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Application of Computed Tomography Pulmonary Angiography with Low-Dose Computed Tomography Venography In The Diagnosis Of Venous Thromboembolism

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Abstract

Aims: This study investigated the use of computed tomography pulmonary angiography (CTPA) combined with low-dose CT venography (CTV) for diagnosing venous thromboembolism (VTE).

Methods: This retrospective study included 185 patients with suspected VTE from May 2015 to April 2020. Patients underwent CTPA with low-dose CTV and venous ultrasound to evaluate the sensitivity, specificity, and predictive values of lower extremity CTV to diagnose deep vein thrombosis (DVT) and compare consistency by Kappa test (P<0.001)of this diagnosis by the two methods.

Results: Among 185 patients, 121 were detected with lower extremity DVT using venous ultrasound. Low-dose CTV use for DVT showed a sensitivity of 71.29%, specificity of 76.19%, positive predictive value of 78.26%, negative predictive value of 68.82%, and accuracy of 73.51%. CTV and venous ultrasound findings of the lower limbs showed moderate consistency (Kappa=0.471, P<0.001), with no significant difference in DVT diagnosis (P=0.253). Seventy-three patients were diagnosed with proximal DVT, and indirect CTV and ultrasound diagnostic results were moderately consistent (Kappa=0.573, P<0.001). The diagnostic positive rate of CTV was 93.15%, significantly higher than that of ultrasound (60.27%, P<0.001). A weak diagnostic consistency of indirect CTV and ultrasound for distal lower limb DVT (Kappa=0.291, P<0.001) was detected, with no statistical difference between the two (P=0.532).

Conclusion: Indirect CTV has high sensitivity and specificity for detecting DVT, enabling early detection of proximal DVT in the lower limbs. Low-dose CTV can compensate for the lack of ultrasound examinations, with high clinical application values.

Keywords: CTPA; CTV; Diagnosis; Venous Thromboembolism

Introduction

Venous thromboembolism (VTE), including pulmonary embolism (PE) and deep vein thrombosis (DVT), is a common vascular disease associated with morbidity and mortality [1, 2]. Most PEs originate from DVT, and more than 90% of acute PEs are caused by leg or pelvic DVTs [3]. Therefore, early diagnosis and timely treatment of lower limb DVT can considerably reduce the incidence of PE [4].

Venography is the gold standard for detecting DVT but is rarely used because of its aggressive nature. In recent years, dual-source low-dose indirect lower extremity deep computed tomography venography (CTV) has been used as a diagnostic method for DVT. However, in clinical practice, venous ultrasound of the lower extremity is often the first choice for DVT examination. Braking equipment, bandages, edema, open wounds, and pain sensitivity will result in insufficient ultrasound examination and reduce the sensitivity and positive predictive value. At this point, CTV may compensate for the lack of ultrasound examination. There are few studies in this aspect. In this study, the diagnostic values of CTV and lower limb venous ultrasound in lower extremity DVT were compared for the early detection of lower limb venous thrombosis and for reduction of the occurrence of PE.

Materials and Methods

General Information

This retrospective study included 185 patients with suspected VTE hospitalized at Tianjin Haihe Hospital between May 2015 and January 2020. The results of computed tomography pulmonary angiography (CTPA) combined with CTV, lower limb venous ultrasound, and related adverse events after CTV were collected. The inclusion criteria were as follows: 1) performance of CTPA combined with CTV and lower extremity venous ultrasound; 2) age ≥16 years; 3) high-quality lower extremity venous ultrasound images: high-definition audiogram, identify blood vessels and their surrounding structures, measure the diameter line, show the filling state of blood flow, trace the blood flow spectrum and conduct quantitative analysis of venous blood flow, and 4) voluntary participation after being informed of the relevant content of this study with their data were included and provision of written informed consent. Patients with severe renal insufficiency, those allergic to contrast media, those without venous access, pregnant women, and children aged <16 years were excluded from the study.

Examination Methods

Lower extremity venous ultrasound was performed using a Philips EPIQ5 (Philips Ultrasound. Inc, Netherland) color Doppler ultrasound instrument, and a 5–10-Mhz linear array probe was selected. The patient was placed supine to expose both lower extremities fully, and each vein from the groin to the ankle was evaluated for thrombus formation.

The CTPA + CTV examination method used a GE Lightspeed 16-slice spiral CT scanner (General Electric Company, USA), and the patient was placed in a supine position with high ankle pads. Pulmonary artery imaging was performed first, and 120–150 mL of contrast agent was injected into the anterior cubital vein for optimal imaging. The injection flow rate was 3.0–3.5 mL/s, and the scanning was delayed for 22–25 s. Lower extremity venous scanning was performed at intervals of 90, 120, 180, and 240 s, ranging from the diaphragmatic to the upper sural venous plexus levels, and two or more experienced radiologists analyzed the data obtained.

Diagnostic Criteria

The CTV diagnostic criteria for DVT were venous cavity filling defects, partially or completely surrounded by opaque blood flow (orbital sign), or complete filling defects [5, 6].

The criteria for the diagnosis of acute DVT by venous ultrasound of the lower extremities were as follows: 1) application of a pressure probe to the thrombus area and uncompressed or partially compressed lumen; 2) solid echoes of varying intensity detected in the venous lumen; and 3) blood flow imaging showing no blood flow signal in the lumen or filling defect in the blood flow signal and an unchanging blood flow spectrum with respiratory movement [7].

The criteria for the results were as follows: 1) the same patient underwent lower limb CTV and lower limb vein ultrasound; 2) if DVT was detected in one or more examinations, the result was recorded as positive; and 3) if no thrombosis was detected in either examination, the result was recorded as negative.

Statistical Methods

Statistical software SPSS 23.0 (Version, IBM, Armonk, US) was used to describe and analyze the obtained data. The count data are presented as frequency (n) and rate (%), and the sensitivity, specificity, positive and negative predictive values, and accuracy rate were calculated using the chi-square test and Fisher's exact probability method. Agreement between groups was analyzed using the Kappa test; P values <0.001 were considered statistically significant. The judging criteria of Kappa values were as follows [8]: Kappa <0, extremely poor consistency strength; 0.0–0.2, weak; 0.21–0.40, weak; 0.41–0.60, moderate; 0.61–0.80, high; and 0.81–1.00, extremely strong.

Results

Diagnostic Results

According to the inclusion criteria, 185 patients (male individuals, n=115; female individuals, n=70; age range, 16–90 years; median age, 66 [52.5, 74.0] years) were included. Among them, 55 patients had a previous history of VTE; 28 had a recent history of fracture, trauma, or surgery; 5 were long-term bedridden; 6 were on hormonal or contraceptive drugs; and 11 had active tumors, among whom 1 had adverse reactions after undergoing CTPA combined with CTV. This patient developed chills and chills immediately after undergoing CTPA combined with a CTV examination, and his body temperature increased to 38℃. No contrast media-related kidney injury events occurred, and only one (0.54%) case of mild adverse reactions related to CTPA combined with CTV was detected.

Among the 185 patients, 10 (5.41%) were detected with abdominal venous thrombosis using CTV, among whom 8 were diagnosed with lower limb DVT and 2 without lower limb DVT (1.08%). Overall, 26 (14.05%) patients were diagnosed with pelvic DVT, and all of them had lower limb DVT. Additional findings included 1 patient with ovarian vein thrombosis, 15 with common iliac vein thrombosis, 14 with internal iliac vein thrombosis, and 21 with external iliac vein thrombosis. Neither abdominal venous thrombosis nor pelvic DVT could be detected by ultrasound.

Lower Limb DVT Diagnosis

As shown in Table 1, the following findings were reported: Among the 185 patients, namely 121 (65.41%) patients with lower limb DVT and 64 patients without lower limb DVT, lower extremity CTV and ultrasound positive predictive value was 38.92%; lower limb CTV and ultrasound negative predictive value was 34.59% (64/185); lower limb CTV positive but ultrasound negative predictive value was 10.81%; and lower limb CTV negative but ultrasound positive value was 15.68%. The sensitivity of lower limb CTV for DVT was 71.29%, specificity was 76.19%, positive and negative predictive values were 78.26% and 68.82%, respectively, and accuracy was 73.51%. Table 2 compares the detection of DVT using the two examination methods. The diagnostic results of CTV and ultrasound of the lower limbs were moderately consistent (Kappa=0.471, P<0.001). Regarding diagnostic accuracy, there was no significant difference between the diagnosis of lower limb DVT using lower limb CTV and ultrasound (P=0.253).

Table 1: Diagnosis of lower limb DVT using CTV and ultrasound

CTV	Ultrasound		Total
	Positive	Negative	
Positive	72	20	92
Negative	29	64	93
Total	101	84	185

Note: Kappa test (Kappa=0.471, P<0.001); paired chi-square test, P=0.253.

CTV: computed tomography venography; DVT: deep vein thrombosis.

A total of 73 patients with proximal lower extremity DVT were identified among 185 patients (Table 2). Lower limb CTV and ultrasound findings were positive in 21.08% of cases; lower limb CTV and ultrasound findings were negative in 60.54%; lower limb CTV findings were positive and ultrasound results were negative in 15.68%; and lower limb CTV findings were negative and ultrasound results were positive in 2.70%. Thrombus formation in the proximal lower limb veins (including the femoral and popliteal veins) detected by the two examination methods was compared, and the diagnostic results of CTV and ultrasound of the lower limbs were moderately consistent (Kappa=0.573, P<0.05). The positive predictive value of lower limb CTV in diagnosing DVT was 93.15%, which was significantly higher than that of ultrasound (60.27%, P<0.001).

Table 2: Diagnosis of lower limb proximal DVT using CTV and ultrasound

CTV	Ultrasound		Total
	Positive	Negative	
Positive	39	29	68
Negative	5	112	117
Total	44	141	185

Note: Kappa test (Kappa=0.573, P<0.001); paired chi-square test, P<0.001.

CTV: computed tomography venography; DVT: deep vein thrombosis.

A total of 110 (59.46%) patients had DVT of the distal lower extremity, and 75 (40.54%) patients had no DVT of the distal lower extremity (Table 3). Lower limb CTV and ultrasound findings were both positive in 24.86% of cases; lower limb CTV and ultrasound findings were negative in 40.54%; lower limb CTV findings were positive, but ultrasound results were negative in 15.68%; and lower limb CTV findings were negative, but ultrasound results were positive in 18.92%. Thrombus formation in the distal lower limb veins (including the posterior tibial, anterior tibial, peroneal, and intermuscular veins) detected by the two examination methods was compared, and the diagnostic results of lower limb CTV and ultrasound were hardly in agreement (Kappa=0.291, P<0.001). There was no significant difference between distal lower limb DVT diagnosis using lower limb CTV and ultrasound (P=0.532).

Table 3: Diagnosis of lower limb distal DVT using CTV and ultrasound

CTV	Ultrasound	Total

	Positive	Negative	
Positive	46	29	75
Negative	35	75	110
Total	81	104	185

Note: Kappa test (Kappa=0.291, P<0.001); paired chi-square test, P=0.532.

CTV: computed tomography venography; DVT: deep vein thrombosis.

In this study, the most common location for DVT detected by lower limb CTV and venous ultrasound was the posterior tibial vein of the lower limb, with 73 and 76 cases, respectively (Table 4); the second most common location for thrombosis detected by lower limb CTV was the popliteal vein (Figure 1); and the second most common location for thrombosis detected by lower limb venous ultrasound was the intermuscular vein. Indirect CTV was used to detect proximal venous thrombosis (Figures 1–3).

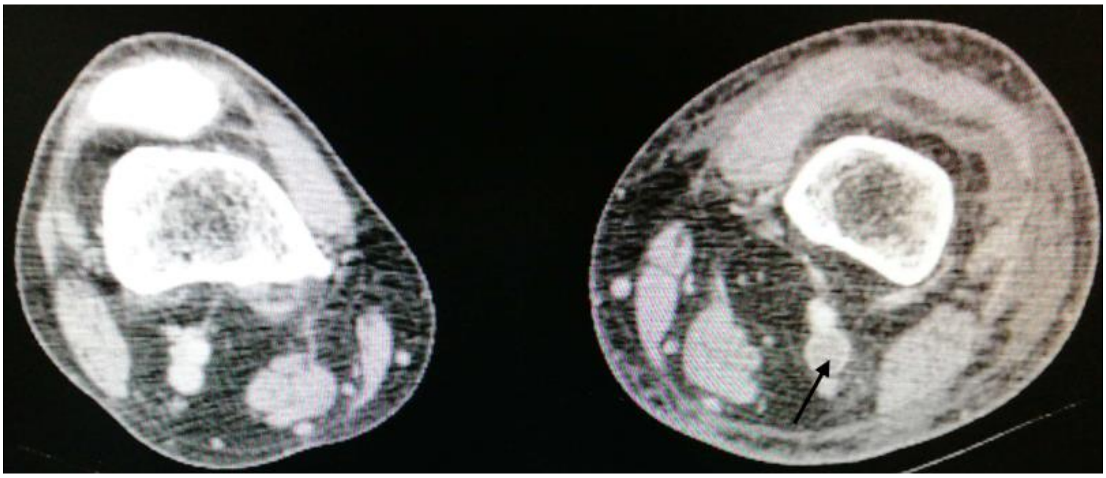

Figure 1: Axial indirect CT venography showing left popliteal vein DVT (arrow)

Figure 2: Axial indirect CT venography demonstrating inferior vena cava thrombosis (arrow)

Figure 3: Curved surface reconstruction showing DVT extending from the right femoral vein (thin arrow) to the right iliac vasculature

Table 4: Location of DVT in 185 patients (n, %)

	Lower extremity CT venography				Venous ultrasound of lower extremity			
Position	Number of cases (component ratio)	Left	Right	Bilateral	Number of cases (component ratio)	Left	Right	Bilateral
Inferior vena cava	2 (0.80%)							
Renalvein	2 (0.80%)	1	1	0				
Ovary vein	1 (0.40%)	1	0	0				
Iliac general vein	15 (6.02%)	6	5	4				
Internal iliac vein	14 (5.62%)	5	2	7				
Extrailiac vein	21 (8.43%)	11	6	4				
Venae femoris	48 (19.28%)	23	14	11	40 (21.05%)	21	14	5
Popliteal vein	56 (22.49%)	22	22	12	12 (6.32%)	6	6	0
Venae tibialis posteriores	73 (29.32%)	30	26	17	76 (40.00%)	28	24	24
Venae tibialis anterior	7 (2.81%)	6	1	0	2 (1.05%)	2	0	0
Peroneal vein	3 (1.20%)	1	2	0	0 (0.00%)	0	0	0
Venae intermuscularis	7 (2.81%)	3	1	3	60 (31.58%)	19	20	21
Total	249	109	80	58	190	76	64	50

Discussion

Lower limb vein ultrasound is a non-invasive examination. Owing to its wide application, low cost, high sensitivity, and accuracy, it has replaced the gold standard in recent years. It has become the preferred examination method for detecting suspected DVT

[9].

However, the application of lower extremity venous ultrasound has some limitations. Studies have shown that the use of CTPA combined with CTV can improve the sensitivity of the diagnosis of thromboembolic diseases with similar specificity, which has become an important auxiliary method for the diagnosis of lower limb DVT; furthermore, CTV can improve the detection rate of VTE [6]. Wu et al. (10) used dual-source low-dose CTV to diagnose lower limb DVT and compared the results with the gold standard digital subtraction angiography test findings. The sensitivity and specificity of the results were 96.2% and 92.6%, respectively, indicating that CTV has a good clinical diagnostic value.

This study confirmed that the diagnostic efficacy of CTV for lower limb DVT was similar to that of lower limb venous ultrasound [11]. Compared with venous ultrasound of the lower extremity, lower extremity CTV appears to have higher accuracy in detecting proximal DVT of the lower extremity and has similar sensitivity and specificity [12, 13]. In this study, the results of lower limb venous ultrasonography were used as the reference standard, and the sensitivity, specificity, positive predictive value, and negative predictive value of CTV in the diagnosis of lower limb DVT were 71.29%, 76.19%, 78.26%, and 68.82%, respectively. Adding CTV after CTPA increased the VTE diagnosis rate by 14.59%.

CTPA combined with lower extremity CTV-related adverse reactions is rare and mild and can screen for abdominal and pelvic DVT, detect clinically hidden DVT, and improve the detection rate of VTE. We consider that the use of CTPA combined with CTV may contribute to the early diagnosis of the disease and allow for early treatment (including anticoagulation therapy) of patients, which has a good application prospect. If further studies confirm our results, this combined imaging approach may play an important role in diagnosing suspected VTE.

The advantages of indirect CTV over ultrasound are as follows. 1) Its addition to CTPA is simple, as during the same examination, an additional image from the upper level of the sural venous plexus to the inferior vena cava can be obtained within a few minutes by expanding the scanned area with contrast media previously injected via the cubital vein; 2) data acquisition is fast and easy to perform, and CT is more objective than ultrasound; and 3) the sensitivity and specificity of ultrasound are highly dependent on the technique of the operator and are subjective. Therefore, indirect CTV is also applicable to obese patients with moderate to severe lower limb edema suspected of VTE, asymptomatic patients with a high risk of VTE, and patients with lower limbs covered with plaster, surgical materials, or wounds [14]. Indirect CTV can also detect lower limb DVT with negative ultrasound findings in the lower limb veins to compensate for the shortcomings of the ultrasound examination. In this study, lower limb DVT with positive indirect CTV findings and negative ultrasound results accounted for 10.81% of cases, which improved the detection rate of VTE. CTPA combined with CTV can also routinely screen the deep veins of the abdomen and pelvis while observing the complex venous anatomy. Herein, the proximal DVTs detected outside the lower extremities included those in the inferior vena cava, renal, ovarian, and iliac veins. These vessels cannot be visualized on lower extremity vein ultrasound. However, they may be important sources of pulmonary emboli, an important advantage of using CTPA combined with CTV.

There was a limitation in this study. Our findings could not be compared with those of digital subtraction venography of the lower extremities, which is the gold standard for diagnosing DVT of the lower extremities. Therefore, this study may have underestimated the incidence of DVT in the lower extremities. In addition, as there is no independent reference standard for DVT, CTV and ultrasound can only be compared for consistency or inconsistency.

In summary, the diagnostic efficacy of indirect CTV for lower limb DVT is similar to that of lower limb venous ultrasound. The accuracy of indirect CTV to diagnose proximal DVTs, except for those of the lower limbs, is high, including those of the inferior vena cava, renal, ovarian, and iliac veins. Therefore, indirect CTV of the lower limbs should be preferred for patients with suspected iliac vein and inferior vena cava thrombosis and PE. In addition, lower extremity DVT with negative ultrasound findings in the lower extremity vein can be detected, which compensates for the deficiency of the ultrasound examination, has few adverse reactions, improves the detection rate of VTE, and has a high clinical application value.

Conflicts of Interest

The authors declare that they have no conflict of interest potentially related to the article.

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