MODERN METHODS OF DEEP VEIN THROMBOSIS DIAGNOSIS: LITERATURE REVIEW

NAUJAUSIŲ RADIOLOGINIŲ TYRIMŲ METODŲ KOJŲ GILIŲJŲ VENŲ TROMBOZEI NUSTATYTI LITERATŪROS APŽVALGA

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SANTRAUKA


Apibendrinus literatūros duomenis, straipsnyje apžvelgiami radiologinės diagnostikos metodai kojų giliųjų venų trombozei nustatyti, radiologinių tyrimų privalumai ir trūkumai.

ABSTRACT

Key words: deep vein thrombosis, compression ultrasound, multidetector computed tomography, magnetic resonance, venography.

Venous thromboembolism consists of two related conditions: deep vein thrombosis and pulmonary embolism. One-third venous thromboembolism cases are manifested as pulmonary embolism and two-third present with deep vein thrombosis alone. Deep venous thrombosis remains an important health care problem as it is related with the complications having a high morbidity and mortality rate: acute and chronic pulmonary embolism, pulmonary hypertension and post-thrombotic syndrome. It is considered the third most common acute cardiovascular disease after ischemic heart disease and stroke and affects millions of people worldwide. Conventional venography was the gold standard in deep vein thrombosis diagnosis and the only imaging test for a long time in order to specify the suspected deep vein thrombosis in legs, pelvis or inferior vena cava [1, 2]. Presently contrast x-ray venography is applied very seldom in conventional medical practice. Contrast x-ray venography is particularly helpful for assessing recurrent acute deep vein thrombosis in patients with a prior history of deep vein thrombosis in whom venous anatomy is often complex and difficult to evaluate using other methods [3] or when to remove an inferior vena cava filter.

Conventional venography is presently replaced with non-invasive or less invasive radiological examination methods: the first-choice method is ultrasound, but there are also other ones – computed tomography venography and magnetic resonance venography. Ultrasound is the imaging examination of choice for suspected lower extremity deep venous thrombosis. Ultrasound has high sensitivity (range, 93.2 %–95.0 %; pooled sensitivity, 94.2 %) and high specificity (range, 93.1 %–94.4 %; pooled specificity, 93.8 %) for diagnosing proximal (thigh) deep vein thrombosis and much lower sensitivity (range, 59.8 %–67.0 %; pooled specificity, 63.5 %) for diagnosing distal (calf) and pelvic veins thrombosis. Compression ultrasound has several limitations, especially in the pelvic region compression ultrasound is not the method of choice. Computed tomography venography and magnetic resonance venography are possible alternatives to compression ultrasound in evaluating the extension of the thrombus to the iliac veins and inferior vena cava.

We made a summary of deep vein thrombosis methods of radiological diagnostics in literature.
INTRODUCTION

Venous thromboembolism (VTE) consists of two related conditions: deep vein thrombosis (DPV) and pulmonary embolism (PE). One-third VTE cases are manifested as PE and two-third present with DVT alone [4].

Lower-extremity deep venous thrombosis (DVT) has an estimated annual incidence of approximately 5 per 10,000 in the general population, with the incidence increasing with advancing age [3, 5].

Pulmonary embolism can occur in 50–60 % of patients with untreated DVT, with an associated mortality rate of 25–30 % [3, 6, 7].

Deep venous thrombosis (DVT) remains an important health care problem as it is related with the complications having a high morbidity and mortality rate: acute and chronic pulmonary embolism, pulmonary hypertension and post-thrombotic syndrome. It is considered the third most common acute cardiovascular disease after ischemic heart disease and stroke and effects millions of people worldwide [8, 9, 10].

The most frequent reason for pulmonary embolism is the thrombus forming in the channels of proximal leg veins and deep pelvis veins. The development of deep venous thrombosis is related with stasis, hypercoagulation and injury of the venous wall (Virchow’s triad).

DVT usually starts in calf veins, but it may develop more proximally and condition life-dangerous pulmonary embolism. From 80 to 90 % of pulmonary embolism masses are caused by DVT or thrombus formed in the pelvis [4].

The prophylaxis and treatment of this disease is very important in the clinical practice, so, an early and exact diagnosis is relevant in order to evaluate the exact location and extent of DVT.

The classical symptoms in patients with acute leg DVT are pain or sensitivity, edema and swollen legs, but these symptoms are not specific and characteristic to this kind of pathology only.

The clinical signs and symptoms of pulmonary embolism also are not specific: dyspnea or tachypnea 70–80 % (respiratory rate > 20/min), hemoptysis 11 %, pleuritic pain 50 % (angina-like chest pain), tachycardia 25–30 % (heart rate > 100/min), cough 20–37 % – nonproductive, and sometimes productive of clear, bloody or occasionally purulent sputum, rales 50 % and deep venous thrombosis 15 %.

It is often difficult in a clinical sense to detect DVT and PE because from one third to 2/3 patients do not have any symptoms of DVT at all according to the data of different literature data.

IMAGING OPTIONS

Ultrasound

US is widely recognized as the most cost-effective and preferred imaging modality for diagnosing proximal DVT [5, 6, 7, 11, 12, 13, 14, 15, 16]. US is a non-invasive and easy-to-perform examination without the effect of ionizing radiation and contrast agent (for example, on the bedside if necessary) and it can be repeated a few times.

Color Doppler ultrasonography (CDUS) has become the initial diagnostic tool due to its high sensitivity for the detection of DVT, and some authors now believe that CDUS should be considered as the gold standard for DVT diagnosis [11].

The venous ultrasonography examination involves a few methods: compression ultrasound (images are obtained by applying the simple B-mode and pressing the region of the visible vein with a transducer) – the best method for the evaluation of proximal leg veins – common femoral, femoral (surface femoral) and popliteal veins, duplex US – the image is obtained by applying the B-mode together with the color Doppler signal and color Doppler imaging alone.

The present medical practice diagnosing venous thrombosis still applies the compression method mostly – DVT is excluded if the venous channel is fully compressed and DVT is confirmed if the venous channel changes just a little. Transversal images are evaluated with a 5 or 7.5 MHz linear transducer as well as sagittal grayscale ones supplemented with color and spectral Doppler images.

Doppler color-flow imaging can assist in characterizing a clot as obstructive or partially obstructive; the uneven color-flow can also help to locate the isoechogenic thrombus.

A recent meta-analysis found US to have high sensitivity (range, 93.2 %–95.0 %; pooled sensitivity, 94.2 %) and high specificity (range, 93.1 %–94.4 %; pooled specificity, 93.8 %) for diagnosing proximal DVT [2]. In the same study, US was found to have a much lower sensitivity (range, 59.8 %–67.0 %; pooled sensitivity, 63.5 %) for diagnosing distal DVT, which confirmed a widely known diagnostic limitation for this technique [2] and the calf US examination is not routinely performed in many centers due to relatively low accuracy. However, if the patient indicates local pain in the calf, the examination of this region should be performed.

The iliac and pelvis veins are not visible consistently with ultrasound mostly due to gas in the intestine.

The use of US images only makes it difficult to differ between acute and chronic DVT. The findings during the US examination in chronic DVT may include: higher-echogenecity thrombus, uneven walls of veins, low-caliber veins or collateral veins, but these symptoms may not occur; the echogenecity of chronic DVT can also change without any previous image data for comparison; it is difficult to differ between acute and chronic DVT.

It has been recognized it is difficult to differ between acute and chronic DVT by applying non-invasive examination methods including US.

Moreover, US may be limited in obese patients, in patients with marked low extremity (LE) edema and in pa-
patients with overlying casts [2] and US might show false negative results in patients with duplicate veins.

**Computed Tomography Venography**

CTV permits routine evaluation of deep veins of the calves [Fig. 1, Fig. 2], the iliac veins/IVC [Fig. 3], and the deep femoral vein [Fig. 4, Fig. 5], none of which are routinely well evaluated with US [2].

CTV can be performed either as direct CTV, using a venous injection of iodinated contrast media in a pedal vein similar to that in contrast x-ray venography, or, more commonly, as an indirect CTV using an antecubital vein for a contrast media injection and a delayed-imaging acquisition suitable for deep-venous opacification [2]. Many studies found, that the amount of contrast agent used in CTV was lower by about 80% than in venography. Studies comparing the findings of CTV with tones of venography showed 100% sensitivity and 96–97% specificity.

CTV enables comprehensive evaluation of some regions in one examination – i.e., pulmonary CT angiography evaluating pulmonary embolism and evaluation of pelvic and deep leg veins. Combined CT venography and pulmonary angiography – CTVPA, is a “one-stop examination”, requiring only a few additional minutes – although the overall radiation dose is higher, there are more images to review, and the dose of IV contrast needs to be higher for optimal venous enhancement compared with CTPA alone [2]. CTPA is readily available in most hospitals.

CTV can be repeated in dynamics during the treatment (anticoagulation therapy) if necessary.

In patients who have a suspected pulmonary embolism, a recent meta-analysis found CTV to have high sensitivity (range, 71%–100%; pooled sensitivity, 95.9%) and high specificity (range, 93%–100%; pooled specificity, 95.2%) comparable to that of US for diagnosing proximal DVT [17].
The advantage of CTV like that of MRI is imaging of transversal sections which can also evaluate extravascular pathology – for example, reasons of external vein compression (adenopathy, pelvic masses) which may cause DVT. Moreover, the latest CT scanners really cause a lower radiation dose during the examination compared with older equipment and also enable performing different reconstructions and 3-dimensional images which makes it easier to make a diagnosis.

The most frequent methodology of CTV in leg DVT is between 120–150 ml of iodinated contrast (depending on the patient’s weight); scanning starts 180 s after injecting the contrast agent into the elbow vein; scanning is performed from the tarsi or knee-joints every 5 mm towards the pelvis (involving the ilial wings).

The radiation dose for the bilateral lower-extremity CTV is 3–8 mSv (less than that of abdominal CT) [18]. Clot is identified as a filling defect within a deep vein. Acute DVT often expands the vein, and has associated peri venous edema and enhancement of the venous wall [19, 20].

The limitations of CTV should also be considered: the examination may not be performed for the patients sensitive to the iodinated contrast agent as well as renal function insufficiency as quite a high amount of contrast agent is used; pregnancy; claustrophobia and patients unable to stay still during the examination; children; metal implants causing artifacts in surrounding tissues; high-circumference patients. The evaluation of changes in the channels of veins is also hindered by atherosclerotic changes in the walls – it may be difficult to differ from real DVT.

Katz D. S. and others [2] believe, that US and CTV are complementary in a subset of patients, and may help to resolve problematic findings encountered on either examination.

**Magnetic Resonance Venography**

MR venography has high accuracy compared with conventional venography for the pelvic and thigh veins, but is less accurate for the calves. By Hofer E. K. et al [18] MRV is effective and accurate, with a sensitivity and specificity for iliac and femoral DVT approaching 100 % compared with venography and a 92 % sensitivity in detecting isolated calf-vein thrombus. A variety of sequences can be utilized, including spin-echo, gradient-recalled echo, and gadolinium-enhanced images [21, 22, 23].

MRI is the alternative to CTV for patients with suspected DVT needing to avoid the effect of ionizing radiation or suffering from allergy to iodine contrast agents. In patients with suspected PE, in whom radiation should be avoided, or who are allergic to iodine contrast agents, magnetic resonance pulmonary angiography (MRPA) has potential as an alternative to CTPA [24, 25, 26, 27].

The advantage of MRV over US is a possibility to evaluate extravascular anatomy and determination of the pathology causing the external vein compression which can condition DVT or DVT-imitating pathologies. MRV may be performed for pregnant women that must avoid the radiation effect, but need the determination of pelvic deep vein thrombosis.

MRV has the advantage over US in evaluating veins above the inguinal ligament, as 20 % of DVTs are isolated to the pelvic veins [28]. MRV may be superior to US for determining the chronicity of DVT, although this has not been well studied [2, 29].

MRV is contraindicated for patients with ferromagnetic implants; metal foreign bodies; high-circumference patients; claustrophobia and patients unable to stay still during the examination.

Lately, there have been more references about the effect of gadolinium contrast agents on patients with the renal dysfunction – nephrogenic systematic fibrosis (NSF) or nephrogenic systematic dermopathy (NFD) after the examination which can be manifested with clinical symptoms or even result in death.

As long as full evidence is not obtained, there is a common agreement not to use any gadolinium contrast agent for dialysed patients or patients with a very limited glomerular filtration speed.

**Nuclear Imaging**

With the emergence of nuclear medicine methods, new perspectives were opened early on for diagnosis of DVT [9]. Radiolabeled peptide that bind to various components of a thrombus have been investigated. Apcitide, a technetium-labeled platelet glycoprotein IIb/IIIa receptor antagonist, is approved for diagnostic studies of DVT [18].

Foci of increased activity indicate an acute thrombus in that location.

In a multicenter evaluation of technetium-99m-apciti- de scintigraphy compared with contrast venography in 243 symptomatic or high-risk patients, 99mTc-apcitiide had a sensitivity of 75.5 % and a specificity of 72.8 %. However, after patients with a history of DVT or PE were excluded, the sensitivity and specificity were 90.6 % and 83.9 %, respectively, for 99 mTc-apcitiide [9, 30].

**CONCLUSIONS**

1. Conventional venography is mostly of historical interest when used solely as a road-mapping technique immediately prior to IVC filter placement. Conventional venography is often limited by its technical difficulty.

2. Ultrasonography has become the first-line accepted imaging method in the diagnostic procedure for patients with clinically suspected DVT. US is highly sensitive and specific noninvasive imaging options for evaluating proximal DVT, and it is less...
accurate for the calf and pelvic veins and in asymptomatic patients.

3. CT venography and MR venography are highly suspecting of having pelvic DVT and can be used to evaluate extravascular anatomy and pathology.

4. CT venography and MR venography can be combined with CT or MR pulmonary angiography and it is nowadays the imaging test of choice in patients with clinically suspected acute pulmonary embolism (PE).

REFERENCES


