Justification of using Computed Tomography and Magnetic Resonance Imaging for Deep Venous Thrombosis and Pulmonary Embolism

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Abstract—Deep vein thrombosis (DVT) is a medical condition, occurs when a blood clot forms in a deep vein and pulmonary embolism (PE) occurs when a blood clot gets lodged in an artery in the lung, affecting blood flow to part of the lung.The frequencies of using computed tomography (CT) and magnetic resonance imaging (MRI) to diagnose deep venous thrombosis and pulmonary embolism is increasing day by day.

Both the technics are noninvasive and provide prompt results. But there are a good number of alternative technics for the same purposes. That is why, till now scholars and respective professionals are interested to know more about the justification and comparative effectiveness of CT and MRI in detecting DVT and PE.

This review aimed to analyze the history of several detecting methods for DVT and PE and to dig out the clear concepts about the effectiveness and patient compliances of CT and MRI in detecting deep venous thrombosis and pulmonary embolism. For proper analysis a lot of research as well as meta-analysis had been studied.

From this article besides scholars and professionals, general readers will get a clear concept about the features, effectiveness and justifications of CT and MRI in treating DVT and PE.

Keywords—computed tomography (CT), magnetic resonance imaging (MRI), deep vein thrombosis, pulmonary embolism (PE), angiography

1 Introduction

1.1 Deep vein thrombosis (DVT)

Deep vein thrombosis (DVT) happens when a blood clot forms in one or more of the deep veins in the human body, which can affect the blood flow of veins and result in poor blood circulation. Moreover, DVT can occur even in the absence of serious disorders. As investigated by some researchers, 'thrombosis can occur in any part of the venous system, but it appears most frequently at the deep veins of the legs' [1].

Thrombosis can occur during travelling and even that can be in an air traveler also. 'Traveler's thrombosis occurs by sitting still in transport-vehicle for a long time and

blood clots are formed and deposited the inside of deep veins of lower limbs', which constitutes DVT [2]. Scurr et al. have indicated 'incidences of 10% of asymptomatic calf vein thrombosis among air travelers >50 years of age and traveling for more than 8 h' [3]. The prevalence of DVT among the general population and the possibilities of the suffering of DVT patients from pulmonary embolism is not so small. Basically, 'DVT is a prevalent disease in nature with an occurrence of between '2.5% to 5%' in the total population, and about '30−40%' of DVT patients finally suffer from 'pulmonary embolism' [4].

A great disappointing thing is the uncertainty of proper diagnostic results of DVT. Generally, of DVT is a great clinical challenge for doctors and clinicians. Besides these, the deterioration of such disease may make the treatment procedure more complicated. Actually, 'the diagnosis or assessment of DVT in clinics is notoriously unreliable because, only about 30% patients have been shown to be positive on objective testing' [5]. That is why, 'suspected DVT cases in the clinical diagnosis, can lead to the 'unnecessary prolonged hospitalization of patients' as well as 'inappropriate anticoagulation therapy' with potentially harmful and dangerous consequences.

1.2 Pulmonary embolism (PE)

Pulmonary embolism is a common but still underdiagnosed condition. Pulmonary embolism (PE), which is the most serious presentation of VTE, is the third most common cause of death from cardiovascular disease after a heart attack and stroke. [6] In a survey, it was found that, "1945 through 2002, PE was unsuspected or undiagnosed ante-mortem in 3268 (84%) of 3876 patients" who had PE discovered at autopsy [7].

It is still undiagnosed, due to the lack of suspicion and availability of appropriate diagnostic testing such as multi-detector computed tomographic angiography (CTA), especially in low resource settings [8]. It is so serious condition that has a '30-day mortality rate' between 9% and 11% [9]. Worldwide, the prevalence of PE is increasing day by day which is most alarming. The incidence of PE (Pulmonary embolism) is growing worldwide, particularly in the high-income countries [10].

Defining PE depending on clinical presentations is very critical and uncertain. Generally, the clinical features of pulmonary embolism are non-specific. In a study, they claimed that, 'Symptoms can vary from mild chest pain to shock be-cause of right ventricular failure in patients with massive PE' [11]. In a study they claimed, 'patients with PE sometimes present without any symptoms, the diagnosis being coincidently when investigating for other conditions [10]'.

Till now, spinal cord injury, immobilization, malignancy, recent surgery and/or trauma, lower limb fractures and joint replacements are considered as the major risk factors of PE. However, 30% of patients with PE have no detectable provoking factors [12] and 'in Sub-Saharan Africa, preliminary studies have shown that PE was scarce' [13].

2 Methodology

Taking into account the specifics of the topic under consideration, the most appropriate when writing this article was the use of the a systematic review of the literature was developed in three main processes, considering the criteria. The established criteria are the following: research planning, development of the search for information, and results found.

3 Diagnosis of deep vein thrombosis and pulmonary embolism

The diagnosis of pulmonary embolism (PE) is a very difficult task, particularly when there is coexisting 'heart or lung disease' and it is notoriously inaccurate when based on clinical signs alone. Sometimes, pulmonary embolism manifests in such a dramatic fashion that, the prompt diagnosis is intuitively obvious and treatment will be started, but the usual presentation is frequently 'vague' and variable in severity and further testing is necessary to establish or exclude the diagnosis [14]. About all the patients of pulmonary embolism will have 'one or more' of dyspnea of sudden onset, tachypnoea (20 breaths per min), or chest-pain (pleuritic/substernal) [15], if the clinician remembers those 3 features, the possibility of pulmonary embolism (PE) will rarely be overlooked. While these clinical features and/er presentations are associated with 'electrocardiographic signs of right ventricular strain' and/or 'radiological signs of plump hilum', pulmonary infarction or oligemia, the likelihood of PE is high and it is further strengthened in the presence of 'risk factors for VTE' and arterial hypo-anemia with hypocapnia [14]. But, the absence of all these 3 clinical features/presentations, virtually excludes the diagnosis of PE (Pulmonary embolism) [16]. Different studies have disseminated that, well characterized clinical empiric estimates or explicit 'prediction rules of pretest likelihood of PE can be applied for the safe management of patients suspected of having the disease [17]. Year after year many diagnostic methods for detecting pulmonary embolism have been introduced in the treatment arena.

3.1 Several diagnostic methods of DVT and PE

There is a tradition of using several diagnostic tools and methods in detecting pulmonary embolism (PE) as well as deep vein thrombosis (DVT). Some are used as independent and some as associate. Here is an overview of several diagnostic tools and methods of PE and DVT.

Electrocardiography. Electrocardiography is a primary diagnostic method for pulmonary embolism. The main value of electrocardiography (ECG) is in excluding other potential diagnoses like myocardial infarction or pericarditis [14]. Generally, in minor pulmonary embolism (PE), there is no real hemodynamic stress and thus the only

finding is sinus tachycardia. In massive pulmonary embolism (PE), the evidence of 'right heart strain' may be seen (Rightward shift of the QRS axis, transient right bundle branch block, Qr pattern in V1, T-wave inversion in leads V1–3, SI QIII TIII pattern, P pulmonale), but these signs are nonspecific [18]. In combination with a 'high clinical pretest probability' or 'echocardiographic signs' of 'right ventricular dysfunction', accuracy of ECG to diagnose PE (Pulmonary embolism) may be improved. [19] Physicians should be aware about that, ECG-report may be 'entirely normal' in up to 20% of patients with PE resulting in a low sensitivity for the exclusion of the diagnosis. [20] Now a day, autonomic dysfunction in anxiety disorder, [21] even drowsiness [22] is assessed by ECG. ECG features are used widely in detection as the prediction input because it is a 'non-invasive' and 'radioactive free diagnostic' tool. [23] But as a single detector ECG is not enough for detecting PE or DVT.

Chest radiography. Chest radiography is the 'initial examination of choice' insuspected patients of pulmonary embolism (PE), especially in the outpatient setting. [24] Generally, radiographs are frequently 'abnormal' in the setting of pulmonary thromboembolism but, show nonspecific findings. Westermark [25] alluded to this fact inthe year of 1938, stated, "The roentgenologic diagnosis of 'embolism of the pulmonary artery' is verydifficult particularly, in cases 'without infarction'." In the year 1940, using 'postmortem radiographs', Hampton and Castleman [26] authored a radiologic-pathologic correlation where they described a 'pulmonary infarct' as a 'wedge-shaped opacity' touching the 'pleural surface', with a 'sharply convex medial margin'. In the year of 1991, Stein et al. [27] described, atelectasis and/or 'pulmonary parenchymal abnormalities' and 'pleural effusion' as the most common 'radiographic findings' in angiographically proven pulmonary embolismpatients. But finally, Milad et al. [24] claimed that, "thefindings and the aforementioned signs described by 'Hampton and Castleman'as well as by 'Fleischner' do not occur any more frequently in pulmonary embolism patients than in 'patients without pulmonary embolism". So, chest radiography has some major limitation as a detector of PE and DVT.

Echocardiography. Transthoracic echocardiography (TE) rarely enables direct visualization of PE (Pulmonary embolus) [28] but may reveal thrombus floating "'in transit" in the 'right atrium or ventricle'. By transesophageal echocardiography, it is also possible to visualize the massive emboli in 'central pulmonary ateries' [29]. In massive pulmonary embolism (PE), the right ventricle is usually dilated and hypokinetic, with the abnormal motion of the interventricular septum. [14] The finding of right ventricular dysfunction is non-specific [28] and certain conditions commonly confused with pulmonary embolism (such as chronic obstructive pulmonary disease exacerbations or cardiomyopathy) are also associated with abnormal right ventricular function. Although, direct echocardiographic visualization (EV) of intra-luminal thrombi in patients with suspected PE is an almost exceptional event and even when echocardiography provides only 'indirect signs' compatible with hemodynamic consequences of massive PE, it is helpful in excluding or suggesting alternative causes for any type of hemodynamic instability. Because, the right ventricle may present no dysfunction even in patients with massive PE (Pulmonary embolism), echocardiography should be considered an ancillary rather than a 'principal diagnostic test' for (PE) pulmonary embolism [30]. So in this method there are also many limitations.

D-dimer test. D-dimer testing involves the conduction of a blood test to measure a substance that is released after a blood clot breaks up. A low or normal d-dimer test result indicates that only a minor amount of the substance released as the clot breaks up; thus, problems resulting from this blood clot are not likely. A higher-than-normal d-dimer level signals the potential for a blood clot issue to develop; d-dimer levels are often higher than normal in patients with abnormal blood clotting [31]. Elevations of D-dimer are non-specific; for instance, D-dimer is increased by aging, inflammation or cancer, and thus an abnormal result has a low positive predictive value. With respect to the role of d-dimer testing in the diagnosis of PE, a negative D-dimer result can assist in the exclusion of PE. The clinical probability estimate, determined by information from the patient's history and physical examination, can be assessed by either a formal numerical model,or an informed intuitive estimate [32]. The high negative likelihood ratio of these assays is sufficient to rule out PE in all patients; thus, these assays may be considered a "standalone" test for the exclusion of PE [33]. Because the 'negative likelihood ratio' and 'predictive value of these tests' are not high enough to rule out pulmonary embolism in consecutive patients, a normal result must be combined with an additional assessment that classifies patients as having a lower pretest probability for pulmonary embolism. European Society of Cardiology guidelines state that, in 32–40% of patients with low to intermediate pretest clinical probability and normal D-dimer levels, PE can be safely excluded without further testing. [34] D-dimer testing as an assistant in the diagnosis of PE can be divided between two types of D-dimer assays, very highly sensitive and moderate-to-highly sensitive. Very highly sensitive D-dimer assays have a sensitivity for PE of around 98% or higher [36].

Lung ultrasound (LUS). Since its emergence approximately 15 years ago, [37] lung ultrasound technology has been increasingly used to complement conventional assessment methods and other imaging modalities of the lung in the diagnosis of PE [38]. Traditionally used to assess pleural effusions and masses, LUS has been revolutionized to image the pulmonary parenchyma, primarily as a point-of-care technique [37]. In general, the ultrasound imaging process has significant differences from radiographic imaging in which x-ray beams are used. LUS can be performed in any position and on the entire chest, laying the probe in the intercostal spaces and avoiding the ribs [37]. The probe is placed both longitudinally, perpendicular to the ribs, and obliquely along the intercostal spaces [37]. Ultrasound machines are lightweight, compact, easy to transport and robust, thus allowing multiple bedside examinations [39]. LUS is also not only easily available at bedside but, similar to MRI scans, can be performed with the absence of an ionizing radiation risk [39]. In addition to lower limb compressive venous ultrasonography and echocardiography, lung ultrasound can play an important role in the diagnosis of PE in selected patients' subgroups [40]. It can be safely used under conditions of both pregnancy and renal insufficiency, and can be highly useful as a bedside test for hemodynamically unstable patients [40].

Computed tomography (CT). As a fast and non-invasive technology, CT is often one of the first-line modalities for imaging of pulmonary circulation in patients with suspected PE [41]. CT can also reveal the extent of the PE, identify signs of right ventricular dysfunction, as well as provide alternative diagnoses. Basically, CT images

are cross-sectional images of a specific area of a human body that allows doctors or surgeons to see the inside of a patient [42]. CT acquires images of the lung using a breath hold technique during the pulmonary arterial enhancement phase following the injection of intravenous contrast material. Similar to observations discovered through means of pulmonaryangiography, the PE would appear as a filling defect in the pulmonary artery as it becomes opaquer from thecontrast. Further advances in CT technology such as multidetector rows have allowed fora highly refined and detailed evaluation of the entire pulmonary vascular tree, and significant improvements in the detection of peripheral PE. Due to its noninvasive nature as well as its sensitivity and specificity, CT is currently considered the first line imaging tool for the evaluation of suspected PE.CT use for diagnosis of PE is increasing at a rapid pace due to large advances in technology that make CT user friendly for both the physician and patient [43]. Compared to conventional x-ray imaging procedures, CT exposes patients to higher doses of radiation. CT 16-array or greater delivers a higher absorbed dose (8–20 mSv^3) to breast tissue than conventional V/Qimaging (0.6–3 mSv) [44]. These differences reflect variations in size and configuration of breast tissue, CT parameter settings, and the methods used to measure radiation dose. [44] An image [45] of CT is shown in Figure 1 for better concept.

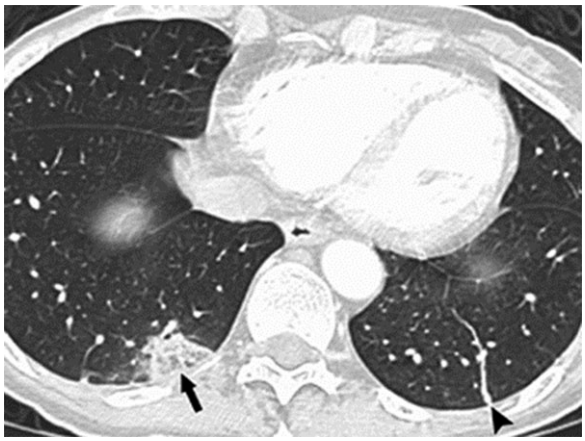

Fig. 1. Acute pulmonary embolism in a 58-year-old woman who presented with chest pain and dyspnea. CT scan shows an acute pulmonary embolus with ancillary findings of a peripheral wedge-shaped area of hyper attenuation in the lung (arrow), a finding that may represent an infarct, as well as a linear band (arrowhead)

Although data on the carcinogenic potential at relatively low dose CT imaging are lacking, the excess stochastic risk of fatal cancer induction in a standard person undergoing CT with the current effective dose of 3–6 mSv is 15–30 excess deaths per 100,000 persons [46]. Various developments in CT imaging such as helical/spiral CT have enhanced the detection of small emboli as well as visuals of peripheral pulmonary arteries [47]. New technologies such as multi-detector row CT have also allowed for improvements towards optimizing contrast material delivery, and reducing radiation

dose [47]. On the other hand, CT Venography (CTV) is an effective for diagnosis of DVT. Duplex ultrasound, including 'both gray-scale and Doppler imaging examination of the lower extremity venous system, has replaced conventional venography as the first-line diagnostic test for DVT, with reported sensitivity and specificity above 90% in symptomatic patients [48]. Ultrasound imaging can be performed at the bedside, does not involve ionizing radiation, is noninvasive, and is relatively inexpensive. The technical quality of the diagnosis de-pends on operator skill and evaluation of the 'pelvic and calf veins' is limited [49]. On the other hand, combined CTPA/CTV fills this role, and the results of one component can be used to guide therapy when the complementary component is not diagnostic, increasing the overall cost-effectiveness [50]. The reported 'sensitivity and specificity' of CTV has been found between 89%–100% and 94%–100%, respectively [51]. In one of the largest series, CTV was 97% sensitive and 100% specific for femoropopliteal DVT [52]. A more recent study using multislice CT showed a sensitivity of 100% and specificity of 97% and positive and negative predictive values of 92% and 100%, respectively [53].

Magnetic resonance imaging (MRI). An Image processing concept called MRI can be used to visualize different structures of human body [54]. MRI techniques are used for diagnosing pulmonary embolism (PE) and deep vein thrombosis include MR angiography or MRA with/without contrast enhancement, 'MR perfusion imaging', and 'real-time MR'. MR angiography covers several advanced techniques like 'contrast-enhanced high temporal resolution' and 'non-contrast- enhanced steady-state free procession (SSFP) sequences [55]. In 1984, findings from some experimental studies as well as some case reports suggested a role for MR imaging (MRI) in patients with pulmonary embolism (PE) [56]. After five years, in 1989, Hatabu and colleagues [57] become able to successfully depict the 'small peripheral pulmonary arteries' with an ECG-gated spin-echo acquisition in diastole and a 'gradient-recalled acquisition' in a steady state with breath holding.The proper combination of real-time MR imaging (RTMR), MR angiography, as well as MR perfusion imaging has been proved to increase the sensitivity for the detection of PE (Pulmonary embolism) [58]. The tremendous development of 'steady-state free precession sequences' also improved the use of MRI for the detection of PE (145) as, a quick sequence with a 'high contrast-to-noise ratio' could be used to generate 'high-spatial-resolution' three-dimensional MR angiographic 'non- enhanced' images [59]. The successful association of 'cine steady-state free precession' imaging into clinical practice also ensured comprehensive evaluation of both the left and right ventricular functions [60]. On the other hand, 'real-time steady-state' free precession MRI provided an additional way to evaluate the 'central pulmonary vasculature' in patients with 'poor breath-holding capability' or with contraindicated to the use of gadolinium-based contrast material [61]. The proper development of 'phase-contrast imaging' in the decades of 1990 made it possible to quantify 'blood flow' in main, right, as well as left pulmonary arteries and to assess 'blood flow' patterns [62]. In fact, MR Pulmonary Angiography (MRPA) is another development of MRI. In the decade 1990, MRPA involved basically two-dimensional time-of-flight (TOF) methods with limited anatomic coverage [63].

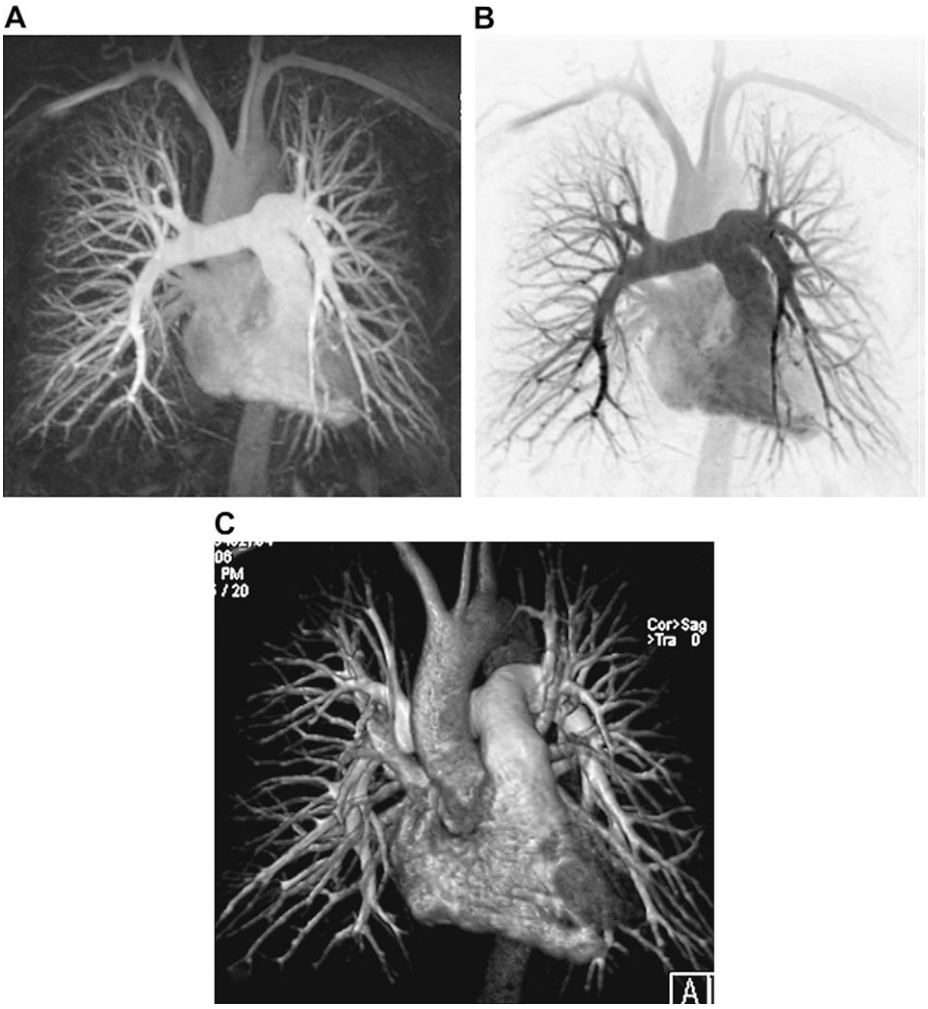

Fig. 2. High spatial resolution 3D CE MRA with parallel imaging with an acceleration factor of 2 in a 44-year-old male patient with shortness of breath and suspected PE. There was no evidence of filling defect or perfusional abnormality. Normal pulmonary arterial anatomy is demonstrated on the maximum intensity projection (MIP) (A), inverted MIP (B), and volume-rendered images (C) [65]

In this technic, breath-holding capability, 'registration artifacts', and 'poor differentiation of slow blood flow' from the thrombus also compromised the image quality [64]. The advent of prompt gradients and effecting reconstruction algorithms has made three-dimensional contrast MRA (MR angiography) feasible [63]. In Figure 2 there are some images of MRA [65] for assessing. Moreover, the technique of computed tomography pulmonary angiography (CTPA) is a faster, less complex, and less operator dependent than any other conventional pulmonary angiography, and has about the same

frequency of technically insufficient examinations (about 5%) [66]. In this method, the thorax can be scanned during the period of a single breath hold.Another one more advantage of computed tomography pulmonary angiography over scintigraphy is that by imaging the 'lung parenchyma' and great vessels, an alternative diagnosis can be made if PE is absent [67].

3.2 Justification of using CT and MRI for DVT and PE

Physicians and surgeons have been using CT and MRI for detecting DVT and PE for many years. CT scanners have the ability to acquire data for a slice typically between 0.5–4 seconds. In the first study to evaluate the accuracy of single-detector spiral CT angiography, Remy-Jardin et al. [68] reported a sensitivity of 100% and specificity of 96% for pulmonary embolism in central pulmonary arteries, when compared with angiography as the diagnostic standard. CTPA studies using multidetector-row CTscanners have showed excellent sensitivity of 96–100% and specificity of 97–98% [69]. In that study, CTV performed as same to contrast venography, with the sensitivity of 100% and a specificity of 96%. Some other studies were conducted on clinically suspected pulmonary embolism (PE) patients', generally without 'any sign and symptoms of the legs', in which the scan (CT) was extended to the legs. In a study it was found that, the estimated pooled sensitivity of 'CTV' was 96% with an 'estimated pooled specificity of 95%' [70]. Of note, the heterogeneity between the studies was substantial.

In Table 1 the sensitivity and specificity of MRI techniques for Acute DVT & PE Diagnosis [55] of a study is shown where the findings of many researchers are available.

Table 1. Sensitivity and specificity of MRI techniques for acute DVT & PE diagnosis [55]

First Author	Year	n	Patients	Technique	Sensitivity	Specificity
Erdman (56)	1990	100	Upper & Low. ex.	Phase contrast	90	100
Evans (58)	1993	61	Lower extremity	Phase con.&MR	100	100
Carpenter (75)	1993	85	Lower extremity	Time of flight	100	96
Spritzer (57)	1993	199	Lower extremity	Time of flight	97	98
Dupas (59)	1995	25	Pelvic vein	Time of flight	100	98
Pulmonary embolism						
Evans (77)	1996	75	Lower extremity	Phase con.&MR	100	100
Catalano (62)	1997	43	Lower extremity	Time of flight	100	94
Fraser (37)	2002	101	Lower extremity	MRDTI	100	100
Fraser (67)	2003	55	Lower extremity	VESPA	100	97
Cantwell (69)	2006	24	Lower extremity	bSSFP	100	98
Westerbeek (36)	2008	43	Lower extremity	MRDTI	95	100
Pedrosa (73)	2009	24	Upper and lower	HASTE	100	91

Note: *In case more sensitivity and specificity figures were mentioned in the article, we report the sensitivity and specificity of the proximal veins.

From the late 1960s onwards, pulmonary angiography had been considered the "gold standard" imaging test for diagnosing PE [71]. Direct angiography allows for the visualization of thrombi as small as 1–2 mm within subsegmental arteries [72]. Today, a wide range of MRI techniques may be applied for diagnosis of VTD and PE [55]. Fraser et al. [73] included 101 patients suspected of DVT in their study that compared contrast venography with MRDTI (Magnetic resonance direct thrombus imaging). For gross DVT diagnosis, they found a good sensitivity of 94% to 96%, regarding the qualifications of the observer. Specificity ranges were from 90% to 92%. A meta-analysis showed a 'pooled estimate sensitivity' of 91.5% and specificity of 94.8% for DVT diagnosis by MRI [74] Compared to contrast venography, MRDTI has a sensitivity of 97% for femoropopliteal DVT and a specificity of 100% [73] This benefit overcomes the limitations of other techniques that detect filling defects and surrogate markers of a thrombus [75] A prospective study on 511 patients with suspected pulmonary embolism (PE) demonstrated that, the sensitivity of CUS of the lower extremities for the presence of pulmonary embolism (PE) on CTPA was only 39% with a specificity of 99% [76]. In a study, it has been found that, distal US has an even 'lower accuracy' for predicting pulmonary embolism (PE) with a sensitivity of 22% and a specificity of 94% [77]. Gadolinium-enhanced MR Angiography is an effective and excellent noninvasive diagnostic method for PE because its 'sensitivity and specificity are high, as confirmed by a good review article and a meta-analysis, and it allows simultaneous study of DVT also [78]. A good advantage of MRA over multidetector 'CT angiography' is those images of ventilation may be obtained if noble gases, like helium 3 or xenon 129 and are used. Besides these, it has no contraindications and is very safe to use even during pregnancy [79]. Nothing that, MRA is more sensitive than Doppler ultrasound (DU) in detecting 'pelvic deep vein thrombosis (DVT) however [80]. As now MR technology improves and it becomes more readily available everywhere, the role of MRV and MRPA in assessing venous thromboembolic disease (VTD) may expand [63]. According to the positive references and findings we can consider CT and MRI as two time-tasted methods for detecting PE and DVT.

4 Conclusion

Day by day the prevalence of pulmonary embolism and deep vein thrombosis is increasing. For the patients of both the diseases are in need of prompt diagnosis. Considering the needed time there are some diagnostic methods like ECG or echocardiogram. But those methods are so effective as in needed. Some diagnostic technics like, ECG, echocardiogram, ultrasonography may be chosen as associated tests but for the clear concepts about the patient's condition of PE or DVT computed tomography (CT) and/ormagnetic resonance imaging (MRI) is a must. Moreover, combined use of CT and MRI may be considered as the method of choice for diagnosing PE and DVT. Besides these, the contentious trends of the development of CT and MRI also a justification of continuation of using those two methods in a wider range.

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