

Original Article

Efficacy of Atorvastatin Against Venous Thromboembolism After Total Hip Arthroplasty

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Abstract

Objective: We examined the effect of atorvastatin on the prevention and management of venous thromboembolism (VTE) after total hip arthroplasty (THA). **Methods:** A total of 300 patients were equally assigned to a treatment group and a control group. The treatment group received oral atorvastatin calcium tablets (20 mg/day) starting on the first day after surgery. The incidence of deep vein thrombosis, pulmonary embolism, incision hemorrhage, postoperative infection, and incision ecchymosis were evaluated in both groups. Additionally, hemoglobin levels, hematocrit, visual analog scale (VAS) pain scores, Harris hip scores, and Harris grading were compared between the two groups. **Results:** The incidence of deep vein thrombosis, pulmonary embolism, incision hemorrhage, postoperative infection, and incision ecchymosis was significantly lower in the treatment group after atorvastatin intervention ($P < 0.05$ vs. control group). The hemoglobin levels, hematocrits, and VAS scores in the treatment group were significantly lower on days 1, 3, 7, and 14 after surgery ($P < 0.05$ vs. control group). The Harris hip scores and the number of patients with excellent Harris grading were significantly higher in the treatment group ($P < 0.05$ vs. control group). **Conclusion:** Atorvastatin is effective in preventing VTE after THA and in improving postoperative joint function.

Keywords: Atorvastatin, Total Hip Arthroplasty, Venous Thromboembolism

Introduction

Venous thromboembolism (VTE) is a common complication following total hip arthroplasty (THA), primarily characterized by deep vein thrombosis (DVT) and pulmonary embolism (PE)¹. The incidence of DVT has been reported as 30.6% after femoral shaft fracture fixation, 15.7% after hip fracture fixation, 14.5% after periprosthetic knee fracture fixation, 10.8% after tibiofibular fracture fixation, and 50% after fixation of multiple fractures². Currently, there is no standardized clinical protocol for the prevention and treatment of venous thrombosis after knee

arthroplasty. Anticoagulant drugs are commonly used in clinical practice to prevent postoperative VTE, with aspirin and rivaroxaban being the most frequently prescribed². However, anticoagulants increase the risk of bleeding in certain patients during clinical application^{3,4}. Therefore, there is an urgent need to identify safer medications with better clinical efficacy for the prevention and treatment of VTE.

Statins have been shown to improve deep vein thrombosis (DVT) and are considered safer than anticoagulants. Their primary effects are thought to be related to their ability to enhance the fibrinolysis system, reduce thrombus formation, and decrease pulmonary embolism (PE) and post-embolization syndrome. It has been concluded that statins play a more beneficial role than aspirin in preventing and controlling thrombosis in atherosclerotic disease⁵. Rosuvastatin has been found to reduce the risk of DVT and PE in healthy individuals⁶, while atorvastatin has been reported to be effective in preventing and treating acute proximal lower extremity DVT⁷. However, no research has yet determined whether atorvastatin has an interventional effect on the development of VTE after total

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hip arthroplasty (THA). In this study, THA patients were either given atorvastatin or not. The clinical data of these patients were compared and analyzed to assess the effect of postoperative atorvastatin use on the prevention and treatment of VTE.

Materials and Methods

Participants

In this study, 300 patients who visited the orthopedics department of our hospital for total hip arthroplasty (THA) between January 2018 and January 2023 were selected as study subjects. The clinical data of these patients were retrospectively analyzed to explore the effect of atorvastatin intervention on the prevention and treatment of venous thromboembolism (VTE) after THA. This study was approved by the Research Ethics Committee of Jiangxi Province Hospital of Integrated Chinese and Western Medicine (2023-005) and conducted in accordance with the principles of the Declaration of Helsinki and good clinical practice guidelines. All patients provided written informed consent. The inclusion criteria were as follows: (1) patients aged ≥ 18 years; (2) meeting the diagnostic criteria for fractures as outlined in the *Guidelines for Imaging Differential Diagnosis of Bone and Joint Disorders*; (3) patients who underwent THA within 3-7 days of admission; and (4) patients with complete clinical data. Exclusion criteria included patients with: (1) preoperative infectious diseases; (2) tumors; (3) severe disorders of the liver, kidney, heart, or lungs; (4) diseases of the hematopoietic or endocrine systems; and (5) cognitive disorders⁸.

Treatment protocol and patients' data collection

The selected patients were divided into a treatment group (n=150) and a control group (n=150) based on whether or not they were treated with atorvastatin. Basic demographic and clinical data were collected, including sex, age, body mass index (BMI), education level, comorbidities (hypertension, diabetes mellitus, hyperlipidemia), affected side, fracture site (intertrochanteric femur/neck of femur), American Society of Anesthesiologists physical status (ASA-PS) classification, and length of hospital stay. Both groups received conventional postoperative nursing care. The treatment group received oral atorvastatin calcium tablets (Pfizer) 20 mg/day, starting on the first postoperative day and continuing until discharge. Adverse reactions, such as nausea, diarrhea, vomiting, and elevated liver enzyme levels, were recorded during the treatment period⁹.

Outcome Measures and Complications Assessment

The following parameters were observed and recorded for patients in both groups:

(1) Occurrence of Complications: The occurrence of lower limb DVT, pulmonary embolism (PE), incision hemorrhage,

postoperative infection, hip dislocation, limb swelling, and incision ecchymosis within 90 days after total hip arthroplasty (THA) was recorded.

(2) Hemoglobin (HB) and Hematocrit (HT): Routine laboratory test results were collected preoperatively and on the 1st, 3rd, 7th, and 14th days after surgery. The values for HB and HT were recorded.

(3) Visual Analog Scale (VAS) Pain Score: The pain level of patients was assessed preoperatively and 90 days postoperatively using the VAS. Scores were classified as follows: 0 points for no pain, 1-3 points for mild pain, 4-6 points for moderate pain, and 7-10 points for severe pain. A lower score indicated less pain¹⁰.

(4) **Harris Hip Score:** The Harris hip score and Harris grading system were used to assess hip function in patients of both groups preoperatively and 90 days postoperatively. The assessment included four aspects: mobility, pain, function, and deformity. A higher score indicated better recovery of joint function¹¹.

Statistical analysis

The SPSS 18.0 statistical software was used for data analysis. Quantitative data following a normal distribution were presented as mean \pm standard deviation ($\bar{x} \pm s$) and were analyzed using a t-test. Categorical data were expressed as percentages (%) and analyzed using the chi-square (χ^2) test. A p-value of < 0.05 was considered statistically significant.

Results

Comparison of General Information Between the Two Groups

In the treatment group, there were 82 males and 68 females. The patients' ages ranged from 37 to 87 years, with a mean age of 63.37 ± 8.37 years. The BMI ranged from 17.34 to 40.31, with an average of 28.19 ± 3.84 . Among them, 83 patients had left-sided injuries, and 67 had right-sided injuries. Regarding the fracture site, 53 patients had intertrochanteric fractures, and 97 had fractures of the neck of the femur. Additionally, 43 patients had hypertension, 31 had diabetes mellitus, and 28 had hyperlipidemia. According to the ASA classification, 41 patients were classified as grade I, and 109 were classified as grade II.

In the control group, there were 77 males and 73 females. Their ages ranged from 37 to 86 years, with a mean age of 63.57 ± 7.79 years. The BMI ranged from 17.84 to 39.42, with a mean of 28.19 ± 4.03 . Of these patients, 71 had left-sided injuries, and 79 had right-sided injuries. There were 60 cases of intertrochanteric fractures and 90 cases of fractures of the neck of the femur. Regarding underlying diseases, 35 patients had hypertension, 36 had diabetes mellitus, and 24 had hyperlipidemia. In the ASA classification, 32 patients were classified as grade I, and 118 as grade II.

Table 1. Baseline characteristics of patients in the two groups.

Variables	Treatment group (n=150)	Control group (n=150)	X ² /t	P
Age (years)	63.37 ± 8.37	63.57 ± 7.79	-0.221	0.825
Sex (%)				
Men	82 (54.7)	77 (51.3)	0.335	0.563
Women	68 (45.3)	73 (48.7)		
BMI (kg/m ²)	28.19 ± 3.84	28.13 ± 4.03	0.133	0.895
Comorbidities (%)				
Hypertension (%)	43 (28.7)	35 (23.3)	1.109	0.292
Diabetes mellitus (%)	31 (20.7)	36 (24.0)	0.480	0.488
Hyperlipidemia (%)	28 (18.7)	24 (16.0)	0.372	0.542
Affected side (%)				
Left	83 (55.3)	71 (47.3)	1.921	0.166
Right	67 (44.7)	79 (52.7)		
Type of Hip Fracture (%)				
Intertrochanteric	53 (35.3)	60 (40.0)	0.696	0.404
Femoral neck	97 (64.7)	90 (60.0)		
ASA-PS classification (%)				
Grade I	41 (27.3)	32 (21.3)	1.466	0.226
Grade II	109 (72.7)	118 (78.7)		
Length of hospital stay (d)	10.53 ± 1.65	10.34 ± 1.39	1.100	0.272

Note: BMI, body mass index; ASA-PS, American Society of Anesthesiologists Physical Status.

Table 2. Incidence of complications observed in the two patient groups.

Complications	Treatment group (n=150)	Control group (n=150)	X ² /t	P
DVT	3 (2.0)	11 (7.3)	4.795	0.029
PE	5 (3.3)	15 (10.0)	5.357	0.021
Incision hemorrhage	6 (4.0)	21 (14.0)	9.158	0.002
Postoperative infection	2 (1.3)	9 (6.0)	4.624	0.032
Hip dislocation	2 (1.3)	4 (2.7)	0.170	0.680
Limb swelling	3 (2.0)	5 (3.3)	0.128	0.720
Incision ecchymosis	4 (2.7)	14 (9.3)	5.910	0.015

Note: DVT, deep venous thrombosis; PE, pulmonary embolism.

There were no significant differences in baseline data, including age, sex, BMI, and ASA-PS classification, between the two groups ($P > 0.05$) (Table 1).

Occurrence of Complications in the Two Groups

In the treatment group, DVT occurred in 3 cases (2.0%), PE in 5 cases (3.3%), incision hemorrhage in 6 cases (4.0%), postoperative infection in 2 cases (1.3%), hip dislocation in 2 cases (2.7%), limb swelling in 3 cases (2.7%), and

incision ecchymosis in 4 cases (2.7%). In contrast, in the control group, DVT occurred in 11 cases (7.3%), PE in 15 cases (10.0%), incision hemorrhage in 21 cases (14.0%), postoperative infection in 9 cases (6.0%), hip dislocation in 4 cases (2.7%), limb swelling in 5 cases (3.3%), and incision ecchymosis in 14 cases (9.3%) (Table 2).

Compared to the control group, the incidence of DVT, PE, incision hemorrhage, postoperative infection, and incision ecchymosis was significantly lower in the treatment group ($P < 0.05$). However, the incidence of hip dislocation and

Table 3. Hemoglobin and hematocrit of patients in both groups.

Variables	Group	DAY 0	DAY 1	DAY 3	DAY 7	DAY 14
HB (g/dl)	Treatment (n=150)	13.72 ± 1.43	11.50 ± 1.50	11.27 ± 1.55	10.50 ± 1.58	10.38 ± 1.45
	Control (n=150)	13.86 ± 1.46	12.46 ± 1.46	11.84 ± 1.46	11.39 ± 1.42	11.08 ± 1.64
	t	-0.817	-5.622	-3.251	-5.137	-3.921
	P	0.414	< 0.001	< 0.001	< 0.001	< 0.001
HT (%)	Treatment (n=150)	41.99 ± 2.04	36.18 ± 2.09	34.04 ± 1.92	32.21 ± 2.00	30.18 ± 2.04
	Control (n=150)	41.74 ± 1.92	38.24 ± 1.89	36.45 ± 2.21	34.21 ± 2.09	33.55 ± 2.07
	t	1.095	-8.927	-10.084	-8.463	-14.208
	P	0.274	< 0.001	< 0.001	< 0.001	< 0.001

Note: HB: hemoglobin; HT: hematocrit.

Table 4. VAS scores and Harris hip scores and grading of patients in the two groups.

Variables	Groups	Before surgery	After surgery	t	P		
VAS	Treatment (n=150)	7.68±1.11	2.09±0.87	50.607	< 0.001		
	Control (n=150)	7.81±1.25	3.27±0.98	32.785	< 0.001		
	t	-0.926	-11.015				
	P	0.355	<0.001				
Harris hip score	Treatment (n=150)	38.98±5.71	84.66±5.95	-71.799	< 0.001		
	Control (n=150)	38.53±5.30	75.67±8.61	-45.460	< 0.001		
	t	0.712	10.520				
	P	0.477	< 0.001				
Groups	Harris hip score grading				Excellent and good rate	X ²	P
	poor	acceptable	good	excellent			
Treatment (n=150) [N (%)]	0	28 (18.7)	88 (58.7)	34 (22.7)	122 (81.3)	60.177	<0.001
Control (n=150) [N (%)]	45 (30.0)	49 (32.7)	53 (35.3)	3 (2.0)	56 (37.3)		

limb swelling did not differ significantly between the two groups ($P > 0.05$) (Table 2).

Comparison of Hemoglobin and Hematocrit Changes Between the Two Groups

Routine laboratory test results for hemoglobin and hematocrit were collected preoperatively (D0) and on days 1 (D1), 3 (D3), 7 (D7), and 14 (D14) postoperatively to assess the changes in hemoglobin and hematocrit between the two groups. At D0, the hemoglobin level in the treatment group was 13.72 ± 1.43 , compared to 13.86 ± 1.46 in the control group, and the hematocrit was 41.99 ± 2.04 in the treatment group and 41.74 ± 1.92 in the control group. No statistically significant difference was observed in either hemoglobin or hematocrit between the two groups at D0 ($P > 0.05$) (Table 3).

At D1, the hemoglobin level in the treatment group was 11.50 ± 1.50 and gradually decreased, reaching $10.38 \pm$

1.45 by D14. In the control group, hemoglobin was 12.46 ± 1.46 at D1 and 11.08 ± 1.64 at D14. Significant differences in hemoglobin levels were observed between the two groups on D1, D3, D7, and D14 ($P < 0.05$).

Regarding hematocrit, the treatment group had values of 36.18 ± 2.09 on D1 and 30.18 ± 2.04 on D14, showing a gradual decrease after atorvastatin administration. In the control group, hematocrit was 38.24 ± 1.89 at D1 and 33.55 ± 2.07 at D14. The changes in hematocrit between the two groups were significantly different on D1, D3, D7, and D14 ($P < 0.05$) (Table 3).

Hip Function Assessment in the Two Groups

The preoperative and postoperative (90-day) pain levels (VAS score) and hip joint function (Harris hip score) were compared between the two groups. The results indicated that there were no significant differences in the VAS and Harris scores between the two groups preoperatively ($P >$

0.05) (Table 4).

At 90 days post-surgery, the mean VAS score in the treatment group was 2.09 ± 0.87 , while in the control group, it was 3.27 ± 0.98 . The VAS score in the treatment group was significantly lower compared to the control group ($P < 0.05$). Regarding the mean Harris hip score, the treatment group scored 84.66 ± 5.95 , while the control group scored 75.67 ± 8.61 . The Harris score was significantly higher in the treatment group compared to the control group ($P < 0.05$) (Table 4).

Further analysis of Harris grading revealed that, in the treatment group, 34 patients had an “excellent” grade, 88 had a “good” grade, 28 had an “acceptable” grade, and none had a “poor” grade, resulting in an excellent/good rate of 81.3%. In the control group, 3 patients were rated as “excellent,” 53 as “good,” 49 as “acceptable,” and 45 as “poor,” giving an excellent/good rate of 37.3%. Overall, the excellent and good rate in the treatment group was significantly higher than in the control group ($P < 0.05$) (Table 4).

Adverse reactions

During atorvastatin administration, 2 cases of nausea, 1 case of vomiting, and 1 case of elevated liver enzyme levels were reported. No cases of diarrhea were observed.

Discussion

Venous Thromboembolism (VTE) is a clinical syndrome often associated with major orthopedic surgery, where abnormal blood coagulation in the veins leads to blockage of venous vessels and impaired venous return [12]. Deep vein thrombosis (DVT) refers to lesions in the deep veins of the lower extremities, while pulmonary embolism (PE) is characterized by dysfunction of pulmonary artery circulation caused by obstruction of the pulmonary artery or its branches due to a thrombus in the venous system or from the right heart [1]. DVT typically presents with sudden onset of swelling, pain in the extremities, localized soft tissue tension, and exacerbation following strenuous activity.

The American College of Chest Physicians (ACCP) published the “Antithrombotic Therapy for VTE Disease: Second Update of the CHEST Guideline and Expert Panel” in 2021, which provides clinical guidelines for antithrombotic therapy for VTE. According to these guidelines, apixaban, dabigatran, edoxaban, or rivaroxaban are recommended as anticoagulants during the therapeutic phase (the first three months) [13]. However, recent studies have highlighted the increased risk of bleeding associated with long-term anticoagulation therapy [14]. For instance, aspirin, commonly used in clinical practice, can lead to increased perioperative bleeding due to its potent inhibitory effect on plasminogen and platelets [15].

Rivaroxaban, a direct factor Xa inhibitor, exerts its anticoagulant effect by binding to antithrombin III, without

directly inhibiting thrombin. Despite its efficacy, rivaroxaban has been associated with adverse reactions, including hemorrhage and albumin reduction [16,17]. Therefore, there is an urgent need to discover and study safer and more effective drugs for the prevention and treatment of VTE.

Statins have been shown to be effective in preventing thrombosis in many studies. Skajaa N et al. [18] reported a significant reduction in the incidence of VTE among statin users in a population-based matched cohort study. One study found that atorvastatin was effective in reducing recurrent VTE in elderly patients [19]. In a study by Wang TF et al. [7], patients with acute proximal lower extremity VTE, with or without PE, were treated with atorvastatin and followed for 90 days. The study revealed that atorvastatin effectively lowered the mean low-density lipoprotein levels and the incidence of VTE in these patients. Additionally, research showed that patients diagnosed with COVID-19 had a five-fold increase in the risk of DVT lasting up to three months and a thirty-three-fold increase in the risk of PE lasting for up to six months. However, after 30 days of atorvastatin intervention, the incidence of VTE was significantly reduced [20]. Moreover, statins, superior to aspirin, have been found to be effective in reducing the incidence of VTE [21]. In the current study, it was observed that the incidence of VTE was significantly reduced within 90 days after THA in patients who received atorvastatin intervention compared to those who did not. While previous studies have reported that atorvastatin reduces the incidence of VTE, the novelty of our study lies in the fact that we are the first to demonstrate that atorvastatin effectively reduces the incidence of VTE in patients following THA and has a preventive and therapeutic effect on VTE.

Lower extremity VTE and PE are common and severe complications after THA. Patients often experience postoperative symptoms such as lower extremity swelling, increased epidermal pigmentation, and pain. If not properly managed or improperly treated with anticoagulants, patients may develop complications such as incision hemorrhage, postoperative infection, and incision ecchymosis. These complications not only affect postoperative recovery but also increase the burden on the patient’s quality of life [12]. Therefore, reducing these complications is crucial for improving recovery and evaluating patients’ clinical outcomes. Additionally, it has been found that high hematocrit and hemoglobin levels in the general middle-aged population may increase the long-term risk of VTE, making them important factors in the induction of VTE [22]. In the present study, the incidence of incision hemorrhage, postoperative infection, hip dislocation, limb swelling, and incision ecchymosis within 90 days after THA was observed. We found that patients in the treatment group (atorvastatin intervention) had a significantly lower incidence of these complications compared to those in the control group. Furthermore, the hip joints of the patients were assessed using the VAS pain scale and Harris hip scores within 90 days after THA. The results showed that atorvastatin intervention significantly

reduced the VAS pain scores and increased the Harris hip scores and grading. This suggests that atorvastatin contributes to the restoration of joint function and serves as an effective adjunctive therapeutic agent for postoperative THA patients. We also observed changes in hemoglobin and hematocrit levels in patients over the first 14 days after surgery. The hemoglobin and hematocrit levels in the treatment group were significantly lower than those in the control group. In conclusion, atorvastatin reduces the incidence of VTE to some extent and supports the postoperative recovery process.

It is believed that the mechanism of action of atorvastatin in inhibiting thrombosis may be related to several factors: activation of the fibrinolytic system, suppression of the hypercoagulable state of the blood, maintenance of venous endothelial function and integrity, and promotion of the repair of damaged endothelial structures²³. Wang D et al.²⁴ reported that atorvastatin improved subdural hematoma in rats by increasing the expression of angiopoietin-1 and VEGF. Additionally, atorvastatin has been shown to reduce the secretion of pro-inflammatory factors after DVT in patients, effectively alleviating inflammation without reducing C-reactive protein expression²⁵. We speculate that this may explain why atorvastatin reduces the incidence of infections and other complications in patients after THA. However, the exact mechanism remains to be elucidated through experimental studies.

To sum up, we found that atorvastatin effectively reduced the incidence of VTE in patients after THA and improved joint function, thereby contributing to better postoperative recovery and quality of life. This study adds valuable insights to the clinical use of atorvastatin and provides new clinical perspectives and data to support the prevention and treatment of VTE in postoperative THA patients. However, due to the limited sample size, as well as financial and time constraints, a larger cohort study was not conducted, and the precise mechanism of action of atorvastatin in improving VTE remains to be fully elucidated.

Postoperative administration of atorvastatin 20 mg/day following THA significantly reduced the incidence of VTE, PE, incision hemorrhage, postoperative infection, and incision ecchymosis. Additionally, patients receiving atorvastatin intervention showed significantly lower hemoglobin levels and hematocrit, reduced VAS pain scores, and improved Harris hip scores and grading compared to those without the intervention. Importantly, atorvastatin intervention did not lead to increased hemorrhage.

Ethics approval

This study was approved by the research ethics committee of Jiangxi Province Hospital of Integrated Chinese and Western Medicine (2023-005) and was conducted in accordance with the principles of the Declaration of Helsinki.

Consent to participate

Written informed consent was obtained from all patients.

Authors' contributions

HL designed and performed research. HL and YK analysed data and contributed to data interpretation. YK wrote the paper. All authors read and approved the final manuscript.

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