

Incidence and Risk Factors of Deep Venous Thrombosis in Asymptomatic Iliac Vein Compression: A Prospective Cohort Study

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Abstract

Background: Deep vein thrombosis (DVT) may be associated with iliac vein compression. Up to now, the majority of data has come from a retrospective study about the correlation between DVT and iliac vein compression. This prospective study was to determine the incidence of DVT in individuals with iliac vein compression and identify risk factors predictive of DVT.

Methods: A total of 500 volunteers without symptoms of venous diseases of lower extremities and overt risk factors of deep venous thrombosis between October 2011 and September 2012 in Shijitan Hospital were enrolled in this cohort study. All the participants underwent contrast-enhanced abdominal computed tomography (CT) to evaluate iliac vein compression. Baseline demographic information and degree of iliac vein compression were collected. They were categorized into $\geq 50\%$ or $< 50\%$ iliac vein compression group. Ultrasound examination was performed to screen DVT at the time of CT examination and 3, 6, 9, and 12 months after the examination. Primary event was DVT of ipsilateral lower extremity. Correlation between DVT and iliac vein compression was estimated by multivariate Logistic regression after adjusting for age, gender, malignancy, surgery/immobilization, chemotherapy/hormonal therapy, and pregnancy.

Results: In 500 volunteers, 8.8% (44) had $\geq 50\%$ iliac vein compression and 91.2% (456) had $< 50\%$ iliac vein compression. Ipsilateral DVT occurred in six volunteers including two in iliofemoral vein, two in popliteal vein, and two in calf vein within 1 year. Univariate analysis showed that the incidence of DVT was 6.8% in $\geq 50\%$ compression group, significantly higher than that in $< 50\%$ compression group (0.7%) ($\chi^2 = 12.84$, $P = 0.01$). Patients with malignancy had significantly higher incidence of DVT than those without malignancy ($\chi^2 = 69.60$, $P < 0.01$). Multivariate Logistic regression indicated that iliac vein compression and malignancy were independent risk factors of DVT. After adjustment for malignancy, patients with $\geq 50\%$ iliac vein compression had 10-fold increased risk of developing DVT (adjusted relative risk [RR] = 10.162, 95% confidence interval [CI]: 1.149–89.865, $P = 0.037$). In subgroup analysis, patients with malignancy and $\geq 50\%$ iliac vein compression had 12-fold increased the risk of DVT than those without malignancy and $\geq 50\%$ compression (RR = 12.389, 95% CI: 2.327–65.957, $P = 0.003$).

Conclusions: Iliac vein compression is common, but the incidence of DVT is low. Only individuals with $\geq 50\%$ iliac vein compression or compression combined with other risk factors might have significantly increased the risk of DVT. Further study is recommended to improve prevention strategies for DVT in significant iliac vein compression.

Key words: Deep Venous Thrombosis; Iliac Vein Compression; Logistic Models

INTRODUCTION

The relationship between iliac vein compression and deep vein thrombosis (DVT) was noted in 1851. Virchow found that the incidence of iliofemoral venous thrombosis in left lower limb was 5 times as high as that in the right lower limb.^[1] In 1965, Cockett and Thomas^[2] pointed out that the iliac venous compression was an important risk factor for the left iliofemoral vein thrombosis.

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The precise incidence of DVT in iliac vein compression is little known as there are too many risk factors for DVT. Currently, no standardized diagnostic criteria have been established for iliac vein compression.^[3] Most data about the effect of iliac vein compression on DVT came from retrospective studies. This prospective cohort study was conducted to investigate the incidence and risk factors of DVT in various degrees of iliac vein compression without symptoms. It might be more helpful for recognizing the clinical significance of iliac vein compression and improving prophylaxis of DVT in individuals with significant iliac vein compression.

METHODS

Volunteers

This prospective study enrolled volunteers without symptoms of venous diseases of lower extremities who underwent contrast-enhanced pelvic or abdominal computed tomography (CT) scans in Beijing Shijitan Hospital because of nonvascular disease from October 2011 to September 2012. The study was approved by the Institutional Review Board of the Beijing Shijitan Hospital. Informed consent was obtained from patients who agreed to participate in this study. The records of routine CT scans performed in our hospital were reviewed for volunteers. As hemodynamically significant, stenosis was usually defined as $\geq 50\%$ reduction of the lumen diameter, the volunteers were categorized into $\geq 50\%$ compression or $< 50\%$ compression group by the degree of iliac vein compression.

The inclusion criteria were (1) aged over 18 years and (2) underwent contrast-enhanced pelvic or abdominal CT examination for nonvascular diseases. The exclusion criteria were (1) history of DVT or chronic venous diseases; (2) symptoms of DVT or chronic venous insufficiency in lower extremity; (3) inferior vena cava involved compression; (4) congenital vein malformation; (5) inherited coagulation abnormality; (6) major trauma or abdominal surgery within 1 year; (7) tumors compressing the iliac vein; (8) cardiac, renal, or pulmonary dysfunction; (9) long-term bedridden or disabled patients; and (10) follow-up time shorter than 1 year.

Measurement of iliac vein compression

A high precise calibration tool of CT image digital films (Duen System UniSight, Beijing Duen Information System Co., Ltd., Beijing, China) was used to measure the diameter of the left common iliac vein [Figure 1]. The degree of compression was calculated by the ratio of the minimal anteroposterior diameter to an average diameter of common iliac vein [Figure 2].

Definition of deep vein thrombosis and underlying risk factors

DVT was diagnosed through ultrasound imaging with or without symptoms.^[4] Risk factors included age, gender, surgery/immobilization, chemotherapy/hormonal therapy, and pregnancy. Grading of risks factors for DVT

was mainly based on the criteria of standard reports of Society of Vascular Surgery: age ≥ 60 years, surgery > 3 h, immobilization > 3 days.^[5]

Follow-up

Duplex ultrasound surveillance of lower extremity veins was performed at the time of CT examination and 3, 6, and 12 months after the examination.

Statistical analysis

Chi-square test was used for univariate analysis. Multivariate stepwise Logistic regression was used to examine the effect of iliac vein compression on the development of DVT, which was determined by the adjusted relative risk (RR) with a 95% confidence interval (CI). A two-tailed $P < 0.05$ was considered statistically significant. All statistical analyses were performed using the SPSS 16.0 software (SPSS Inc., Chicago, IL, USA).

RESULTS

Five hundred and twenty asymptomatic volunteers were eligible for enrollment among 626 candidates. Five hundred volunteers (96.2%) were followed for 1 year. Demographic characteristics are shown in Table 1. The mean age of the patients was 55.4 ± 14.7 years (range: 18–89 years). There were 272 men (54.4%) and 228 women (45.6%). The degree of compression ranged from 0% to 72.6% with a median of 16.2%. Forty-four (8.8%) volunteers had $\geq 50\%$ iliac



Figure 1: Iliac vein compression. The left iliac vein was compressed by the right iliac artery and the fifth lumbar vertebral body (arrow).

Table 1: Demographic characteristics of the volunteers with/without iliac vein compression syndrome

Characteristics	n (%)
Age	
≥ 60 years	319 (63.8)
< 60 years	181 (36.2)
Gender	
Male	272 (54.4)
Female	228 (45.6)
Iliac vein compression	
$\geq 50\%$	44 (8.8)
$< 50\%$	456 (91.2)

vein compression and 189 (37.8%) had $\geq 25\%$ iliac vein compression.

Six volunteers (1.2%) developed DVT involving eight lower extremities within 1 year. Ipsilateral DVT occurred in six volunteers including two in iliofemoral vein, two in femoropopliteal vein, and two in calf vein. One patient had bilateral calf vein thrombosis, but only left iliac vein was compressed. One patient had bilateral femoropopliteal vein thrombosis with only left iliac vein compression.

During a one-year follow-up, malignancy was detected in 18 volunteers including four cases of lung cancer, three of ovarian cancer, two of cervical cancer, two of pancreatic cancer, two of breast cancer, two of gastric cancer, two of ureteral cancer, and one of hepatic cancer. Fifty-one volunteers had surgery or immobilization. Eighty-seven volunteers received chemotherapy or hormonal therapy including oral contraceptive. Six were pregnant.

The incidence of DVT was 6.8% in $\geq 50\%$ compression group and 0.7% in $< 50\%$ compression group. The results of univariate analysis are shown in Table 2. The incidence of DVT was significantly higher in volunteers with $\geq 50\%$ compression than that in those with $< 50\%$ compression ($\chi^2 = 12.84$, $P = 0.01$). Patients with malignancy (22.2%) had a significantly higher incidence than those without malignancy (0.4%) ($\chi^2 = 69.60$, $P < 0.01$). Age ($\chi^2 = 1.00$, $P = 0.43$), gender ($\chi^2 = 0.05$, $P = 1.00$), surgery/immobilization ($\chi^2 = 0.28$, $P = 0.48$), chemotherapy/hormonal therapy ($\chi^2 = 4.49$, $P = 0.07$), and pregnancy ($\chi^2 = 12.25$, $P = 0.07$) were not significant risk factors.

Multivariate stepwise Logistic regression showed that iliac vein compression and malignancy were independent risk factors of DVT [Table 3]. After adjustment for malignancy, $\geq 50\%$ iliac vein compression had 12-fold increased risk factors of DVT than $< 50\%$ iliac vein compression (adjusted $RR = 12.389$, 95% CI : 2.327–65.957, $P = 0.003$).

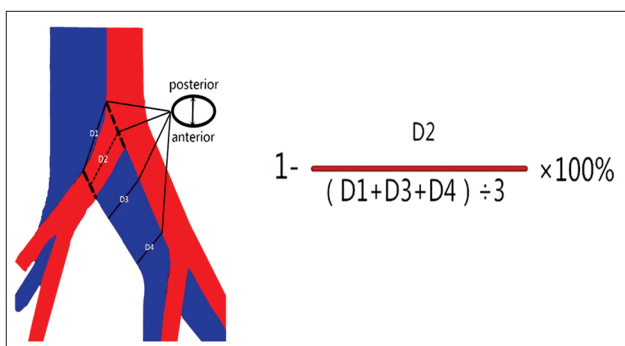


Figure 2: Calculation of degree of iliac vein compression. Degree of iliac vein compression = $(1 - D2 / (D1 + D3 + D4) / 3) \times 100\%$. D1, D3, D4: The anterior-posterior diameter of the left common iliac vein in before, after and distant segment; D2: The anterior-posterior diameter of the left common iliac vein in the compressed sit.

DISCUSSION

Iliac vein compression is not uncommon in the general population.^[6,7] Baron *et al.*^[8] reported about 20% of adults had iliac vein compression. Liu *et al.*^[9] reported that the prevalence of iliac vein compression syndrome (IVCS) in their cohort was 14.8%. Wolpert *et al.*^[10] performed magnetic resonance venography in 24 patients with isolated left leg edema and found that 37% patients had IVCS. Kibbe *et al.*^[11] investigated fifty volunteers without venous related symptoms or signs and found that 24% had $> 50\%$ left iliac venous compression and 66% had $> 25\%$ compression. This study also showed that 37.8% had $\geq 25\%$ iliac vein compression, and 8.8% had $\geq 50\%$ compression.

Many reports demonstrated that most patients with left iliofemoral thrombosis had iliac vein compression.^[12] However, most of them were retrospective studies. The real stenosis of iliac vein is difficult to define precisely as the vein thrombosis. That is the reason why we conducted the prospective study to investigate the incidence of DVT in individuals with iliac vein compression. Approximately, 70–80% of iliac veins develop a variable degree of obstruction following an episode of acute

Table 2: Univariate analysis for predictors of DVT

Variables	DVT, n	No DVT, n	χ^2	P
Age				
≥ 60 years	5	314	1.00	0.43
< 60 years	1	180		
Gender				
Male	3	269	0.05	1.00
Female	3	225		
Malignancy				
Yes	4	14	69.60	< 0.01
No	2	480		
Surgery/immobilization				
Yes	1	50	0.28	0.48
No	5	444		
Iliac vein compression				
$\geq 50\%$	3	41	12.84	0.01
$< 50\%$	3	453		
Chemotherapy/hormonal therapy				
Yes	3	84	4.49	0.07
No	3	410		
Pregnancy				
Yes	1	5	12.25	0.07
No	5	489		

DVT: Deep vein thrombosis.

Table 3: Multivariate analysis for predictors of DVT

Variables	B	SE	Wald	P	RR	95% CI	
						Lower	Upper
Malignancy	2.319	1.112	4.437	0.037	10.162	1.149	89.865
Iliac vein compression	2.517	0.853	8.703	0.003	12.389	2.327	65.957

DVT: Deep vein thrombosis; B: Standard coefficient; SE: Standard error; RR: Relative risk; CI: Confidence interval.

DVT.^[13] DVT is caused by the mechanical obstruction of the left common iliac vein by the right common iliac artery, resulting in stasis rather than a primary hypercoagulable state.^[14] However, the incidence of DVT is low in iliac vein compression. The variant exists in a significant portion of the population but is usually asymptomatic.^[15] In this study, only 6.8% developed DVT. Greater than 50% compression was an independent risk factor in the multivariate analysis, indicating that DVT may be associated with significant compression. This is consistent with another study.^[16]

Volunteers were recruited in one medical center, hence, bias may be present for this prospective study. Although there are many risk factors for DVT, the goal of the present study was to observe the incidence of DVT in variable iliac vein compression. It was not surprising to find a high incidence of malignancy in this study. We just considered it as one of the risk factors for DVT combined with iliac vein compression. In this study, the relationships between deep venous thrombosis and other risk factors such as age, gender, malignancy, and surgery were also assessed. Univariate analysis showed that malignancy was a significant risk factor. Multivariate analysis suggested that iliac vein compression and malignancy were independent risk factors. This might be due to the selection criteria of volunteers. Those with the overt risk of thrombosis had been excluded at the time of recruitment. Since our hospital is a cancer center, patients might come to undergo CT scanning for tumor. Malignancy becomes the primary risk factor for DVT. The contribution of chemotherapy or surgery to DVT could be concealed by malignancy due to the interactive effect. Although significant iliac vein compression was an independent risk factor for DVT, it seems that significant iliac vein compression combined with other risk factors would have more increased risk of DVT.^[17] Now that the malignancy is a strong risk factor, the effect of iliac vein compression might be underestimated.

Venous thromboembolism including DVT and pulmonary embolism becomes the second cause of death in cancer.^[18] There were several biomarkers and predictive models to assess the risk of venous thromboembolism in patients with cancer,^[19] but none of them refer to iliac vein compression.^[20] More targeted prophylaxis of venous thromboembolism in cancer patients could reduce mortality and morbidity. Once significant iliac vein compression is detected in malignancy, active prevention of DVT should be advocated. However, the incidence of DVT in iliac vein compression was low, so the cost-effectiveness of screening iliac vein compression for prediction of DVT needs to be further studied.

In summary, iliac vein compression is not uncommon, but the incidence of DVT is low. Only patients with $\geq 50\%$ iliac vein compression or compression combined with other risk factors may have significantly increased risk of DVT. Further study is recommended to improve prevention strategies for DVT in patients with significant iliac vein compression.

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Conflicts of interest

There are no conflicts of interest.

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