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

Jeffrey P. Kanne, MD; Tasneem A. Lalani, MD

Abstract—During the 1990s, computed tomography (CT) and magnetic resonance (MR) imaging underwent extensive technological advancement and expanded clinical use in patients with venous thromboembolic disease, particularly with regard to evaluation of the pulmonary vasculature. In many institutions, helical (spiral) CT pulmonary angiography has become the initial imaging study of choice to evaluate patients with suspected pulmonary embolism, supplanting ventilation/perfusion scintigraphy. In addition, CT venography of the pelvis and lower extremities is often incorporated into the CT angiography protocol to identify or exclude concurrent deep venous thrombosis. MR pulmonary angiography and MR venography are second-line diagnostic tools because of their higher cost, limited availability, and other logistical constraints. As the technology improves and becomes more widely available, MR imaging may play a greater role in the evaluation of patients with venous thromboembolic disease. (Circulation. 2004;109[suppl I]:I-15-I-21.)

Key Words: thrombosis ■ pulmonary heart disease ■ imaging ■ MRI

During the 1990s, technological advances in computed tomography (CT) and magnetic resonance (MR) imaging made these techniques applicable to the diagnosis of venous thromboembolic disease, particularly for the pulmonary vasculature in patients with suspected pulmonary embolism (PE). At the opening of the third millennium, in many institutions, helical (spiral) CT pulmonary angiography (CTPA) has become the initial imaging study of choice for evaluating patients with suspected PE, supplanting ventilation/perfusion (V/Q) scintigraphy by reducing indeterminate examinations.1–4 CT venography (CTV) of the pelvic and lower extremity veins after CTPA of the pulmonary arteries has been advocated by some as an adjunct to helical CT for detection of concurrent deep venous thrombosis (DVT) using a single imaging technique for detection of venous thromboembolic disease.

Although MR imaging produces high tissue contrast without ionizing radiation, currently, this technique is less popular than CT for evaluation of acute venous thromboembolism (VTE) because of technical limitations, higher costs, limited availability, and other logistical considerations. As technology improves, however, MR pulmonary angiography (MRPA) and MR venography (MRV) may play a greater role in the evaluation of patients with venous thromboembolic disease.

This article reviews applications of CT and MR imaging in the clinical evaluation of patients with suspected venous thromboembolic disease.

CT Pulmonary Angiography

CTPA has gained acceptance as a first-line imaging study in cases of suspected acute PE, replacing traditional V/Q scintigraphy at many institutions. In general, V/Q scanning is reserved for patients in whom motion artifact or poor right heart function limit the quality of CT examination and those with contraindications to intravenous radiographic contrast.

After contrast administration, CTPA provides visualization of the pulmonary arterial system in the axial plane, and multiplanar and three-dimensional reconstructions can be generated from raw data to enhance diagnostic accuracy. The cardinal sign of acute PE on CTPA is an intravascular filling defect in a pulmonary artery that partially or completely occludes the vessel and is often associated with increased diameter of the affected vessel (Figures 1 through 3). The most specific sign of acute PE is a filling defect that forms acute angles with the vessel wall. Although the filling defect of acute PE can produce obtuse angles or complete occlusion of the vessel, these patterns are also seen in cases of chronic thromboembolic disease.2,3

The sensitivity and specificity of CTPA for diagnosis of acute PE have been reported to range from 53% to 100% and 67% to 100%, respectively, varying on the basis of patient selection, extent of thrombus, area of the vasculature imaged, interpretation criteria, and experience of the reader.1 The most specific sign of acute PE is a filling defect that forms acute angles with the vessel wall. Although the filling defect of acute PE can produce obtuse angles or complete occlusion of the vessel, these patterns are also seen in cases of chronic thromboembolic disease.2,3

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Using thin (2 mm) collimation, sensitivities of 94% to 96% and specificities of 94% to 100% have been achieved.\textsuperscript{5,6} Although normal V/Q scintigraphy essentially excludes PE, a high-probability V/Q scan has a sensitivity of 88% for PE compared with pulmonary angiography. In the prospective investigation of pulmonary embolism diagnosis (PIO-PED) study, only 41% of patients with PE had a high-probability scan,\textsuperscript{7} and 57% of patients had nondiagnostic (indeterminate or low-probability) V/Q scans. In other studies, CTPA demonstrated acute PE in 14% to 44% of patients with nondiagnostic V/Q scans, including several in whom lower extremity ultrasound imaging did not find DVT.\textsuperscript{8–11} CTPA gave the correct diagnosis in 92% of cases with discordant V/Q and CTPA\textsuperscript{12} and, when used as the initial diagnostic examination in cases of suspected PE, reader confidence was significantly higher with CTPA than with V/Q scanning (90% versus 54%, respectively).\textsuperscript{13}

For PE in the main, lobar, or segmental pulmonary arteries, the diagnostic accuracy of CTPA compares favorably with that of pulmonary angiography,\textsuperscript{14–16} but how best to evaluate the subsegmental pulmonary arteries remains controversial. The subsegmental pulmonary arteries are more difficult to evaluate because of their smaller size, limited contrast enhancement in relation to the finite spatial resolution of CT, and the orientation of these vessels in space.\textsuperscript{17} The true incidence of isolated subsegmental PE is unknown, and reported incidences vary widely (4% to 17%), depending on patient population and other factors. However, in large series, isolated subsegmental emboli were identified in 4% to 6% of patients with clinically suspected PE.\textsuperscript{7,18–20} The clinical significance of isolated subsegmental pulmonary emboli also is unclear, especially in patients without evidence of DVT or cardiopulmonary dysfunction. Although many clinicians still hold pulmonary angiography as the gold standard, balloon occlusion studies have shown that even pulmonary angiography can miss subsegmental PE\textsuperscript{21,22} and interobserver agreement is poor (13% to 66%).\textsuperscript{18,23,24} One study comparing thin collimation (1 mm) CTPA and pulmonary angiography in a cast porcine model showed no statistical difference in sensitivity between the two modalities at the subsegmental levels (each 87%).\textsuperscript{25}

It has been suggested that clinical outcome (rather than pulmonary angiography) serve as the standard against which...
to evaluate the diagnostic accuracy of the various imaging modalities for acute PE.\textsuperscript{26} The majority of subsequent PEs occur within the first few weeks after an index event, with 50\% of recurrences and 90\% of PE-related deaths occurring within the first 2 weeks.\textsuperscript{27,28} In patients with chronic underlying risk factors such as malignancy, however, the occurrence of a thromboembolic event after a negative diagnostic examination for VTE does not mean that the original examination was necessarily a false-negative result. In several outcome studies limited by a relatively high proportion of patients lost to follow-up and relatively sparse autopsy data, patients with negative CTPA were monitored without anticoagulation with negative predictive values ranging from 93\% to 100\%;\textsuperscript{1,6,9,29–38} these results are comparable to those obtained with pulmonary angiography.\textsuperscript{39–46}

Detailed delineation of the pulmonary parenchyma and extrapulmonary structures by CTPA offers additional information about the lungs and pleura not provided by V/Q scintigraphy or pulmonary angiography. In one study, CTPA identified pleural or parenchymal abnormalities that explained indeterminate defects on V/Q scans in 57\% of patients;\textsuperscript{11} in other studies, alternative intrathoracic findings were identified in 11\% to 85\% of patients undergoing CTPA;\textsuperscript{6,8,9,13,32,47–51} these additional findings were nonspecific, occurring both in patients with and without PE.\textsuperscript{52} Although other such intrathoracic abnormalities may not imply a need for further evaluation, their identification may affect patient management.

Identification of PE on CTPA is a clear indication for initiating appropriate therapy, but uncertainty about subsegmental thromboemboli contributes to ongoing uncertainty about the diagnostic accuracy of both CTPA and pulmonary angiography. As multislice CT technology becomes more commonplace, future studies employing thinner collimation, faster scan times, and cardiac gating are expected to result in better visualization of the smaller pulmonary arteries, and these enhancements may ultimately determine whether a negative CTPA is sufficient evidence to withhold therapy from a patient with signs or symptoms suggestive of PE.

Multislice CT

In the past several years, multislice CT has become commonplace in major U.S. medical centers. Most university medical centers and other tertiary care centers have at least one multislice scanner. Sixteen-slice scanners, now offered by most vendors, are currently appearing in many radiology departments and offer even faster scan times, result in lower radiation doses than 4- and 8-slice scanners, and provide isotropic imaging (z-axis spatial resolution equal to x- and y-axis spatial resolution). As availability of these newer multislice scanners increases, updated studies of the diagnostic accuracy of CTPA using newer techniques can be expected.

**Advantages and Disadvantages of CTV**

<table>
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<tr>
<th>Advantages</th>
<th>Drawbacks</th>
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<tr>
<td>One exam for both DVT and PE</td>
<td>Iodinated contrast nephrotoxicity</td>
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<tr>
<td>High diagnostic accuracy similar to colorflow duplex and CTPA</td>
<td>Radiation exposure</td>
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<tr>
<td>Detects other nonthromboembolic pathology (eg, cancer)</td>
<td>Cannot be performed at bedside (risk of transporting critically ill)</td>
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<tr>
<td>After-hours availability (unlike duplex in many locations)</td>
<td>Higher cost</td>
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<tr>
<td>Accuracy in diagnosis of calf vein thrombosis</td>
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**CT Venography 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.\textsuperscript{53} Ultrasound imaging can be performed at the bedside, does not involve ionizing radiation, is noninvasive, and is relatively inexpensive. The technical quality of the examination depends on operator skill, however, and evaluation of the pelvic and calf veins is limited.\textsuperscript{54–56} In many institutions, ultrasound may not be as readily available after hours as CTV.

CTV provides direct imaging of the inferior vena cava, pelvic, and lower extremity veins immediately after CTPA without injection of additional contrast material, adding only a few minutes to the examination. Because DVT is the most important factor predisposing to PE,\textsuperscript{50} a single examination capable of evaluating both the pulmonary arterial system and the pelvic and lower extremity venous system offers distinct advantages over other tests directed at either diagnosis alone. 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.\textsuperscript{57,58}

Like CTPA, CTV is occasionally plagued by technical limitations such as streak artifact from orthopedic hardware or poor venous enhancement. Table 1 summarizes the advantages and disadvantages of CTV. Additionally, errors in interpretation related to anomalous vessels, adjacent pathology, and reader inexperience may result in inaccurate interpretation. The reported sensitivity and specificity of CTV has been reported between 89\% to 100\% and 94\% to 100\%, respectively.\textsuperscript{60–62} In one of the largest series, CTV was 97\% sensitive and 100\% specific for femoropopliteal DVT.\textsuperscript{63} 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.\textsuperscript{64}

There are several drawbacks to combining CTV with CTPA as a single comprehensive imaging modality for VTE. In a number of published studies of combined CTPA and CTV, \(\approx 150\) mL of iodinated contrast was required to produce adequate opacification of the pulmonary arteries and pelvic and lower extremity veins,\textsuperscript{61,63–68} more than the amount usually required for adequate opacification of the pulmonary arteries alone. Given that the nephrotoxicity of iodinated radiocontrast is dose related,\textsuperscript{69} minimizing the dose is important, especially in critically ill patients with underlying renal
angiography, selective pulmonary arterial phase enhancement acquisition time for MR exceeds that for CT or conventional breath-holding for longer intervals. Additionally, because the image matrix size can improve spatial resolution and breath-holding make evaluation of the bulk of medical radiation exposure. In part because of these issues, the value of combining CTV with CTPA is still debated, and in many institutions, including our own, CTV is not routinely included in the CTPA protocol.

Exposure to ionizing radiation is also greater with combined CTRA/CTV over either test alone, and this is particularly pertinent to radiosensitive tissues such as the ovaries and testes. Protocols using spaced sections rather than helical acquisition help reduce radiation doses but risk missing smaller venous thrombi. Although concern about exposure need not preclude clinically indicated examinations, physicians should be aware of the deleterious effects, particularly in younger patients, and remember that CT imaging contributes to the bulk of medical radiation exposure. In part because of these issues, the value of combining CTV with CTPA is still debated, and in many institutions, including our own, CTV is not routinely included in the CTPA protocol.

**MR Pulmonary Angiography**

In the 1990s, MRPA involved mainly two-dimensional time-of-flight (TOF) techniques with limited anatomic coverage. Breath-holding capability, registration artifacts, and poor differentiation of slow blood flow from thrombus also compromised image quality. The advent of faster gradients and better reconstruction algorithms has made three-dimensional contrast MR angiography feasible. These scans can be completed in 10 to 30 seconds—during a single breath-hold—with increased signal-to-noise ratio and improved image quality through administration of intravenous gadolinium (Figure 4). Despite these advances, limitations on spatial resolution and breath-holding make evaluation of the segmental and subsegmental pulmonary arteries difficult. Increasing the image matrix size can improve spatial resolution at the cost of longer imaging time and, therefore, require breath-holding for longer intervals. Additionally, because the acquisition time for MR exceeds that for CT or conventional angiography, selective pulmonary arterial phase enhancement cannot be achieved, making it difficult to distinguish arterial from venous structures.

In an animal model, 81% and 61% of fifth-order (subsegmental) vessels were visualized using 192×192 and 160×160 matrices, respectively, on a single breath-hold scan. Without breath-holding, the same matrices yielded definition of only 26% (192×192) and 20% (160×160) of subsegmental pulmonary arteries. In another study, the sensitivity and specificity for detection of lobar and segmental emboli was 87% and 97%, respectively. In a subsequent study, sensitivity for detection of subsegmental emboli was only 68%, making this technique inferior to CTPA or angiography.

Newer techniques using navigator pulses that allow free breathing are promising for dyspneic patients undergoing MR, as tracking of diaphragmatic excursions facilitate cumulative data acquisition at the same phase of the respiratory cycle. Additionally, improved gating reduces the cardiac pulsation artifact that affects MR more than CT imaging. Improvements in the speed of data acquisition, faster gradients, and radial acquisition of raw data rather than current Cartesian acquisition methods promise to further improve the future diagnostic accuracy of MRPA.

**MR Venography**

MRV may be used to evaluate central venous pathology, anatomic variants, and DVT of the extremities (Figure 5). The technique is less stringent than most MR angiography techniques because venous flow profiles are relatively uniform, vessel size is greater, and flow is slower. Additionally, venous pathology is usually more extensive than arterial pathology, requiring lower image resolution. MRV can be performed without intravenous contrast using TOF and phase-contrast (PC) techniques. Alternatively, intravenous gadolinium can be administered to enhance the venous signal. Contrast-enhanced MRV has several advantages over both TOF and PC techniques, including faster acquisition, better signal-to-noise ratio, and greater accuracy in states of slow flow or tortuous venous anatomy.

MRV shares with CTV the advantage of better delineating the inferior vena cava and pelvic veins than does sonography, and does not require venous compression, which is pertinent to examination of limbs in plaster casts or other impediments to compression sonography. Studies comparing MRV with sonography have found MRV superior for diagnosis of DVT in the thigh. One study of 25 patients undergoing both MRV and sonography of the pelvic and common femoral veins found the sensitivity and specificity of MRV to be 100% and 98%, respectively, whereas sonography had a sensitivity of 91% and a specificity of 97%.

**Conclusions**

Even with modern technology, VTE is an elusive clinical entity and no perfect diagnostic test has been developed. Helical CTPA will likely continue to serve as the initial diagnostic imaging examination of choice for patients with clinically suspected acute PE in the absence of contraindications to radiograph contrast material, especially as multislice technology proliferates. Should future studies find multislice CTPA technology superior to pulmonary angiography at the
larger iodinated contrast load and additional radiation exposure in the hepatic region and superior in the pelvis. Although involving a subsegmental arterial level with better interobserver agreement, CTPA would become the first and only imaging study needed for diagnosis of acute PE in most patients.

Several authors advocate including CTV in the CTPA protocol for more complete evaluation of VTE and to increase the overall sensitivity of the examination. This technique seems comparable to ultrasound in the femoropopliteal region and superior in the pelvis. Although involving a larger iodinated contrast load and additional radiation exposure, it may prove more cost-effective and result in appropriate anticoagulation therapy for a higher proportion of patients with DVT, thereby reducing the risk of a life-threatening PE.

MRV and MRPA remain second-line diagnostic tools because of higher cost, technical limitations, limited availability, and logistical constraints. As MR technology improves and becomes more readily available, the role of MRV and MRPA in evaluating venous thromboembolic disease may expand. Pulmonary angiography is generally reserved for patients in whom the clinical suspicion of PE remains high despite negative CTPA and bilateral lower extremity venous evaluations (by CTV or ultrasound), or for those with contraindications to CTPA and an indeterminate V/Q scan.

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