Review of the Latest Published Research

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Summaries and commentaries from the section editors and invited reviewers present a clinical context for practitioners' application of the latest published research relevant to the care of patients with pulmonary hypertension. In this issue, Kelly Chin discusses the role of computed tomography and 6-minute walk distance in the diagnosis of pulmonary hypertension patients.

Sugiura T, Tanabe N, Matsuura Y, et al. Role of 320-Slice computed tomography in the diagnostic workup of patients with chronic thromboembolic pulmonary hypertension. *Chest.* **2012 Oct 22. [Epub ahead of print]**

Sugiura et al evaluated the accuracy of 320 slice computed tomography (CT) scanning in patients undergoing evaluation for chronic thromboembolic pulmonary hypertension (CTEPH). Forty-four patients were identified as having probable CTEPH based on VQ scan and echocardiography. Patients then underwent 320 slice CT scan, right heart catheterization, and pulmonary angiography. The CT scans were obtained using 0.5 mm slice thickness with ECG gating, and required 2 gantry rotations in order to simultaneously image the lungs and the entire heart. Two independent reviewers read each CT scan, and their results were compared with pulmonary arteriogram, set as the gold standard test for the analysis.

Overall, CT performed well. The sensitivity of the 320 slice CT scan for detecting lobar PEs was 97%, and the specificity was 97.1%, with excellent inter-observer agreement (Kappa=0.91, Table). At the segmental level, the sensitivity was 85.8% and the specificity was 94.6%, with very good inter-observer agreement (Kappa=0.79). The subsegmental arteries were not included in the analysis, mainly due to a lack of an acceptable reference standard. The authors also attempted to estimate systolic pulmonary arterial pressure (sPAP) by looking at the curvature of the interventricular septum, finding a strong correlation between their measured estimate and the actual sPAP (r=-0.79, *P*<0.001).

Interestingly, the sensitivity and specificity results were calculated at the level of the *individual vessel*. In other words, they calculated the number of correctly identified vessels (normal vs clot) in the 344 main and lobar arteries and in the 860 segmental arteries that were evaluated; the number of correct CTEPH *diagnoses* was not reported. Out of 44 patients, only 18 subsequently underwent pulmonary thromboendarterectomy; the disposition of the other patients was not discussed.

The authors concluded that CT pulmonary angiography was a less invasive alternative to conventional angiography for the diagnosis of CTEPH, but acknowledged that the study was a retrospective, single-center study of a highly selected cohort, and that further study was needed.

Sugiura et al provide an interesting look at how multisclice CT may be used in the future, though with several caveats. Notably, the patient population included only those with "suspicion" for CTEPH, so it is impossible to determine what the sensitivity and specificity of the test would be in a less select population, nor is it possible to compare its accuracy vs VQ scan. Additionally, although the accuracy of the specific vessels involved seems to have been quite good, they do not discuss how or whether they used this information in determining "operability," a critical and challenging aspect of the CTEPH evalua-

Table: Summary of pathological vascular findings as delineated by CTPA and PDSA, and statistical analysis of findings in CTPA compared to findings in PDSA

	CTPA	PDSA	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	K (95% CI)
Main/lobar arteries (N=344)							
Number of normal vessels	271	277					
Chronic thromboembolic findings	73	67	97.0	97.1	89.0	99.3	0.91 (0.86–0.96)
Segmental arteries (N=860)							
Number of normal vessels	661	670					
Chronic thromboembolic findings	199	190	85.8	94.6	81.9	95.9	0.79 (0.74–0.84)

Definition of abbreviations: CTPA = Pulmonary angiography on 320-slice CT, PDSA = pulmonary digital subtraction angiography, PPV = positive predictive value, NPV = negative predictive value, K = Cohen's Kappa, 95%CI = 95% confidence interval. Copyright 2012 by the American College of Chest Physicians. Reprinted with permission.

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tion. Importantly, prior studies have suggested that conventional CT angiography is less sensitive than VQ scan in the diagnosis of CTEPH.[1,2] Further study is needed prior to more widespread adoption of 320 slice CT as either a screening or confirmatory test for CTEPH.

Savarese G, Paolillo S, Costanzo P, et al. Do changes of 6-minute walk distance predict clinical events in patients with pulmonary arterial hypertension? A meta-analysis of 22 randomized trials. *J Am Coll Cardiol.* 2012;60(13): 1192-1201.

Savarese et al performed a meta-analysis of 22 clinical trials in pulmonary arterial hypertension (PAH) looking at mortality and change in 6-minute walk distance (6MWD). They were specifically interested in whether change in 6MWD predicted survival and other outcomes, such as PAH-related hospital admission. Similar to prior meta-analyses, they found that active treatment led to a reduction in all-cause death (odds ratio [OR] 0.43, $P<0.01$), and active treatment also reduced hospitalization for PAH and/or lung transplantation (OR 0.44, $P<0.01$) and the initiation of PAH rescue therapy (OR 0.56, $P<0.01$). However, they did not identify any relationship between change in 6MWD and outcome. They did find a significant relationship between change in 6MWD and change in pulmonary vascular resistance (r=-0.63, $P<0.01$). In an accompanying editorial, Dr Stuart Rich reviewed the history of the 6MWD as a primary endpoint in PAH phase III clinical trials, and suggests that now is the time to consider novel clinical trial strategies[3].

Saverese et al found that *change* in 6MWD does not correlate well with mortality and other outcomes. Notably, other studies have reported similar findings, suggesting that achieving a particular walk threshold (>380-440 meters) is more important than the absolute value of the change in 6MWD achieved.[4,5]

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5. Sitbon O, Humbert M, Nunes H, et al. Long-term intravenous epoprostenol infusion in primary pulmonary hypertension: prognostic factors and survi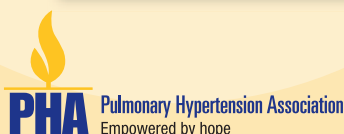val. *J Am Coll Cardiol.* 2002;40(4):780-788.