Nuclear imaging in chronic thromboembolic pulmonary hypertension: increasingly central to diagnosis and management

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Pulmonary hypertension (PH) is defined by elevated pulmonary artery pressure which is associated with symptoms of dyspnea and exercise limitation, impaired health-related quality of life, and typically premature mortality due to right ventricular (RV) failure. PH specifically due to multiple or recurrent pulmonary emboli is classified as WHO Group 4 chronic thromboembolic PH and defined as PH due to persistent pulmonary arterial obstruction by organized thrombi.[1–3] Chronic Thromboembolic Pulmonary Hypertension (CTEPH) is a common, important cause of PH that is usually progressive resulting in RV failure, and is often fatal, especially if unrecognized and/or untreated. CTEPH has been the focus of extensive clinical research, leading to several international clinical practice guidelines and consensus statements with strong recommendations in support of accurate diagnostic approaches and several effective treatment options to improve clinical outcomes including quality of life and survival.[1,4,5]

Improving clinical outcomes in CTEPH patients requires appropriate clinical suspicion, timely diagnosis, and management. Nuclear ventilation/perfusion (V/Q) lung scan has long been the recommended imaging modality for the assessment of CTEPH. Initially, planar imaging was performed in multiple views and then SPECT imaging became the more common protocol.[1,6] Recently, hybrid SPECT-CT imaging is also utilized in some advanced nuclear labs for better delineation of segmental or subsegmental perfusion defects. An example of fusion imaging where SPECT perfusion defects are overlapped with anatomical CT slices in a patient with multiple pulmonary emboli is shown on Figure 1 (Western University, Nuclear Medicine).

For the assessment of CTEPH, Tc99m MAA should be freshly prepared. The reduction of number of particles also should be considered in patients with severe PH and in patients with significant R-L shunt.[7] In young and pregnant patients, the administered dose can also be reduced.[8] Normal or near-normal V/Q lung scan with small, non-segmental perfusion defects effectively excludes surgically accessible chronic thromboembolic pulmonary disease (CTEPD) with a sensitivity of 90% to 100% and a specificity of 94% to 100%.[1,9] Perfusion defect patterns can be different in CTEPH than in acute PE, and familiarity with these patterns is crucial to accurate interpretation of both pre and post therapy scans.[10] Lung perfusion SPECT imaging has largely replaced classic planar V/Q lung scan, given higher sensitivity, and specificity.[6]

In order to delineate the anatomic extent, distribution, and potential operability of CTEPD, specifically with regards to the presence of adequate large-vessel thromboembolic material in an individual patient to predict successful surgical pulmonary endarterectomy (PEA), anatomic visualization is recommended. Catheter-based selective pulmonary angiography is the

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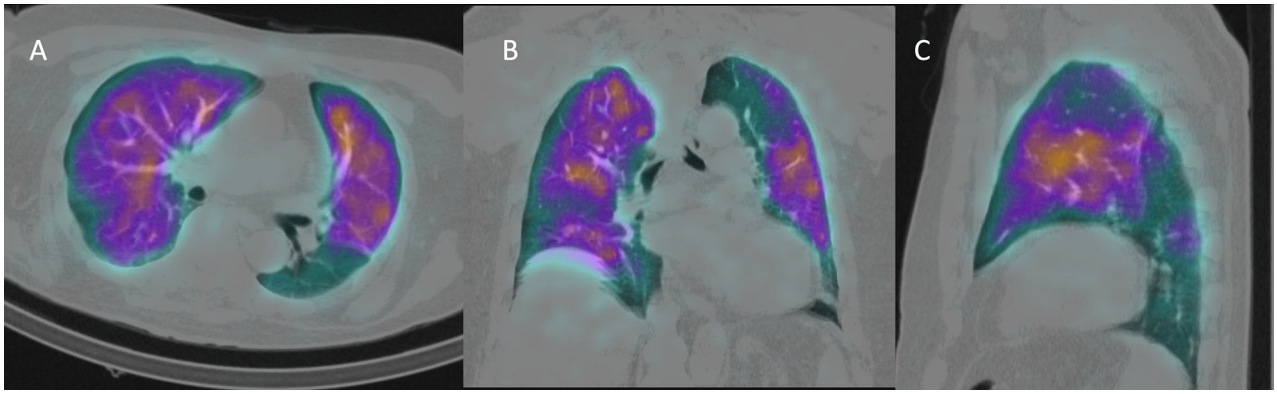

Figure 1. Hybrid Tc99m MAA SPECT-CT imaging in a patient with multiple segmental and subsegmental perfusion defects in keeping with pulmonary emboli. A. Axial, B. Coronal, and C. Sagittal views. The overlapping low-dose, non-enhanced CT slices provide an anatomic map and help better localization of each pulmonary emboli..

reference-standard for diagnosis of CTEPH.[5] CT pulmonary angiography is a non-invasive imaging modality which can accurately assess anatomic extent and distribution of CTEPD for assessment of eligibility for definitive PEA, as well as for BPA although false negativity rate can be up to 25% of cases.[11]

With regards to management, long-term anticoagulation in all CTEPH patients, including inoperable patients as well as patients post-PEA, is always required to prevent progressive pulmonary vascular thrombosis or PE recurrence.[12] Warfarin is recommended at present as first choice for all CTEPH patients, but there is increasing clinical use of direct oral anticoagulants[13] for CTEPH, given effectiveness and common use for multiple other thromboembolic conditions.

Surgical PEA is the most definitive treatment of CTEPH, potentially curative, and thus is strongly recommended for all eligible patients by guidelines.[12] Long-term clinical outcomes in CTEPH patients are markedly improved following successful PEA, including reduced symptoms, improved exercise capacity (e.g., 6-min walk test distance), HRQoL, and survival.[14] Clinical benefits are correlated with improvements in pulmonary vascular hemodynamics, including meanPAP, PVR and cardiac index. Approximately 30% of CTEPH patients do not undergo PEA because of personal choice or are declined because of significant co-morbidities or insufficient resectable thrombotic material in larger pulmonary arteries.[14,15] In addition, about 30% of patients have limited benefit post-PEA with persistent CTEPH and residual PH which is typically addressed with PH-targeted medical therapy.[5]

Balloon Pulmonary Angioplasty (BPA) is an increasingly common global therapeutic intervention for patients with inoperable CTEPH as well as those with residual PH post-PEA.[9,16]. Systematic reviews of uncontrolled data suggest improved resting mean pulmonary artery pressure (mPAP), symptoms, functional capacity, and survival.[9,16]

A few studies have investigated the role of lung perfusion scan in evaluating the response to BPA in small patient groups.[17] In the post-procedural period (post-PEA or post-BPA), reperfusion edema may occur.[18] This may reflect on the perfusion images as initially areas of normal MAA distribution, showing relatively lower counts or areas of photopenia after treatment.[19] Also, areas of hyperperfusion can be seen as preferential blood flow occurs within the regions of endarterectomy, creating a vascular steal.[20] Therefore, attention should be paid to the artifactual patterns on the immediate post procedure lung perfusion scan. Lung SPECT-CT may be valuable in recognition of the pseudo-defects. Over time, the pulmonary vasculature adapts to normalized pressures and the hyperemia resolves. Accordingly, these defects resolve within 9–12 months.

In this issue of Journal of Nuclear Cardiology, Hashimoto et al. assessed 20 patients with inoperable CTEPH with a hybrid imaging model of lung perfusion SPECT and CT, to determine the perfused functional lung volume before and after BPA treatment.[9] The importance of baseline scan and the value of SPECT in selection of target vessels have been emphasized. The immediate success of each BPA procedure was defined by prompt visualization of the flow through the treated pulmonary arteries. BPA was associated with hemodynamic, clinical, and functional improvements, including mPAP, World Health Organization functional classification, and 6MWD. Functional volume of lung (FVL) was calculated from lung perfusion SPECT (LPSPECT)

and indicated the preservation rate (%) of normal perfused, functional lung volume. This was calculated by dividing the functional volume of the lungs calculated from the lung perfusion SPECT, by the lung volume calculated from the chest CT. At baseline, FVL-LPSPECT was moderately correlated with mPAP ($r = -0.728$, $P < .001$), as was 6MWD ($r = -0.571$, $P = .009$). Despite the short time interval to follow-up perfusion lung scan (28–56 days) following BPA, improvements in perfused functional lung volumes (FVL-LPSPECT) were observed, without evidence of significant pseudo-defects. In multiple regression analysis, FVL-LPSPECT was found to be the most significant predictor of improvement in mPAP after BPA ($P < .001$).

This study in a small cohort of patients demonstrates lung perfusion SPECT's potential value in assessing the effectiveness of BPA in patients with CTEPH. This needs to be confirmed in a larger study. Moreover, we are excited about the potential for lung perfusion SPECT to be clinically useful in the assessment of other patients. For example, quantification of functional perfused lung may identify CTEPH patients most likely to benefit from interventions, including BPA and possibly PEA. In addition, it remains uncertain which patients post-acute PE are at highest risk of developing CTEPH, but guidelines recommend against routine screening of all patients post-acute PE because CTEPH only occurs in 2% to 4% of survivors. Patients post-acute PE at highest risk for development of CTEPH potentially could be identified earlier if, for example, they have more severely disturbed lung perfusion on SPECT. Nuclear lung perfusion imaging has long been central to the diagnosis of CTEPH, and new 3-D imaging protocols and analysis methods hold promise for more detailed and clinically useful assessment of pulmonary vascular perfusion in many PH patients.

Disclosure

The authors have no conflicts of interest to declare.

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