

## Update in Echocardiography: Chronic Thromboembolic Pulmonary Hypertension

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Chronic thromboembolic pulmonary hypertension (CTEPH) is the result of clot persistence and fibrosis in the pulmonary vasculature after acute pulmonary embolism. This condition leads to elevated pulmonary pressures and eventually right heart failure. Patients are often severely limited by exertional dyspnea and can experience significant morbidity and mortality when left untreated [1-3]. The condition is also associated with impairment of left ventricular diastolic function and filling. Pulmonary thromboendarterectomy (PTE) is currently the only curative treatment for CTEPH and greatly alters the clinical course of the disease.

Described in detail by Moser, et al. in 1987, PTE has greatly improved CTEPH-related mortality [4]. The rapid hemodynamic and echocardiographic changes following PTE have provided an ideal model for assessing the interaction between the left and right heart. While early studies focused on the right ventricular dysfunction seen in CTEPH, more recent studies have addressed the associated left ventricular (LV) dysfunction. This article highlights two of the latest echocardiographic publications in CTEPH, one which addresses right ventricular function using strain imaging, and the other which explores the role of left atrial volume in the associated LV diastolic impairment.

### Right Ventricular Strain in CTEPH

The importance of the right ventricle (RV) in overall cardiac function is not fully understood, but RV function has been shown to correlate with long-term outcomes in the setting of pulmonary hypertension [5,6]. In CTEPH, increased RV afterload causes RV hypertrophy and dilation, leading to eventual RV dysfunction and failure [7,8]. Intervention through PTE results in improved mean pulmonary pressure, pulmonary vascular resistance, and cardiac output [9]. Many investigators have tried to identify simple echocardiographic surrogate measures of RV function, such as tricuspid annular plane systolic excursion (TAPSE) and right ventricular fractional area change (RVFAC). Although useful, these are indirect and imperfect measures of RV volume and contractility [10-15]. No simple parameters have overcome the problem of the RV's crescentic, asymmetric shape [16,17].

Deformation imaging through 2-D speckle tracking strain analysis appears to be a more robust technique to assess RV function and contractility. Strain is defined as the deformation of an object by an applied external force. Thus, right heart strain can be measured as the percentage change in shortening or thickening of the RV myocardium in the longitudinal or radial dimension [13]. In the setting of pulmonary hypertension, RV longitudinal strain has been shown to be a predictor of clinical outcomes with greater prognostic power than TAPSE [18]. Furthermore, RV strain has been shown to correlate well with invasive right heart catheterization (RHC) pressures measurements in pulmonary hypertension [19]. Recently, Sunbul, et al. reported a correlation between the 6-minute walk time (6MWT) and RV strain in CTEPH patients prior to PTE. Greater 6MWT distances correlated with higher RV basal and mid-free wall strain [20]. In addition, several studies have shown that 6MWT and New York Heart Association (NYHA) class improve after PTE [21-23]. One might infer, then, that RV strain would improve after PTE as well.

This has led to interest in using strain in CTEPH as a marker for

functional improvement of the RV after PTE. At 6 months post-PTE, Giusca et al. showed gradual strain improvement in the basal and mid-apical segments while Mauritz et al. found similar longitudinal strain improvement by cardiac magnetic resonance (CMR) imaging [24,25]. There appears to be progressive remodeling and geometric changes after PTE, which was demonstrated by Berman et al. who demonstrated a reduction in RV mass through CMR as early as 3 months after PTE [21].

Our group at UC San Diego recently studied strain imaging in the pre- and early post-PTE periods and found that RV basal strain correlated very well with preoperative PA pressure and PVR [26]. Surprisingly, though, RV strain did not improve early after PTE, despite marked reductions in PA pressure and PVR [26]. Despite the immediate decrease in RV afterload and reduction in RV size, we found an overall absolute decrease in RV strain early after PTE. This may be due to transient RV ischemia or stunning, and as a result, early postoperative RV strain cannot be used as a marker of successful PTE.

### LA Volume and Left Heart Dysfunction in CTEPH

The interplay between the right and left heart in pulmonary hypertension, which was noted long before the development of PTE, is still not fully understood. Patients with pulmonary hypertension often have diminished early LV filling (the E wave on Doppler imaging) with a relatively preserved atrial kick (A wave.) Theories for the LV diastolic dysfunction in CTEPH (i.e., E<A ratio) have included elevated RV diastolic pressures, decreased LV volume and compliance due to septal shifting, as well as true intrinsic dysfunction of the LV [27]. With the advent of PTE, it became clear that the LV diastolic "dysfunction" improved immediately with relief of RV overload [28]. This rapid recovery suggested that there was no intrinsic LV dysfunction, and later studies confirmed this concept [15,29,30].

A closer look at the E/A ratio in patients with CTEPH revealed that early diastolic filling (E) was much more diminished in CTEPH than the atrial kick (A). This low LV preload was reversed by PTE, and the E wave velocity promptly increased [31]. Thus, these studies all support the theory of LV underfilling as the primary cause of LV diastolic "dysfunction" in CTEPH.

Given this, we and others have focused more on the left atrium (LA), the chamber effectively between the RV and the LV. LA volume has been identified as a prognostic marker for a variety of cardiovascular diseases, and appears to play an integral role in

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overall LV function [32]. The importance of LA volume in CTEPH has not been previously examined, but recent evidence suggests that RV outflow tract dimensions may actually affect left atrial filling and volume in patients with CTEPH [33]. From front to back, space within the mediastinum is limited by the sternum anteriorly and the spine posteriorly. An enlarged RV outflow tract may restrict LA expansion and thereby affect LA filling [33]. A similar phenomenon of LA volume restriction has been described in patients with large mediastinal hiatal hernias [34]. The concept of LA size limitation from spatial restriction was tested in an animal model by Hoit, et al. [35]. Dogs that underwent pericardiectomy had a significant increase in LA compliance, reservoir function, and early diastolic LV filling compared to a control group [35]. Together, these studies suggest that impaired LA filling and volume may be caused by physical restrictions within the mediastinal space.

Our group recently examined the relationship between left atrial volume (LAV) index and pulmonary artery pressure in CTEPH [36]. We found that LAV index was in the low-normal range prior to PTE (mean: 19 cm<sup>3</sup>/m<sup>2</sup>) but increased significantly by 18% after surgery. Additionally, lower preoperative left atrial volumes were inversely associated with higher pulmonary vascular resistance (R=-0.45), higher mean pulmonary artery pressures (R=-0.28), and lower cardiac output (R=0.48). Increases in LAV following PTE were associated with decreased improved PVR (R=-0.36), higher cardiac index (R=0.41), and increased mitral E/A ratio (R=0.44) [36]. These last two findings are especially interesting because they suggest that postoperative increases in left atrial volume lead to increased early diastolic filling and, in turn, improved LV cardiac output. Further studies should address whether this is due more to an anatomical limitation to LA volume or to LA underfilling from depressed right ventricular output.

In summary, there have been several recent advances in our understanding of atrial and ventricular function (and interaction) in CTEPH. Further studies in this area should include assessments of global and regional right ventricular strain, as well as left heart strain before and after PTE.

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