Implications for Management

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**Background:** End-stage renal disease (ESRD) patients undergoing intertrochanteric fracture surgery face complex coagulation challenges. This study aimed to identify risk factors for coagulation dysfunction in ESRD patients during the perioperative period of intertrochanteric fracture surgery.

**Methods:** This retrospective study included 127 patients who underwent surgical treatment for intertrochanteric femoral fractures between January 2019 and June 2023, of whom 33 had end-stage renal disease (ESRD) and were receiving maintenance dialysis. Propensity score matching was performed at a 1:1 ratio based on age, gender, BMI (body mass index), fracture classification, anesthesia type, and APACHE II score, yielding 33 matched non-ESRD controls. Perioperative data, including coagulation parameters, biochemical indices, and clinical outcomes, were collected. Multivariable regression analysis was conducted to identify risk factors associated with coagulation dysfunction.

**Results:** The dialysis group showed significantly different coagulation profiles compared to controls, particularly in platelet count (71.6 ± 21.3 vs 159.1 ± 35.7×$10^9$/L, $P = 0.003$) and blood loss (609.9 ± 89.2 vs 559.3 ± 55.5 mL, $P = 0.007$). Regression analysis revealed that blood loss in the dialysis group was primarily influenced by platelet count ($P < 0.001$) and anticoagulant dose ($P < 0.001$), while in the control group it was mainly affected by surgery duration ($P < 0.001$). Although mean surgery duration did not differ significantly between groups, its relationship with blood loss varied markedly between ESRD and non-ESRD patients. The dialysis group experienced more complications, with most bleeding events occurring 5–7 days postoperatively when platelet counts reached their nadir.

**Conclusion:** ESRD patients face increased bleeding risk during intertrochanteric fracture surgery, primarily associated with platelet count and anticoagulant use. The critical period for bleeding complications occurs 5–7 days postoperatively, suggesting the need for careful platelet monitoring and individualized anticoagulation protocols during this timeframe.

**Keywords:** anticoagulation, bleeding risk, coagulation, end-stage renal disease, intertrochanteric fracture, perioperative care, platelet count, surgery

## Introduction

Despite the aging population worldwide, the patients with end-stage renal disease (ESRD) tend to be younger and the disease prevalence continues to rise.[1] The total number of patients with ESRD in China was 2.16 million in 2014, increasing to 2.57 million in 2016 and 2.9 million in 2017, respectively. This number is expected to exceed 4 million by 2030, exhibiting an increasing annual trend. Renal insufficiency can lead to secondary osteoporosis.[2] The incidence of hip fracture in patients with ESRD is 4–17 times higher than that in the general population.[3–5]

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Patients with ESRD present a unique hemostatic challenge characterized by a paradoxical coagulation dysfunction—often termed the "uremic hemostatic paradox". These patients simultaneously exhibit increased bleeding tendencies due to uremic platelet dysfunction, reduced platelet count, and impaired platelet-vessel wall interactions, while also demonstrating a hypercoagulable state that predisposes them to thrombotic complications.[6,7] This dual pathology is further complicated by the necessity of anticoagulation during hemodialysis, creating a delicate balance in perioperative management where both hemorrhagic and thrombotic risks must be carefully considered.

Recent studies have demonstrated poorer outcomes in ESRD patients on dialysis after intertrochanteric fracture. A nationwide cohort study showed that the in-hospital mortality rate was 13.79% for dialysis patients, with a 1-year mortality rate reaching 35.34%, significantly higher than non-dialysis patients.[8] The perioperative risks remain elevated even after controlling for demographics and comorbidities.[9] The primary cause of these deaths was cardiovascular disease, which is strongly associated with coagulation.[10] Additionally, patients with uremia commonly exhibit hypercoagulable activity and platelet activation, and are in a hypercoagulable state, leading to thrombosis.[6] Conversely, these patients have a reduced platelet count and bleeding tendencies due to the action of various metabolites (toxins).[11] The use of anticoagulants during blood purification makes the coagulation system more prone to dysfunction.

Currently, standardized guidelines for perioperative anticoagulation management in ESRD patients undergoing orthopedic surgery remain lacking. Existing protocols are largely extrapolated from general populations or other surgical subspecialties, failing to account for the unique hemostatic challenges in this population. This gap in evidence-based guidance contributes to variable clinical practices and potentially suboptimal outcomes. Therefore, this study examined blood loss-related factors in 33 patients with ERSD experiencing intertrochanteric fracture to identify risk factors for coagulation dysfunction in these patients.

# Materials and Methods

## Study Design and Setting

This retrospective cohort study was conducted at Beijing Friendship Hospital. All eligible patients who underwent intertrochanteric fracture surgery between January 2019 and June 2023 were included. The study protocol was approved retrospectively by the Ethics Committee of Beijing Friendship Hospital (approval number: 2024-P2-169-02) for analysis of de-identified clinical data and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

## Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) newly developed and unilateral intertrochanteric fracture; (2) patients with ERSD undergoing dialysis with complete clinical information; (3) patients receiving surgical treatment at our center.

The exclusion criteria were as follows: (1) multiple fractures; (2) old fractures; (3) pathological fractures; (4) patients receiving temporary renal replacement therapy for acute kidney injury; (5) patients receiving no surgical treatment.

## Sample Size Determination and Patient Selection

Sample size calculation referenced a systematic review and meta-analysis by Mathew et al on perioperative bleeding risk in patients with chronic kidney disease, which demonstrated that patients with renal dysfunction exhibited significantly higher risk of blood transfusion with a pooled odds ratio of 2.7 (95% CI: 2.1–3.4).[12] Based on this effect size and considering a clinically significant difference of 50 mL in blood loss with a pooled standard deviation of 75 mL between groups, we initially estimated a minimum requirement of 30 patients per group ($\alpha$=0.05, power 0.8) using G*Power 3.1 software.

Between January 2019 and June 2023, we initially screened 368 patients who underwent intertrochanteric fracture surgery. According to our inclusion and exclusion criteria, 241 patients were excluded due to multiple fractures (n=38), pathological fractures (n=12), temporary renal replacement therapy for acute kidney injury (n=8), incomplete medical records or mortality (n=156), and non-surgical treatment (n=27). Among the remaining 127 eligible patients, 33 had ESRD undergoing maintenance dialysis, and 94 had normal renal function.

We applied propensity score matching using a logistic regression model with an initial caliper width of 0.2 standard deviations of the propensity score logit. The matching variables included age, gender, BMI, fracture classification, anesthesia type, and APACHE II score. This approach yielded 28 matched pairs, which was fewer than our initial target. To achieve our predetermined sample size, we slightly adjusted the caliper width to 0.22, which resulted in 33 well-matched pairs. Among 94 eligible non-ESRD patients, propensity score matching identified 33 patients with the closest baseline characteristics to our 33 ESRD patients. The remaining 61 non-ESRD patients differed in matching variables (primarily age, gender, BMI, fracture classification, anesthesia type, or APACHE II scores) and were thus excluded to minimize confounding. While this selective matching improves internal validity by creating comparable groups, we acknowledge it may limit generalizability to the broader intertrochanteric fracture population. The matched control group represents non-ESRD patients with demographic and clinical profiles similar to ESRD patients, rather than a random sample of all intertrochanteric fracture patients.

Post-hoc power analysis confirmed that our final sample size (33 patients per group) provided 83% statistical power at an alpha level of 0.05, sufficient to detect the observed differences in our primary outcome measures, fulfilling our study design requirements. Baseline characteristics were comparable between the matched groups as shown in Table 1, with no significant differences observed (all $P > 0.05$). The patient selection process is illustrated in Figure 1.

# Perioperative Management

## Preoperative Preparation

All patients underwent comprehensive preoperative assessments, including detailed medical history, physical examination, and laboratory tests focusing on coagulation parameters. Patients in the dialysis group received their regular dialysis schedule before surgery with a final preoperative heparin-free dialysis session scheduled within 24–48 hours before the operation. Platelet counts were carefully monitored, and patients with counts below $50\times10^9$/L received platelet transfusions to minimize bleeding risk.

**Table 1** Baseline Characteristics of Study Participants

| | Dialysis Group (n=33) | Control Group (n=33) | *P* value |
|---|---|---|---|
| Gender (Female/Male) | 17/16 | 15/18 | 0.813 |
| Age (years) | 61.3 ± 7.3 | 62.2 ± 6.5 | 0.609 |
| BMI (kg/m$^2$) | 23.1±3.2 | 22.8±2.9 | 0.724 |
| Fracture Classification (AO/OTA) | | | 0.762 |
| A1 | 14 (42.4%) | 16 (48.5%) | |
| A2 | 12 (36.4%) | 11 (33.3%) | |
| A3 | 7 (21.2%) | 6 (18.2%) | |
| Anesthesia Type | | | 0.566 |
| General | 9 (27.3%) | 7 (21.2%) | |
| Spinal | 24 (72.7%) | 26 (78.8%) | |
| APACHE II score | 14.0 ± 2.9 | 13.0 ± 1.8 | 0.061 |
| HBG (g/L) | 74.5 ± 14.4 | 99.1 ± 8.8 | < 0.001 |
| HCT (%) | 24.8 ± 5.3 | 36.3 ± 4.2 | < 0.001 |
| Harris functional score | 70.4 ± 4.2 | 68.5 ± 3.2 | 0.307 |
| Length of hospital stay (Day) | 12.6 ± 2.9 | 10.1 ± 1.1 | 0.001 |

**Note**: Data are presented as mean ± standard deviation or n (%). *P* values were calculated using paired *t*-test for continuous variables and McNemar's test for categorical variables. All patients underwent closed reduction with INTERTAN intramedullary nailing.
**Abbreviations**: AO/OTA, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association; APACHE, Acute Physiology and Chronic Health Evaluation.


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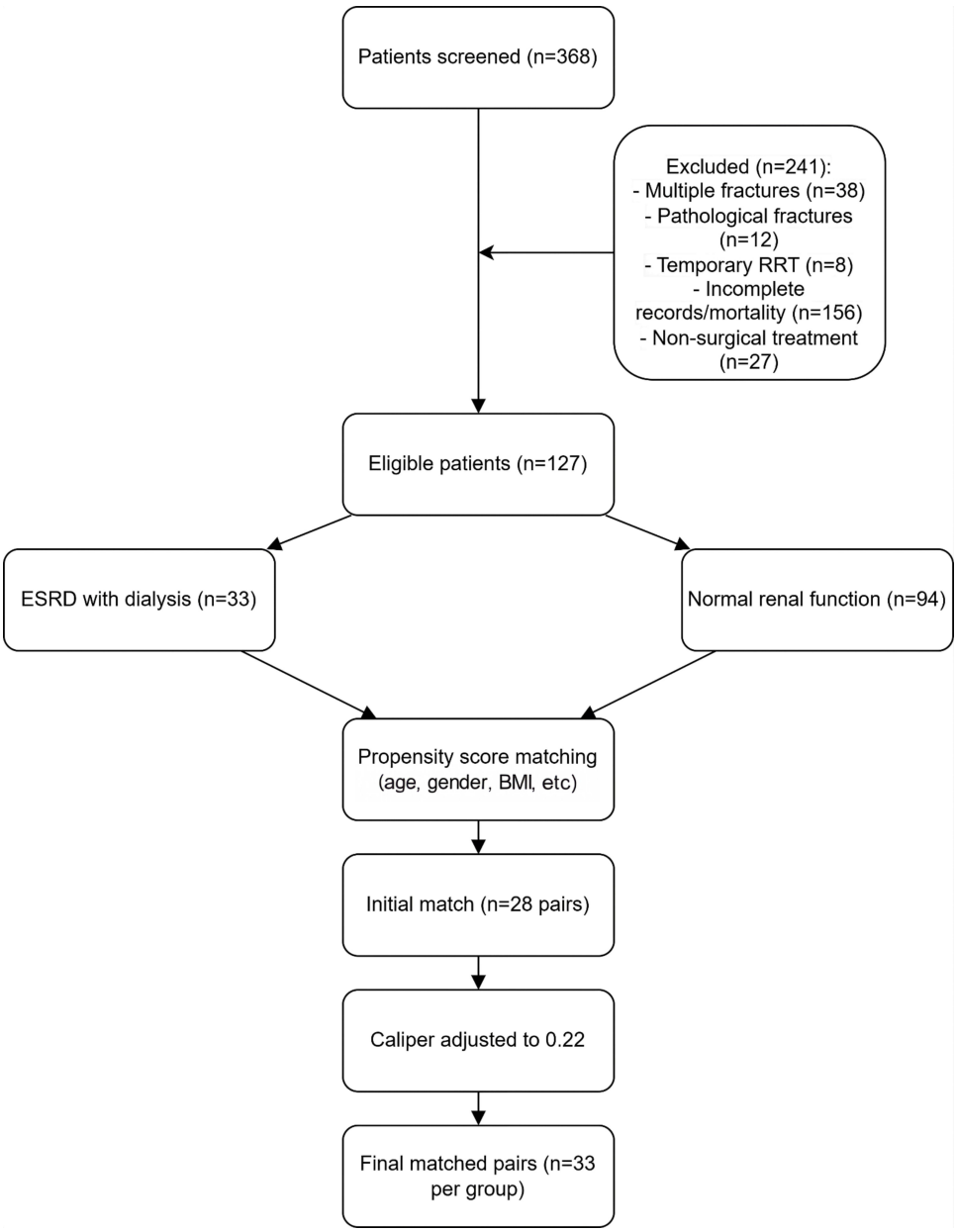


**Figure 1** Patient selection flowchart. Flow diagram showing the selection process from 368 initially screened patients to final analysis cohort of 66 matched patients (33 ESRD and 33 non-ESRD). After excluding 241 patients based on specified criteria (multiple fractures n=38, pathological fractures n=12, temporary renal replacement therapy n=8, incomplete medical records/mortality n=156, non-surgical treatment n=27), 127 eligible patients remained (33 ESRD, 94 non-ESRD). Propensity score matching (PSM) with caliper width 0.22 based on age, gender, and APACHE II score was applied to eligible patients, yielding 33 well-matched pairs for final analysis.
**Abbreviations**: ESRD, end-stage renal disease; PSM, propensity score matching.

## Surgical Procedure

All operations were performed by senior orthopedic surgeons with at least 10 years of experience in intertrochanteric fracture surgery. Surgical procedures were standardized according to the hospital's clinical pathway. An internal fixation with a closed restoration intramedullary nail (TRIGEN™ INTERTAN, Smith & Nephew, USA) was performed under lumbar or general anesthesia. The surgery was performed within 24 hours after the final dialysis session for patients in the ESRD group.

## Postoperative Management

Regular dialysis was resumed the day after surgery for ESRD patients, with careful monitoring of coagulation parameters. Anticoagulation therapy was administered to all patients to prevent deep vein thrombosis, with protocols individualized based on coagulation status:

## Anticoagulation Regimen

For patients with ESRD, low-molecular-weight heparin (LMWH; nadroparin calcium) was administered at a reduced prophylactic dose of 41 IU/kg/day, corresponding to approximately a 50% reduction from the standard dose. This adjustment was based on the known prolonged half-life and accumulation of LMWH in patients with severe renal impairment due to reduced renal clearance, as well as institutional protocols informed by prior pharmacokinetic evidence in dialysis populations.[13,14] Dose selection also accounted for the increased bleeding risk associated with uremic platelet dysfunction.[15] Individual dose modifications were implemented according to platelet count ($<50 \times 10^9$/L) and anti–factor Xa activity monitoring, with a target prophylactic range of 0.2–0.3 IU/mL.[16]

For control patients: Standard prophylactic dosing of nadroparin calcium (86 IU/kg/day) was employed according to manufacturer guidelines and institutional protocols for orthopedic surgery thromboprophylaxis in patients with normal renal function.

## Blood Management

Blood transfusions were provided if hemoglobin levels fell below 6 g/dL or if patients exhibited symptoms of anemia.

Platelet transfusions were considered for patients with counts below $50\times10^9$/L who exhibited bleeding tendencies.

## Monitoring Protocol

Daily assessment of coagulation parameters during the first week, with particular vigilance during days 5–7 when platelet counts typically reached their nadir.

Ultrasound examinations were performed if hematoma formation was suspected.

## Rehabilitation Protocol

Rehabilitation began on the first postoperative day with a standardized protocol:

Early mobilization: Passive exercises started on day 1, with progressive weight-bearing initiated based on radiographic evidence of healing and patient tolerance.

Physical therapy: Tailored rehabilitation programs were implemented, with adjustments for ESRD patients to accommodate dialysis schedules and energy limitations.

Follow-up schedule: Patients were evaluated at 2 weeks, 1 month, 3 months, 6 months, and 12 months postoperatively, with assessment of functional outcomes using the Harris Hip Score and radiographic evaluation of fracture healing.

Throughout the perioperative period, all patients received standard prophylactic antibiotics, pain management, and nutritional support according to institutional protocols, with special attention to electrolyte balance in the ESRD group.

## Data Collection and Outcome Measurements

Two trained orthopedic residents independently collected data using standardized forms. All data points were part of standard care documentation and were extracted from medical records. The data included general information (sex, age, length of dialysis, blood pressure, and blood glucose), biochemical and coagulation-related indicators (coagulation function, renal function, hemoglobin level, platelet count, and electrolyte level), and surgery-related indicators (surgery duration, blood loss, bleeding, preoperative APACHE II score, postoperative Harris function score, length of stay, complications, and anticoagulation modality). The clinical observation was performed by outpatient follow-ups and telephone follow-ups. Data extraction was cross-verified between the two residents.

Coagulation dysfunction-related complications were classified as follows: (1) Bleeding events—including major hemorrhage (melena, hematemesis, arterial nosebleeds), minor bleeding (venous nosebleeds, subconjunctival bleeding,

prolonged bleeding from dialysis catheter sites), and local hematomas requiring intervention; (2) Thrombotic events—including deep vein thrombosis confirmed by ultrasonography and myocardial infarction diagnosed by electrocardiography, cardiac enzymes, and clinical presentation.[17]

Perioperative blood loss was quantified using the validated Gross formula, which comprehensively accounts for both measurable intraoperative blood loss and occult blood loss through analysis of hematocrit changes. The formula is expressed as:

Blood loss = PBV × (Hct_pre - Hct_post)/Hct_avg + V_transfused

Where PBV represents patient blood volume (calculated as 70 mL/kg for males and 65 mL/kg for females), Hct_pre and Hct_post denote pre- and postoperative hematocrit values respectively, Hct_avg is the mean of these values, and V_transfused indicates the volume of transfused red blood cells administered during the perioperative period.

## Statistics

Statistical analyses were performed using SPSS 28.0 (IBM Corp, Armonk, NY, USA). The normality of continuous variables was assessed using the Shapiro–Wilk test. Continuous variables were presented as mean ± standard deviation or median (interquartile range) as appropriate. For the 1:1 propensity score matched pairs, paired *t*-test or Wilcoxon signed-rank test was used for continuous variables, and categorical variables were compared using McNemar's test.

Multiple regression analysis with backward stepwise selection (entry threshold $P < 0.10$, removal threshold $P > 0.05$) was performed to identify factors associated with blood loss. Standardized coefficients were calculated to compare predictor importance, and model assumptions were verified through appropriate diagnostic tests. Variance inflation factors were examined to assess multicollinearity.

For platelet count dynamics analysis, a multilevel model was constructed with time points as level 1 and individuals as level 2, including group, time, and their interaction terms. Statistical significance was set at $P < 0.05$.

# Results

## General Information

The dialysis group included 33 patients (17 women and 16 men) with a mean age of 61.3± 7.3 years. The control group also comprised 33 patients (15 women and 18 men) with a mean age of 62.2 ± 6.5 years.

The propensity score matching successfully balanced key baseline characteristics between groups. No significant differences were observed in age ($P = 0.609$), gender distribution ($P = 0.813$), BMI ($P = 0.724$), fracture classification according to AO/OTA system ($P = 0.762$), or anesthesia type (general vs spinal, $P = 0.566$). While the APACHE II scores showed no statistically significant difference between groups ($P = 0.061$), this borderline p-value suggests the possibility of subtle physiological differences in overall disease severity that matching could not completely eliminate. However, with mean scores of 14.0 ± 2.9 versus 13.0 ± 1.8, both groups fell within the same mild-to-moderate risk category, and this minor difference is unlikely to substantially confound our primary outcomes. Significant differences were found in hemoglobin level ($P < 0.001$), hematocrit ($P < 0.001$), and length of hospital stay ($P = 0.001$) Table 1.

## Differences in Clinical Indicators

Statistical analysis revealed significant differences between groups in platelet count, blood urea nitrogen (BUN), creatinine (Cr), prothrombin time (PT), D-Dimer, fasting blood glucose (FBG), anticoagulant use, and blood loss (all $P < 0.05$). However, surgery duration showed no significant difference between groups ($P = 0.544$) Table 2.

## Blood Loss-Related Factors

Multiple stepwise regression analysis identified different predictors of blood loss for each group. The regression equations were:

Dialysis group:

Blood loss (mL) = 653.17–2.373 × PLT ($\times 10^9$/L) + 3.066 × anticoagulant dose (IU/kg/day)

95% CI for PLT coefficient: –3.412 to –1.334

95% CI for anticoagulant dose coefficient: 1.894 to 4.238

$R^2 = 0.724$, adjusted $R^2 = 0.706$, $P < 0.001$

**Table 2** Comparison of Perioperative Coagulation Parameters Between Groups

| | Dialysis Group | Control Group | P value |
|---|---|---|---|
| PLT ($\times 10^9$/L) | 71.6 ± 21.3 | 159.1 ± 35.7 | 0.003 |
| BUN (mmol/L) | 12.9 ± 2.6 | 6.5 ± 1.7 | < 0.001 |
| Cr (umol/L) | 227.5 ± 36.4 | 81.2 ± 14.8 | < 0.001 |
| PTs (s) | 14.2 ± 2.1 | 11.4 ± 1.2 | 0.003 |
| D-Dimor (mg/L) | 7.8 ± 3.5 | 7.3 ± 2.8 | 0.001 |
| Fbg (g/L) | 2.3 ± 0.6 | 2.8 ± 0.9 | 0.024 |
| Blood loss (mL) | 609.9 ± 89.2 | 559.3 ± 55.5 | 0.007 |
| Surgery duration (min) | 48.3 ± 9.9 | 46.9 ± 8.1 | 0.544 |
| Anticoagulant use* (IU/kg/day) | 41.4 ± 12.7 | 85.3 ± 24.2 | < 0.001 |

**Note**: Data are presented as mean ± standard deviation. *Anticoagulant is nadroparin calcium injection (ASPEN Notre Dame de Bondeville), 1 mL is equivalent to 9500 IU anti-X factor, excluding the anticoagulant dose in extracorporeal circulation during dialysis.
**Abbreviations**: PLT, Platelet; BUN, Blood Urea Nitrogen; Cr, Creatinine; PT, Prothrombin Time; Fbg, Fibrinogen.

Control group:

Blood loss (mL) = 414.07 + 3.09 × surgery duration (min)

95% CI for surgery duration coefficient: 2.107 to 3.893

$R^2 = 0.682$, adjusted $R^2 = 0.673$, $P < 0.001$

To comprehensively investigate factors influencing perioperative blood loss, we conducted multiple regression analysis incorporating clinically relevant variables including age, platelet count, anticoagulant dose, surgery duration, hemoglobin, and D-dimer levels (Table 3). A backward stepwise regression approach was employed with entry threshold $P < 0.10$ and removal threshold $P > 0.05$.

In the dialysis group, platelet count emerged as the strongest predictor (standardized $\beta = -0.563$, $P < 0.001$), followed by anticoagulant dose (standardized $\beta = 0.435$, $P < 0.001$). By contrast, surgery duration was the only significant predictor in the control group (standardized $\beta = 0.826$, $P < 0.001$). Although mean surgery duration showed no significant difference between groups ($P = 0.544$), regression analysis revealed that within the control group, surgical duration significantly predicted blood loss variability ($P < 0.001$). This finding demonstrates that regression analysis explains within-group variability rather than between-group differences, highlighting the distinct pathophysiological mechanisms affecting blood loss in ESRD versus non-ESRD patients. The final models demonstrated good fit with adjusted $R^2$ values of 0.706 and 0.673 for dialysis and control groups, respectively.

**Table 3** Multiple Regression Analysis of Factors Influencing Perioperative Blood Loss

| Variable | Dialysis Group | | | Control Group | | |
|---|---|---|---|---|---|---|
| Intercept | Coefficient (95% CI) | Standardized $\beta$ | VIF | Coefficient (95% CI) | Standardized $\beta$ | VIF |
| Age | −0.213 (−1.456, 1.030) | −0.017 | 1.21 | 0.187 (−0.981, 1.355) | 0.022 | 1.18 |
| Platelet count | −2.373 (−3.412, −1.334)** | −0.563 | 1.34 | −0.058 (−0.127, 0.011) | −0.037 | 1.26 |
| Anticoagulant dose | 3.066 (1.894, 4.238)** | 0.435 | 1.28 | 0.741 (−0.388, 1.870) | 0.032 | 1.17 |
| Surgery duration | 1.327 (−0.092, 2.746) | 0.147 | 1.14 | 3.090 (2.107, 3.893)** | 0.826 | 1.09 |
| Hemoglobin | −0.417 (−1.355, 0.521) | −0.067 | 1.32 | −0.319 (−1.105, 0.467) | −0.050 | 1.25 |
| D-dimer | 0.729 (−0.631, 2.089) | 0.085 | 1.19 | 0.251 (−0.498, 1.000) | 0.042 | 1.15 |
| Model Statistics | | | | | | |
| Adjusted $R^2$ | 0.706 | | | 0.673 | | |
| F-statistic | 41.36** | | | 68.47** | | |
| Durbin-Watson | 1.98 | | | 2.04 | | |

**Note**: **$P < 0.001$; VIF: Variance Inflation Factor Model selection was performed using backward stepwise regression with entry threshold $P < 0.10$ and removal threshold $P > 0.05$. Residual diagnostics confirmed normality (Shapiro–Wilk $P > 0.05$) and homoscedasticity (Breusch-Pagan $P > 0.05$) for both models.

Multicollinearity was not observed among the predictors, as evidenced by variance inflation factors all below 1.5. Model diagnostics confirmed normality of residuals (Shapiro–Wilk test, $P > 0.05$) and homoscedasticity (Breusch-Pagan test, $P > 0.05$) for both regression models. While the adjusted $R^2$ of 0.706 for the dialysis group suggests good model fit, we acknowledge that with our sample size, these coefficients should be interpreted as estimates requiring validation in larger independent cohorts rather than as definitive values for clinical calculator applications. These findings reinforce the distinctive nature of bleeding risk factors between ESRD and non-ESRD patients undergoing intertrochanteric fracture surgery.

## Platelet Count Dynamics

Figure 2 demonstrates the platelet count differences in the two groups. Table 4 displays the comparative results between the two groups, where the time and group variables show the respective main effects. Overall, patients' postoperative platelet count decreased after treatment, with the greatest decrease occurring on day five. The postoperative platelet count on day 10 was increased compared to day five. The total platelet count of patients in the dialysis group was lower than that in the control group. The results of the interaction term (Table 4) show a statistically significant interaction for group and time. Therefore, there was a statistically significant difference in the platelet count changes between the two groups. The parameter estimates indicate that this difference is greatest on day five. Figure 2 shows that the difference in the postoperative platelet count between the two groups was at its highest at the time of fracture and at its lowest on day five.

## Complications and Adverse Events

The coagulation dysfunction-related complications included disseminated intravascular coagulation (DIC), bleeding events, and lower limb venous thrombosis. Bleeding events included hemorrhage (melena, hematemesis, and arterial nosebleeds), minor bleeding (venous nosebleeds, subconjunctival bleeding, and prolonged bleeding from the cannula site after removal of the dialysis needle), and local hematomas.[18] Thrombosis events include lower limb venous thrombosis and myocardial infarction.

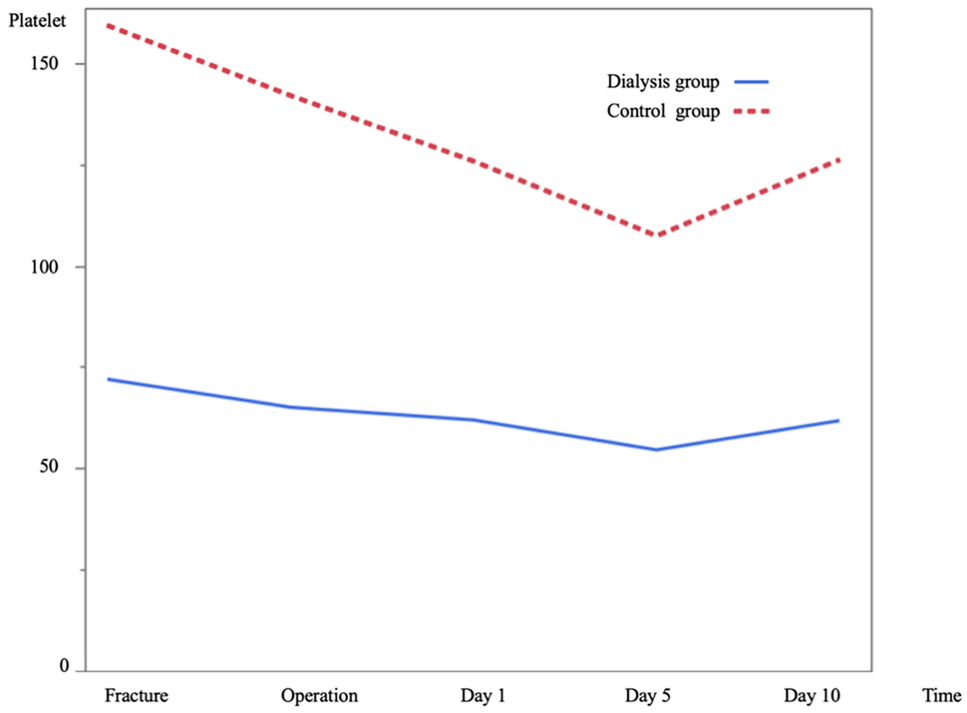


**Figure 2** Platelet count dynamics in ESRD and non-ESRD patients during the perioperative period. The time-course analysis of platelet counts demonstrates the difference between dialysis and control groups from preoperative baseline through postoperative day 10. The most significant difference between groups was observed at the time of fracture (maximum difference) while the lowest platelet counts in both groups occurred on postoperative day 5. The dialysis group (solid line) consistently showed lower platelet counts compared to the control group (dashed line). Data are presented as mean values with error bars indicating standard deviation.
**Abbreviation**: ESRD, end-stage renal disease.

**Table 4** Platelet Count Differences

| Effect | Comparative Results | Parameter Estimates | Standard | *p* value |
|---|---|---|---|---|
| Intercept | | 159.18 | 3.9046 | < 0.001 |
| Time | Perioperative vs preoperative | −12.0909 | 1.8813 | < 0.001 |
| Time | Day 1 vs preoperative | −21.7424 | 1.8813 | < 0.001 |
| Time | Day 5 vs preoperative | −34.6515 | 1.8813 | < 0.001 |
| Time | Day 10 vs preoperative | −21.6515 | 1.8813 | < 0.001 |
| Group Variables | Dialysis group vs Control group | −69.0061 | 5.1913 | < 0.001 |
| Group and Time | Perioperative vs preoperative | 10.3636 | 2.9761 | 0.001 |
| Group and Time | Day 1 vs preoperative | 23.4242 | 2.9761 | < 0.001 |
| Group and Time | Day 5 vs preoperative | 34.4545 | 2.9761 | < 0.001 |
| Group and Time | Day 10 vs preoperative | 22.9394 | 2.9761 | < 0.001 |

**Note**: All time effects are compared to preoperative values. Dialysis group compared to control group.

In the dialysis group, seven bleeding events occurred: one gastrointestinal hemorrhage and six local hematomas. Additionally, six cases of lower limb venous thrombosis were observed, and one patient died during the perioperative period due to cardiac failure combined with artery disease. In the control group, three cases of lower limb venous thrombosis were recorded. Notably, the onset of local hematoma and gastrointestinal hemorrhage primarily occurred 5–7 days postoperatively.

# Discussion

Patients with end-stage renal disease (ESRD) undergoing intertrochanteric fracture surgery present with complex hemostatic abnormalities, characterized by a paradoxical coexistence of bleeding tendencies and thrombotic risks. This study highlights the unique hemostatic disorders in these patients and provides valuable insights for individualized perioperative management, particularly in anticoagulation strategies and platelet monitoring.

## Platelet Dysfunction as a Primary Determinant of Bleeding Risk

Multivariate regression analysis revealed that platelet count was the strongest predictor of perioperative blood loss in ESRD patients (standardized $\beta = -0.563$, $P < 0.001$), whereas surgical duration was the primary factor in patients with normal renal function. The significantly lower platelet count observed in dialysis patients ($71.6 \pm 21.3$ vs $159.1 \pm 35.7 \times 10^9$/L, $P = 0.003$) is consistent with previous findings regarding quantitative and qualitative platelet abnormalities in ESRD.

Multiple mechanisms contribute to platelet dysfunction in these patients. A 2024 review article[18] noted that uremic toxins impair platelet adhesion and aggregation by interfering with glycoprotein receptor expression and calcium mobilization. Furthermore, repeated hemodialysis sessions lead to platelet activation, granule depletion, and functional exhaustion. Recent studies utilizing rotational thromboelastometry and multiple electrode aggregometry have also confirmed the coexistence of both hypo- and hypercoagulable states in ESRD patients.[19] However, the retrospective design limits our ability to establish definitive causality, and prospective studies with protocolized interventions are needed to confirm these associations.

Our time-series analysis demonstrated that the nadir of platelet count occurred on postoperative day 5, coinciding with the peak incidence of bleeding complications. This finding suggests that intensified monitoring and preventive strategies are particularly necessary during this critical period. Current literature recommends maintaining platelet counts above $50\times10^9$/L for major orthopedic procedures,[20] which aligns with our finding that the seven bleeding events in our dialysis group occurred in patients with an average platelet count of $51.3\times10^9$/L.

It is noteworthy that a recent study on cardiac surgery reported that even with normal platelet counts, ESRD patients exhibited increased bleeding risk due to platelet dysfunction.[21] This underscores the limitation of relying solely on

platelet counts and suggests that functional platelet assessments should also be considered. This underscores the importance of comprehensive platelet assessment beyond simple numerical counts in ESRD patients undergoing surgery.

## Anticoagulation Management: Balancing Bleeding and Thrombotic Risks

Anticoagulant dosage was identified as the second most significant factor affecting blood loss (standardized $\beta = 0.435$, $P < 0.001$), further highlighting the complexity of anticoagulation management in ESRD. These patients are simultaneously predisposed to bleeding and hypercoagulability, a phenomenon sometimes referred to as the "uremic hemostatic paradox".[7]

Low-molecular-weight heparins (LMWH), primarily cleared by the kidneys, tend to accumulate in ESRD patients, thereby increasing bleeding risk.[22] In this study, dialysis patients received significantly lower doses of nadroparin calcium compared to controls (41.4 ± 12.7 vs 85.3 ± 24.2 IU/kg/day, $P < 0.001$), yet bleeding events still occurred. This finding suggests that dose reduction alone may not suffice to mitigate bleeding risk, while insufficient anticoagulation could increase thrombotic events. Indeed, we observed six cases of lower extremity deep vein thrombosis in the dialysis group, reflecting their underlying hypercoagulable state.

Prior research indicates that modifiable bleeding risk factors in anticoagulated patients are limited, mainly involving hypertension control.[23] This further emphasizes the importance of individualized dose adjustments in ESRD patients. Of the seven bleeding events in the dialysis group, six were delayed hematomas that resolved after discontinuation of anticoagulants and ultrasound-guided puncture drainage. One patient experienced recurrent local hematoma. Angiography revealed a deep femoral artery rupture, and the hematoma was successfully controlled following embolization therapy. A recent review by Ponchia et al suggested that conventional thromboprophylaxis protocols may be inadequate for ESRD patients and should be tailored based on individualized bleeding and thrombotic risk assessments.[24]

Given our single-center experience and modest sample size, these dosing suggestions should be validated in larger, multicenter prospective trials before widespread adoption. Integrating our findings with previous evidence,[13–16] we recommend individualized LMWH dose adjustments with close monitoring of anti-Xa activity, aiming to maintain levels between 0.2–0.3 IU/mL to balance bleeding and thrombosis risks.

## Temporal Patterns of Coagulation Dysfunction

A key discovery from our study is the temporal pattern of platelet changes in ESRD patients. Multilevel model analysis revealed distinct trends between dialysis and control groups (Table 4), with the greatest between-group difference preoperatively and platelet counts reaching their nadir on postoperative day 5.

This temporal pattern has obvious clinical implications. First, ESRD patients' preoperatively low platelet counts likely reflect chronic uremic thrombocytopenia, further exacerbated by recurrent dialysis-induced platelet activation and sequestration.[25] Second, the day 5 platelet nadir suggests a cumulative effect from surgical trauma, dialysis, and anticoagulation.

Zhu's research last year found that perioperative platelet distribution width (PDW) changes predict acute kidney injury,[26] suggesting platelet parameters might have broader clinical significance beyond bleeding risk assessment.

Notably, six of our seven bleeding events occurred as delayed hematomas 5–7 days postoperatively, aligning perfectly with the platelet count nadir. This pattern matches recent literature describing a bimodal distribution of bleeding complications in ESRD patients after orthopedic surgery, with a second peak approximately one week postoperatively.[27]

While our longitudinal platelet data reveal clear patterns, the generalizability of the specific day-5 nadir requires confirmation across diverse clinical settings. These findings suggest that traditional perioperative bleeding risk assessment, which typically focuses on the immediate 24–48 postoperative hours, may inadequately address ESRD patients' unique needs. Extended monitoring through days 5–7 seems warranted. Additionally, the timing of postoperative dialysis resumption deserves reconsideration, as extracorporeal circulation anticoagulation could worsen bleeding risk during this vulnerable period.

## Integrated Approach to Perioperative Management

Our research shows that blood loss in ESRD patients is primarily associated with platelet count and anticoagulant dosage (Blood loss [mL] = 653.17–2.373 × PLT [$\times 10^9$/L] + 3.066 × anticoagulant dose [IU/kg/day]). In contrast, control group bleeding mainly correlated with surgical duration. This difference suggests that optimizing platelet function and precisely

adjusting anticoagulant dosage might matter more than simply minimizing operative time in ESRD patients. Our regression findings provide direction for risk factor prioritization and monitoring strategies rather than precise quantitative predictions. External validation in independent cohorts is necessary before implementing specific numerical thresholds.

Emerging technologies like thromboelastography and thrombin generation testing could improve risk stratification. A study demonstrated that global coagulation assays can detect subtle coagulation abnormalities missed by conventional tests, revealing that chronic kidney disease patients exhibit a hypercoagulable state compared to healthy controls.[28] Their research showed that these advanced tests could identify paradoxical patterns in thrombin generation, potentially helping identify high-risk patients and tailor individualized treatment plans.

We have begun implementing several interventional strategies in our practice: prophylactic platelet transfusion for ESRD patients with counts below $50\times10^9$/L during the high-risk period,[29] and bedside thromboelastography for more precise coagulation assessment.[30]

Managing coagulation issues in ESRD patients requires collaboration between orthopedic surgeons, nephrologists, anesthesiologists, and hematologists. As Polania Gutierrez and Rocuts emphasized in their review, perioperative anticoagulation management in special populations requires multidisciplinary decision-making regarding anticoagulant interruption and resumption.[31]

## Study Limitations and Future Directions

This study has several noteworthy limitations. The relatively small sample size from a single center may not fully represent the broader ESRD patient population, potentially introducing selection bias. Despite achieving adequate statistical power for our primary outcomes based on post-hoc analysis (83% power), we acknowledge that our sample size limits detection of smaller effect sizes and increases the width of confidence intervals for secondary outcomes. All causal language has been tempered accordingly, and our findings should be interpreted as hypothesis-generating for this specific population rather than definitive. The retrospective design limits our ability to control for all potential confounding variables, although propensity score matching mitigated this to some extent. Additionally, while our propensity score matching focused on key demographic and clinical variables, unmeasured confounders may still exist. The borderline APACHE II matching ($P = 0.061$) indicates that despite propensity score matching, some residual differences in overall physiological status may exist between groups, representing a potential source of unmeasured confounding.

Another important methodological consideration is the potential inaccuracy of blood loss estimation using the Gross formula in dialysis patients. This formula relies on hematocrit changes to calculate occult blood loss. However, ESRD patients undergo significant fluid shifts during dialysis (hemodilution before dialysis vs hemoconcentration after dialysis) that can alter hematocrit independent of actual hemorrhage. In our study, we attempted to minimize this confounding by: (1) standardizing the timing of blood draws (preoperative values obtained immediately before the final pre-surgical dialysis; postoperative values on day 3 at a fixed time point relative to dialysis schedule); (2) carefully documenting dialysis timing and ultrafiltration volumes; and (3) accounting for fluid balance in our calculations. Nevertheless, we acknowledge that fluid status variations may have introduced some degree of measurement error in our blood loss estimates, potentially either overestimating or underestimating true surgical blood loss in individual patients. Future studies should consider more direct measurement methods or volume kinetic modeling approaches that account for dialysis-related fluid shifts.

The one-year follow-up period might not capture all long-term outcomes, particularly late thrombotic events. Our calculation of blood loss using the Gross formula, while validated, may not perfectly account for all sources of perioperative bleeding. We were also unable to perform advanced platelet function testing such as thromboelastography, which might have provided additional insights into coagulation dysfunction mechanisms.

Future research would benefit from large-scale multicenter studies with extended follow-up periods to validate our findings. Prospective studies incorporating advanced coagulation assays and standardized intervention protocols would be particularly valuable. Additionally, studies comparing different anticoagulation regimens specifically designed for this patient population are needed to establish evidence-based guidelines.

Despite these limitations, our study provides valuable insights into the unique coagulation challenges ESRD patients face during intertrochanteric fracture surgery, laying groundwork for improving perioperative management in this high-risk population.

## Conclusion

ESRD patients undergoing intertrochanteric fracture surgery face significantly higher bleeding risks. Our research shows that, unlike in patients with normal renal function, bleeding in ESRD patients is primarily associated with platelet count and anticoagulant dosage. Notably, postoperative days 5–7 represent a critical period for bleeding complications, coinciding precisely with when platelet counts reach their lowest point.

Based on these findings, we recommend: comprehensive preoperative platelet function assessment; intensified coagulation monitoring during the critical postoperative period (particularly days 5–7); considering prophylactic platelet transfusion for patients with counts below $50\times10^9$/L; and establishing multidisciplinary care protocols specifically tailored for ESRD patients. The individualized anticoagulation approaches with careful dose adjustment—informed by platelet counts, anti-Xa monitoring, and patient-specific bleeding/thrombotic risk factors—are essential for this population.

We believe that through individualized approaches targeting the unique coagulation abnormalities in ESRD patients, surgical outcomes can be improved and perioperative complications reduced in this challenging patient population.

## Disclosure

The authors report no conflicts of interest in this work.

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