



OPEN The waiting time of admission to operation was associated with preoperative deep vein thrombosis in geriatric hip fracture

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This study evaluated the association between admission to operation (ATO) time and preoperative deep vein thrombosis (DVT) in geriatric hip fractures under anticoagulation and mechanical thromboprophylaxis. Geriatric patients with hip fractures were screened between January 2015 and September 2019. We collected demographic information and DVT screening results from the medical system. Multivariate binary logistic regression and generalized additive models were used to identify the linear and non-linear associations between ATO and preoperative DVT. Also, we performed Propensity Score Matching (PSM) to test the robustness of our results in a real-world study. This study included one thousand seven hundred and thirty-five patients. There were 443, 726, and 566 patients in $ATO \leq 2d$, $2d < ATO \leq 4d$, and $ATO > 4d$ groups, respectively. Preoperative DVT occurred in 543 (31.3%) patients. There was a "J" type in curve fitting, and the result showed a curvilinear relationship between ATO and preoperative DVT. ATO of 3d was the inflection point. ATO increasing was not associated with an increase of preoperative DVT when $ATO < 3d$ (OR = 0.83; 95%CI: 0.66–1.03; $P = 0.09$), whereas ATO increasing was associated with DVT (OR = 1.08; 95%CI: 1.04–1.14; $P < 0.01$) at $ATO > 3d$. In a real-world population of 1:1 under PSM, we found that the results were stable and the inflection point was the same as the total population. ATO is nonlinearly associated with preoperative DVT in geriatric patients with hip fractures under anticoagulation and mechanical thromboprophylaxis. The 3d was the important point in DVT formation. Each one-day increase in ATO was associated with an 8% increase in the incidence of preoperative DVT when $ATO > 3d$. Study Registration: This study was registered on the website of the Chinese Clinical Trial Registry (ChiCTR: ChiCTR2200057323).

Keywords Hip fracture, Admission to operation, Deep vein thrombosis, Risk

Deep vein thrombosis (DVT) of the lower extremities is a common preoperative complication in hip fracture patients¹. The DVT may lead to pulmonary embolism, long-term limb dysfunction, or even death, which will bring great pain to the patients and prolong the recovery time^{2,3}. Therefore, preoperative prevention of DVT has become an important clinical intervention in the management of elderly hip fracture patients.

Studies have shown that the occurrence of DVT is associated with a variety of factors, including age, past DVT history, and the patient's activity level^{4,5}. However, among these factors, the interval between admission and surgery, called the time of admission to operation (ATO), appears to be an overlooked but potentially clinically important variable^{6,7}. In elderly patients, fractures are often accompanied by pain, limited mobility, and the effects of underlying disease, and prolonged bed rest further exacerbates venous stasis and contributes to thrombus formation⁸. The delay in ATO usually means that patients may be bedridden for long periods while waiting for surgery, which slows blood flow and venous reflux, increases inflammatory response^{9,10}, and increases the state of hypercoagulability of the blood¹¹, which in turn provides favourable conditions for thrombosis¹². The delayed ATO affects a patient's overall prognosis¹³ and may also increase the risk of lower extremity thrombosis in some cases. A previous study found that patients who waited more than 48 h for surgery had a significantly higher rate of DVT compared to those who underwent earlier surgical intervention⁷. To better understand this association, some surgeons have begun to focus on the relationship between ATO and lower extremity DVT^{7,14,15}. Clinically, early diagnosis and prevention of DVT are critical to a patient's postoperative

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recovery, and surgeons have developed various thromboprophylaxis measures, such as anticoagulation therapy, mechanical thromboprophylaxis, and the use of antithrombotic stockings¹⁶.

Among the factors related to DVT, the ATO appears to be an overlooked but potentially clinically important variable. The effectiveness of existing thromboprophylaxis measures is closely related to the timing of the patient's surgery, the type of surgery, and the presence of a preoperative thrombus. However, how to rationalize the ATO and minimize the time interval between the time to operation of hip fracture to reduce the occurrence of preoperative DVT effectively remains to be further explored.

With the increasing understanding of the relationship between ATO and DVT, the purpose of this study is to explore how to reduce the incidence of DVT through early intervention and optimization of surgical timing, aiming to help develop more precise treatment strategies in clinical practice, improve the prognosis of elderly hip fracture patients, and reduce the incidence of DVT.

Materials and methods

Institutional review boards approval

In this retrospective cohort study, we included older adults with hip fractures in the medical records from January 1, 2015, to September 30, 2019. All human procedures followed the 1964 Declaration of Helsinki and its later amendments.

This retrospective study was approved by the Ethics Committee of Xi'an Honghui Hospital (No. 202201009), and the Institutional Review Boards of Xi'an Honghui Hospital waived participants' informed consent. All methods were performed following the relevant guidelines and regulations¹⁷.

Participants

The demographic and clinical data of the patients were obtained from their original medical records. The inclusion criteria were as follows: (1) age of ≥ 65 years; (2) X-ray or computed tomography diagnosis of the femoral neck or intertrochanteric; (3) patients who were receiving surgical or conservative treatment in the hospital; and (4) availability of clinical data in the hospital. The exclusion criteria were as follows: (1) patients with previous pulmonary embolism or DVT history; (2) patients who already had the DVT before the admission, which were examined in other hospitals; (3) patients without the Doppler ultrasonography results of lower extremities in our hospital; (4) Patients who received antiplatelet aggregation therapy and anticoagulant therapy for other diseases before admission to the hospital.

Hospital treatment

Patients were examined before the operation. Prophylaxis for DVT was initiated on admission. Mechanical thromboprophylaxis was used. In patients without contraindications, low-molecular-weight heparin was injected subcutaneously to prevent DVT. Doppler ultrasonography was performed to diagnose DVT before the operation. The diagnostic criterion was the presence of a constant intraluminal filling defect. All patients received an ultrasonography examination of the bilateral lower extremities the day before the scheduled surgery.

Variables

The variables collected in this study were as follows: age, sex, injury mechanism, fracture classification, hypertension, diabetes, coronary heart disease, arrhythmia, hemorrhagic stroke, ischemic stroke, cancer, associated injuries, dementia, chronic obstructive pulmonary disease, hepatitis, gastritis, age-adjusted Charlson comorbidity index (aCCI), time from injury to admission, and time from injury to operation.

The dependent variable in this study was preoperative DVT in bilateral lower extremities, and the independent variable was the ATO. The other variables were potentially confounding factors.

Statistics analysis

Continuous variables were reported as mean $\pm$ standard deviation (Gaussian distribution) or median (minimum and maximum) (skewed distribution), and categorical variables were presented as frequencies and percentages. We used χ^2 (categorical variables), one-way ANOVA (normal distribution), or the Kruskal–Wallis H test (skewed distribution) to test for differences among different delayed ATO values (tertiles). We used univariate and multivariate binary logistic regression models to test the association between ATO and preoperative DVT using three distinct models. Model 1 was a non-adjusted model without adjusted covariates. Model 2 was a minimally adjusted model with adjusted sociodemographic variables. Model 3 was a fully adjusted model with the covariates. To account for the non-linear relationship between ATO and preoperative DVT, we also used a generalized additive model to address the nonlinearity. In addition, a two-piecewise binary logistic regression model was used to explain nonlinearity further. Also, we performed Propensity Score Matching (PSM) to test the robustness of our results in a real-world study.

All analyses were performed using statistical software packages R (<http://www.R-project.org>, R Foundation) and EmpowerStats (<http://www.empowerstats.com>, X&Y Solutions Inc., Boston, MA, USA). Odds ratios (ORs) and 95% CIs were calculated. Statistical significance was set at a two-sided *P* value of < 0.05 (two-sided).

Results

Patient characteristics

In this retrospective cohort study, we screened and included 1735 patients who met the inclusion criteria. Table 1 lists the demographic and clinical characteristics of the study population after dividing the ATO tertiles into the $ATO \leq 2$ d, $2 < ATO \leq 4$ d, and $ATO > 4$ d groups. There were 443, 726, and 566 patients in every group, and females accounted for 71.3%, 72.0%, and 69.1% of the total number of patients in each group, respectively. As for

ATO	ATO ≤ 2d	2 d < ATO ≤ 4d	ATO > 4d	P-value	P-value*
N	443	726	566		
Age (year)	79.39 ± 6.74	79.25 ± 6.87	79.22 ± 6.79	0.92	0.89
Sex				0.50	–
Male	127 (28.7%)	203 (28.0%)	175 (30.9%)		
Female	316 (71.3%)	523 (72.0%)	391 (69.1%)		
ATO (d)	1.91 ± 0.29	3.51 ± 0.50	6.78 ± 2.50	< 0.01	< 0.01
Injury mechanism				0.29	–
Falling	426 (96.2%)	709 (97.7%)	545 (96.3%)		
Accident	13 (2.9%)	16 (2.2%)	16 (2.8%)		
Other	4 (1.0%)	1 (0.1%)	5 (0.9%)		
Fracture classification				0.40	–
Intertrochanteric fracture	282 (63.7%)	434 (59.8%)	342 (60.4%)		
Femoral neck fracture	161 (36.3%)	292 (40.2%)	224 (39.6%)		
aCCI	4.06 ± 1.03	4.15 ± 1.07	4.32 ± 1.13	< 0.01	< 0.01
Hypertension	195 (44.0%)	374 (51.5%)	307 (54.2%)	< 0.01	–
Diabetes	65 (14.7%)	140 (19.3%)	138 (24.4%)	< 0.01	–
CHD	202 (45.6%)	349 (48.1%)	329 (58.1%)	< 0.01	–
Arrhythmia	118 (26.6%)	196 (27.0%)	212 (37.5%)	< 0.01	–
Hemorrhagic stroke	8 (1.8%)	15 (2.1%)	7 (1.2%)	0.5	–
Ischemic stroke	125 (28.2%)	216 (29.8%)	188 (33.2%)	0.20	–
Cancer	9 (2.0%)	17 (2.3%)	21 (3.7%)	0.19	–
Associated injuries	27 (6.1%)	56 (7.7%)	42 (7.4%)	0.57	–
Dementia	16 (3.6%)	26 (3.6%)	25 (4.4%)	0.71	–
COPD	17 (3.8%)	38 (5.2%)	42 (7.4%)	0.04	–
Hepatitis	11 (2.5%)	18 (2.5%)	21 (3.7%)	0.36	–
Gastritis	5 (1.1%)	10 (1.4%)	11 (1.9%)	0.54	–
Treatment strategy				0.21	–
ORIF	281 (63.4%)	441 (60.7%)	341 (60.3%)		
HA	157 (35.4%)	262 (36.1%)	213 (37.6%)		
THA	5 (1.1%)	23 (3.2%)	12 (2.1%)		
Time to admission (h)	103.70 ± 330.52 10 (1–5040)	76.18 ± 205.61 9 (1–2160)	68.05 ± 178.58 13 (1–2880)	0.05	0.21
Time to chemoprophylaxis after admission (h)	4 (1–7)	5 (1–9)	4 (1–8)	0.99	0.96
Chemoprophylaxis				0.44	–
Enoxaparin sodium	171 (38.6%)	266 (36.6%)	210 (37.1%)		
Nadroparin calcium	164 (37.0%)	260 (35.8%)	215 (38.0%)		
Dalteparin sodium	66 (14.9%)	114 (15.7%)	95 (16.8%)		
Other	42 (9.5%)	86 (11.8%)	46 (8.1%)		
Mechanical thromboprophylaxis				0.60	–
Venous foot pumps	89 (20.0%)	164 (22.6%)	122 (21.5%)		
Lower extremities Intermittent pneumatic compression	354 (80.0%)	562 (77.4%)	444 (78.5%)		
Operation time (mins)	90.11 ± 31.87	93.09 ± 32.55	97.74 ± 38.37	< 0.01	< 0.01
Blood loss (mL)	226.60 ± 149.28	242.20 ± 138.91	240.19 ± 163.28	0.21	0.03
Infusion (mL)	1566.93 ± 381.91	1573.95 ± 374.84	1621.19 ± 382.30	0.04	0.08
Transfusion (U)	0.86 ± 1.19	0.93 ± 1.19	0.98 ± 1.26	0.25	0.27
Preoperative DVT	142 (32.1%)	200 (27.6%)	201 (35.5%)	< 0.01	–

Table 1. The demographic and clinical characteristics. Mean + standard deviation/N(%). P value*: For continuous variables, we used the Kruskal–Wallis rank-sum test and Fisher's exact probability test for count variables with a theoretical number of < 10.

the delay in ATO, the index of aCCI increased in every group, from 4.06 to 4.32. In the comorbidities, there were more patients with hypertension, diabetes, CHD, arrhythmia, and COPD in the ATO > 4d group. Also, patients in the ATO > 4d group had longer operation time, and more operative infusion. As for time to admission, the ATO > 4d group had a mean of 68.1 h, less than 103.7 and 76.2 h in the ATO ≤ 2d and 2d < ATO ≤ 4d group.

Preoperative DVT occurred in 543 (31.3%) patients with hip fractures. There were 142 (32.1%), 200 (27.6%), and 201 (35.5%) patients with lower extremity DVT in ATO ≤ 2d, 2d < ATO ≤ 4d, and ATO > 4d groups, respectively.

Univariate analysis of the association between variables and DVT

We investigated the association between these variables and DVT to identify the potential confounding factors in this study, as the criteria of $P < 0.1$, shown in Table 2. Sex, fracture classification, associated injuries, dementia, transfusion, and treatment strategy were identified as confounding factors.

Multivariate analysis between ATO and DVT

We used multivariate logistic regression to perform multifactorial logistic regression to demonstrate the association between ATO and DVT, as shown in Table 3. In addition, ATO was used as a categorical variable, followed by a continuous variable for P for trend test.

There were an identified association in non-adjusted model (OR = 1.05, 95%CI: 1.01–1.09, $P = 0.02$) and adjusted model I (OR = 1.05, 95%CI: 1.01–1.09, $P = 0.02$). Also, we found that ATO was associated with preoperative DVT when adjusting for the confounding factors in adjusted model II (OR = 1.05, 95%CI: 1.01–1.09, $P = 0.02$). However, there was no statistical association when dividing ATO into three groups: $ATO \leq 2$ d, $2 \text{ d} < ATO \leq 4$ d, and $ATO > 4$ d, or in the trend test calculated as a dummy variable. Therefore, the results were unstable in different statistical methods, and a non-linear association should be considered.

Curve fitting and analysis of threshold effect

The curve fitting between ATO and preoperative DVT is shown in Fig. 1. Therefore, the threshold effect was analyzed to identify the curvilinear relationship and the inflection point, shown in Table 4. Interestingly, the result showed a curvilinear relationship, and the ATO value of 3 d was the inflection point in the curve. More specifically, ATO was not correlated with preoperative DVT when $ATO < 3$ d (OR = 0.83; 95%CI: 0.66–1.03; $P = 0.09$), whereas ATO was associated with DVT (OR = 1.08; 95%CI: 1.03–1.14; $P < 0.01$) at $ATO > 3$ d. The P for

	Statistics	Preoperative DVT	P-value
Age (year)	79.28 ± 6.80	1.00 (0.99, 1.02)	0.74
Sex			
Male	505 (29.1%)	1	
Female	1230 (70.9%)	1.34 (1.07, 1.69)	0.01
Injury mechanism			
Falling	1680 (96.8%)	1	
Accident	45 (2.6%)	1.11 (0.59, 2.07)	0.75
Other	10 (0.6%)	2.21 (0.64, 7.67)	0.21
Time to admission (h)	80.56 ± 236.87	1.00 (1.00, 1.00)	0.21
Fracture classification			
Intertrochanteric fracture	1058 (61.0%)	1	
Femoral neck fracture	677 (39.0%)	0.68 (0.55, 0.84)	< 0.01
aCCI	4.18 ± 1.09	0.98 (0.89, 1.07)	0.65
Hypertension	876 (50.5%)	1.12 (0.92, 1.38)	0.26
Diabetes	343 (19.8%)	0.94 (0.73, 1.22)	0.66
CHD	880 (50.7%)	1.11 (0.90, 1.36)	0.32
Arrhythmia	526 (30.3%)	1.08 (0.87, 1.35)	0.47
Hemorrhagic stroke	30 (1.7%)	1.70 (0.82, 3.52)	0.16
Ischemic stroke	529 (30.5%)	0.86 (0.69, 1.08)	0.19
Cancer	47 (2.7%)	1.03 (0.55, 1.92)	0.93
Associated injuries	125 (7.2%)	1.46 (1.00, 2.12)	0.05
Dementia	67 (3.9%)	1.71 (1.05, 2.81)	0.03
COPD	97 (5.6%)	0.79 (0.50, 1.26)	0.33
Hepatitis	50 (2.9%)	0.77 (0.40, 1.45)	0.41
Gastritis	26 (1.5%)	0.39 (0.14, 1.15)	0.09
Admission to operation (d)	4.17 ± 2.42	1.05 (1.01, 1.09)	0.02
Treatment strategy			
ORIF	1063 (61.3%)	1	
HA	632 (36.4%)	0.71 (0.57, 0.88)	< 0.01
THA	40 (2.3%)	0.48 (0.22, 1.05)	0.07
Operation time (mins)	93.84 ± 34.50	1.00 (1.00, 1.01)	0.12
Blood loss (mL)	237.54 ± 149.88	1.00 (1.00, 1.00)	0.30
Infusion (mL)	1587.57 ± 379.57	1.00 (1.00, 1.00)	0.56
Transfusion (U)	0.93 ± 1.21	1.13 (1.04, 1.22)	< 0.01

Table 2. Effects of factors on DVT measured by univariate analysis.

Exposure	Non-adjusted model	Adjusted model I	Adjusted model II
ATO (d)	1.05 (1.01, 1.09) 0.02	1.05 (1.01, 1.09) 0.02	1.05 (1.01, 1.09) 0.02
ATO tertile			
ATO $\leq 2d$	1	1	1
$2d < ATO \leq 4d$	0.81 (0.62, 1.04) 0.10	0.80 (0.62, 1.04) 0.10	0.81 (0.62, 1.05) 0.11
ATO $> 4d$	1.17 (0.90, 1.52) 0.25	1.18 (0.90, 1.53) 0.23	1.17 (0.90, 1.53) 0.24
P for trend	0.16	0.15	0.16

Table 3. Univariate and multivariate results by linear regression. Data in the table: odds ratio (95% CI) P value. Outcome variable: DVT. Exposed variables: ATO. The minimally adjusted model was adjusted for sex. The fully adjusted model was adjusted for sex, fracture classification, associated injuries, dementia, transfusion, and treatment strategy.

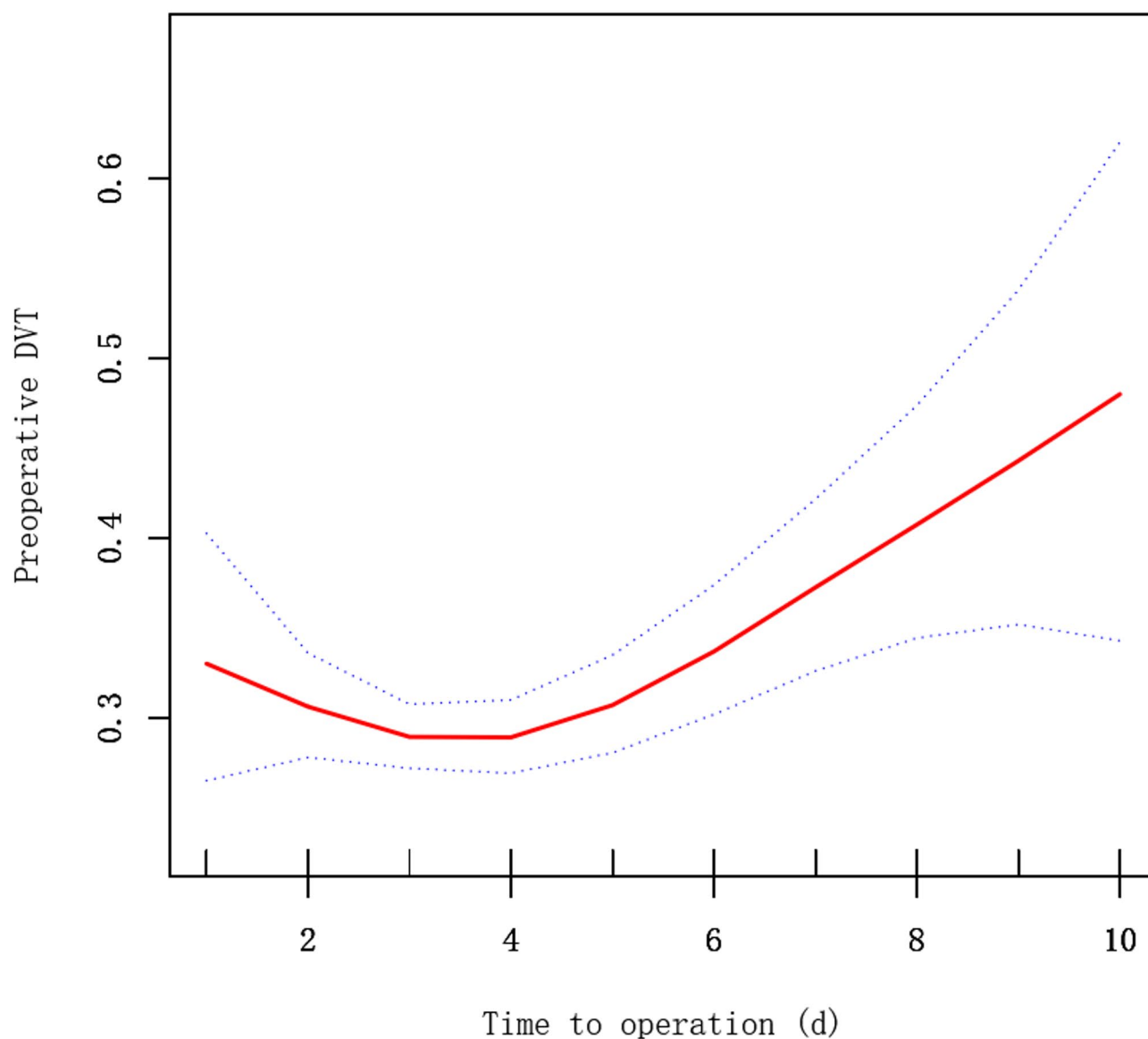


Fig. 1. Curve fitting between ATO and DVT. Adjusted for sex, fracture classification, associated injuries, dementia, transfusion, and treatment strategy.

Outcome	OR (95%CI) P-value
Fitting model by linear regression	1.05 (1.01, 1.09) 0.02
Fitting model by two-piecewise linear regression	
Inflection point	3 d
< 3 d	0.83 (0.66, 1.03) 0.09
> 3 d	1.08 (1.03, 1.14) <0.01
P for log-likelihood ratio test	0.03

Table 4. Nonlinearity of ATO and DVT. Adjusted for sex, fracture classification, associated injuries, dementia, transfusion, and treatment strategy.

log-likelihood ratio test was 0.03, which means the difference between fitting the model by stand linear regression and two-piecewise linear regression is significant, and two-piecewise linear regression is more appropriate.

Propensity score matching (PSM)

To test the robustness of our results in the real world, we performed a sensitivity analysis using PSM. In total, 998 patients (57.5%) were successfully matched according to the ratio of 1:1 in each group. Sex, fracture classification, associated injuries, dementia, treatment strategy, and transfusion did not match between the two groups (Table 5). In the regression analysis under the PSM and PSM-adjusted models, we found that the results were stable and the inflection point was 3 d (Table 6).

Discussion

In this study, we aim to emphasize the detailed curve association between ATO and the development of preoperative DVT in geriatric patients with hip fractures. There was an obvious “J” type curve. In the early stage of ATO, the incidence of preoperative DVT was relatively low. When beyond some point of ATO, the incidence of preoperative DVT began to rise quickly. This study presents several new facts contributing to our understanding of this relationship. Firstly, through two-piecewise multivariate logistical regression, we have discovered a curve association between ATO and preoperative DVT in geriatric hip fracture patients. Specifically, an ATO of 3 d was identified as the inflection point in the curve fitting. When the ATO exceeded 3 d, we observed that each one-day increase in ATO was associated with an 8% increase in the incidence of preoperative DVT. Secondly, we obtained consistent results regarding the inflection point at 3 d of ATO using the PSM sample in a real-world study. However, the magnitude of the association between ATO and DVT was even more pronounced in the PSM analysis. In the PSM model, each one-day increase in ATO was associated with a 13% increase in the incidence of preoperative DVT(OR = 1.13). In the PSM-adjusted model, it was associated with an 11% increase (OR = 1.11). These findings further support the notion that ATO delay is a crucial risk factor for preoperative DVT in geriatric hip fracture patients.

Our results provide new insights into the timing of DVT risk in this patient population. While earlier studies showed surgery 48 h later was a risk factor for developing proximal DVT, our study pinpoints 3 d as a more precise and clinically relevant threshold. This distinction has important implications for clinical practice. Given that ATO delay is a significant risk factor for DVT, early surgical intervention may play a pivotal role in reducing the incidence of DVT in these patients. Our findings thus provide additional evidence for the potential advantages of early operation in geriatric hip fracture patients, which could guide the development of more optimal treatment strategies to minimize the risk of DVT and its associated complications.

As for the association between delay in operation and preoperative DVT, some studies reported that the delay in time from injury to admission and the delay in time from injury to surgery were the risk factors for preoperative DVT. Taoka et al. reported that a delay in surgery beyond 48 h after a hip fracture injury is a risk factor for developing venous thromboembolism and proximal DVT⁷. In a systematic review and meta-analysis, it was reported that a longer time from injury to admission and a longer time from injury to surgery were correlated with a high risk of DVT^{4,18}. The time from injury to surgery often contains the time from injury to admission and the time of ATO. The management for individual patients varied in time from injury to admission, such as finding a fall, calling an emergency, and transferring to a trauma center so that the confounding factors would be diverse in the population in epidemiological analysis. Therefore, it was necessary to choose a stable independent to find the real association in the field of DVT after hip fractures. ATO was a stable and united indicator, under which an individual patient with hip fracture began to receive the same management in a standard trauma center. As for the association between ATO and preoperative DVT, two retrospective studies reported a linear correlation^{14,15}. Zhang et al. reported that ATO was an independent risk factor for preoperative DVT in elderly patients with hip fractures, with OR = 1.881¹⁴. In the study by Xue et al., preoperative time was reported as an independent risk factor for preoperative DVT and the OR = 1.28 in multivariate logistic linear regression analysis¹⁵. These two studies reported the linear association between ATO and preoperative DVT. However, we found the curve association and 3 d was the inflection point in the curve fitting. Meanwhile, the PSM models showed the same results in a real-world study. Thus, curve association is the real relationship between ATO and DVT.

The popular pathogenesis of DVT formation is based on slow blood flow, damaged vascular endothelial cells, and a high coagulation state, proposed by Virchow¹⁹. DVT formation is a dynamic physiological process. Before

Variables	Preoperative DVT: No (<i>n</i> = 499)	Preoperative DVT: Yes (<i>n</i> = 499)	Standardized diff.	P-value
Age (y)	79.36 ± 6.54	79.41 ± 6.31	< 0.01	0.90
Sex			0.20	< 0.01*
Male	171 (34.3)	125 (25.1)		
Female	328 (65.7)	374 (74.9)		
Injury mechanism				0.05
Falling	492 (98.6)	480 (96.2)	0.15	
Accident	5 (1)	15 (3)	0.14	
Other	2 (0.4)	4 (0.8)	0.05	
Fracture classification			0.36	< 0.01*
Intertrochanteric fracture	252 (50.5)	338 (67.7)		
Femoral neck fracture	247 (49.5)	161 (32.3)		
aCCI				0.87
2	22 (4.4)	17 (3.4)	0.05	
3	101 (20.2)	104 (20.8)	0.01	
4	199 (39.9)	212 (42.5)	0.05	
5	123 (24.6)	120 (24)	0.01	
6	41 (8.2)	32 (6.4)	0.07	
7	11 (2.2)	11 (2.2)	0	
8	2 (0.4)	3 (0.6)	0.03	
Hypertension	242 (48.5)	260 (52.1)	0.07	0.28
Diabetes	97 (19.4)	94 (18.8)	0.02	0.87
CHD	252 (50.5)	260 (52.1)	0.03	0.66
Arrhythmia	146 (29.3)	159 (31.9)	0.06	0.41
Hemorrhagic stroke	9 (1.8)	11 (2.2)	0.03	0.82
Ischemic stroke	159 (31.9)	145 (29.1)	0.06	0.37
Cancer	12 (2.4)	15 (3)	0.04	0.70
Associated injuries	27 (5.4)	46 (9.2)	0.15	0.03*
Dementia	13 (2.6)	27 (5.4)	0.14	0.04*
COPD	30 (6)	25 (5)	0.04	0.58
Hepatitis	20 (4)	12 (2.4)	0.09	0.21
Gastritis	12 (2.4)	3 (0.6)	0.15	0.04
Treatment strategy				< 0.01*
ORIF	256 (51.3)	336 (67.3)	0.33	
HA	234 (46.9)	156 (31.3)	0.32	
THA	9 (1.8)	7 (1.4)	0.03	
Transfusion (U)				< 0.01*
0	316 (63.3)	271 (54.3)	0.18	
1	0 (0)	2 (0.4)	0.09	
2	162 (32.5)	188 (37.7)	0.11	
4	21 (4.2)	35 (7)	0.12	
6	0 (0)	3 (0.6)	0.11	
Time to admission (h)	77.14 ± 208.81	92.73 ± 216.17	0.07	0.25
Operation time (mins)	92.37 ± 32.53	95.52 ± 38.41	0.09	0.16
Blood loss (mL)	234.43 ± 137.74	240.96 ± 155.37	0.04	0.48
Infusion (mL)	1588.52 ± 354.38	1597.62 ± 398.94	0.02	0.70

Table 5. The balance test of propensity score matching (*N* = 988). *Variables were not successfully matched.

admission, patients with hip fractures would enter a gap time without the strategy of prevention of DVT, such as pharmacologic anticoagulation and physical prophylaxis.

The hypercoagulation state was reported to start soon after fractures²⁰. More than 50% of patients remained hypercoagulable 6 weeks after hip fracture despite thromboprophylaxis¹¹. The hypercoagulable state promotes slower blood flow, while post-fracture bed rest further slows blood flow. In addition, other mechanisms of DVT formation have been reported, such as the inflammatory response after fracture^{9,21,22}, which is also a key factor in the early formation of DVT, and C-reactive protein, IL-6, IL-8, TNF- α ²³, Gab2-MALT1 axis²⁴ and NF- κ B signalling pathway²⁵ have been reported to be involved in the response. An immune response was also involved in DVT formation after hip fracture²⁶. With the multiplicity of these underlying factors, DVT has begun to form, and it has been reported that the fastest time to form DVT was the first day after fracture²⁷, and 68.2% of DVTs

Outcome	PSM model	PSM-adjusted model
Fitting model by stand linear regression	1.09 (1.03, 1.15) <0.01	1.07 (1.00, 1.15) 0.07
Fitting model by two-piecewise linear regression		
Inflection point	3	3
< Inflection point	0.86 (0.66, 1.12) 0.25	0.85 (0.65, 1.11) 0.24
> Inflection point	1.13 (1.05, 1.21) <0.01	1.11 (1.02, 1.21) 0.01
P for log-likelihood ratio test	0.04	0.05

Table 6. Multivariate results by the regression. Data in the table: OR (95% CI) P value. Outcome variable: DVT Exposed variables: ATO. Adjusted variables in the propensity score matching (PSM)-adjusted model: Sex, fracture classification, associated injuries, dementia, treatment strategy, and transfusion. .

were diagnosed within 24 h of injury²⁸. After admission, patients routinely receive anticoagulation and physical DVT prophylaxis after contraindications to anticoagulation have been ruled out. Because of the suppression of these strategies for preventing DVT, the speed of DVT formation after admission does not rise rapidly^{29,30}. This also explains why the formation of DVT does not correlate with the ATO in the first 3 d of ATO.

However, it was reported that the median time of DVT 9 [IQR 4–17] in geriatric hip fractures³¹, and the DVT trend was stabilized within 1 week²⁷. Actually, the hypercoagulable state, inflammatory response, and immune response will peak after fracture, so drug and physical prevention did not wholly prevent DVT formation. At the same time, the longer the ATO, the more often it is associated with poor patients' comorbidities⁸, higher American Society of Anesthesiologists classes, and the Charlson Comorbidity Index, increased waiting time³². Because of these reasons, the formation of DVT will be increased in the late stage of the ATO, which explains the “J” shape of the curve fitting.

Previous studies have established a linear relationship between ATO and DVT^{14,15}, whereas our study not only found a more meaningful curvilinear relationship, but also the key time point of 3d. In this study, we performed multifactorial logistic regression by adjusting confounding factors for DVT formation to explore a more reliable relationship between ATO and preoperative DVT. Later, the PSM method in the real-world setting was used to enhance the stability and reliability of our results. This is the first study to deeply explore the curve relationship between ATO and preoperative DVT formation in a large sample size. Also, this study has some limitations. First, this study was designed as a retrospective, providing limited evidence compared to a prospective study. Second, this study could not prove the causal relationship between ATO and preoperative DVT formation.

In conclusion, the ATO is nonlinearly associated with preoperative DVT in geriatric patients with hip fractures under anticoagulation and mechanical thromboprophylaxis. The 3d was the important point in DVT formation. Each one-day increase in ATO was associated with an 8% increase in the incidence of preoperative DVT.

Data availability

The data was implemented by Xi'an Honghui Hospital. According to relevant regulations, the data could not be shared, but could request from correspondence author.

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Author contributions

According to the definition given by the International Committee of Medical Journal Editors (ICMJE), the authors listed above qualify for authorship based on making one or more of the substantial contributions to the intellectual content of the following: Conceived and designed the study: Bin-Fei Zhang. Performed the study: Wen-Si Qiang, Lu Dang, Yi-Lun Wu and Bin-Fei Zhang. Analyzed the data: Bin-Fei Zhang. Wrote the manuscript: Wen-Si Qiang.

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Declarations

Ethics approval and consent to participate

The study was approved by the Ethics Committee of the Honghui Hospital, Xi'an Jiaotong University (No. 202201009), and the Institutional Review Boards of Xi'an Honghui Hospital waived participants' informed consent.

Consent for publication

The work described has not been published before (except in the form of an abstract or as part of a published lecture, review, or thesis); it is not under consideration for publication elsewhere; and all co-authors have approved its publication.

Competing interests

The authors declare no competing interests.

Additional information

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