Stressing the Cardiopulmonary Vascular System: The Role of Echocardiography

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The cardiopulmonary vascular system represents a key determinant of prognosis in several cardiorespiratory diseases. Although right heart catheterization is considered the gold standard for assessing pulmonary hemodynamics, a comprehensive noninvasive evaluation including left and right ventricular reserve and function and cardiopulmonary interactions remains highly attractive. Stress echocardiography is crucial in the evaluation of many cardiac conditions, typically coronary artery disease but also heart failure and valvular heart disease. In stress echocardiographic applications beyond coronary artery disease, the assessment of the cardiopulmonary vascular system is a cornerstone. The possibility of coupling the left and right ventricles with the pulmonary circuit during stress can provide significant insight into cardiopulmonary physiology in healthy and diseased subjects, can support the diagnosis of the etiology of pulmonary hypertension and other conditions, and can offer valuable prognostic information. In this state-of-the-art document, the topic of stress echocardiography applied to the cardiopulmonary vascular system is thoroughly addressed, from pathophysiology to different stress modalities and echocardiographic parameters, from clinical applications to limitations and future directions. (J Am Soc Echocardiogr 2018;■:■-■.)

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The past decade has seen an increased awareness of the importance of interactions between the right heart and the pulmonary vascular bed, or the cardiopulmonary vascular system.[1] Prognosis is closely related to right heart function and pulmonary circulation in a variety of conditions, including left-sided heart failure (HF),[2] valvular heart disease (VHD),[3] and, most classically, precapillary pulmonary hypertension (PH).[4] Despite recognition of the cardiopulmonary vascular system's influence, great challenges exist in its noninvasive assessment.

Stress echocardiography has been a mainstay in the evaluation of various left-sided pathologies.[5-9] These studies have helped clinicians in diagnosing functionally significant obstructive coronary artery disease (CAD) and in guiding the timing of therapeutic procedures and have contributed in the prognostic stratification. More recently, stress echocardiographic applications beyond CAD have gained attention for the significant potential clinical implication of applying such a dynamic and versatile technique to many different conditions.[10,11]

In this state-of-the-art document, we review the physiopathology of the cardiopulmonary vascular system, the echocardiographic measures of right ventricular (RV) function and hemodynamics, and how they fare in response to stress testing. Clinical applications including the role in diagnosis and prognosis are reviewed, and limitations and knowledge gaps are discussed to lay out future research.

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Abbreviations

2D = Two-dimensional
3D = Three-dimensional
AS = Aortic stenosis
CAD = Coronary artery disease
CHD = Congenital heart disease
CO = Cardiac output
Ea = Arterial elastance
EDE = Exercise Doppler echocardiography
Ees = End-systolic elastance
EVLW = Extravascular lung water
FAC = Fractional area change
HF = Heart failure
LA = Left atrial
LAP = Left atrial pressure
LV = Left ventricular
mPAP = Mean pulmonary artery pressure
MR = Mitral regurgitation
MS = Mitral stenosis
NYHA = New York Heart Association
PAH = Pulmonary arterial hypertension
PH = Pulmonary hypertension
PVR = Pulmonary vascular resistance
RA = Right atrial
RHC = Right heart catheterization
RV = Right ventricular
$RVOT_{TVI}$ = Right ventricular outflow tract time-velocity integral
RVSP = Right ventricular systolic pressure
sPAP = Systolic pulmonary artery pressure
SSc = Systemic sclerosis
SV = Stroke volume
TAPSE = Tricuspid annular plane systolic excursion
TRV = Tricuspid regurgitation velocity
VHD = Valvular heart disease
Vo_2 = Oxygen uptake

PHYSIOPATHOLOGY

Stress testing is traditionally applied in medicine to uncover alterations in function at early stages of disease. An exercise-induced increase in mean pulmonary artery pressure (mPAP) >30 mm Hg had previously been included in the definition of PH.[12] The practice of exercise measurements of the pulmonary circulation[13] was discouraged in the last American and European guidelines on PH because of uncertainty about exact cutoff values and prognostic implications.[14,15] The rationale and clinical relevance of testing the pulmonary circulation under stress conditions still hold.[16,17] Data continue to accumulate in support of the notion that exercise Doppler echocardiography (EDE) is useful to evaluate and unmask abnormalities of pulmonary vascular function as well as the state of the right heart.[18,19]

RV Function

The right ventricle is coupled to the pulmonary circulation. RV-arterial coupling depends on the adequacy of the matching of contractility to afterload.[20-22] The gold standard of contractility is end-systolic elastance (Ees), or the ratio of end-systolic pressure to end-systolic volume. An acceptable gold standard of afterload is arterial elastance (Ea), or the ratio of end-systolic pressure to stroke volume (SV). Both Ees and Ea can be measured on a simple pressure-volume loop, which describes ventricular pressure as a function of ventricular volume during a cardiac cycle. The optimal RV-arterial coupling allowing flow ejection at a minimal energy cost corresponds to an Ees/Ea ratio of 1.5 to 2.0.[20-22] In patients with PH, the right ventricle basically adapts to the increase in pulmonary arterial afterload by an increased Ees to preserve Ees/Ea.[23] Insufficient RV systolic function adaptation to afterload results in the Starling mechanism with increased RV volumes to preserve flow output at the price of systemic congestion and negative ventricular interaction.[22] Therefore, an assessment of RV function can be made with afterload-dependent indices but also, more accurately, with indices integrating RV function and RV afterload, with a possibly more realistic estimate of Ees/Ea.[24] An exercise increase in RV systolic pressure (RVSP) predicts survival in patients with severe PH, with a cutoff value of change in systolic pulmonary artery pressure (sPAP) > 30 mm Hg.[4] However, RVSP is an indirect estimate of RV contractile reserve and, in fact, correlates poorly with Ees in exercising patients with PH.[25] Furthermore, exercise changes in RVSP vary considerably in healthy subjects, so that it is difficult to define limits of normal of the response.[26] Because the blunting of the increase in Ees to preserve the Ees/Ea ratio in PH is associated with an increase in RV dimensions, assessment of RV function during exercise probably best integrates estimates of both contractility and dimensions. Accordingly, surrogates to the Ees/Ea ratio such as the ratio between RVSP and RV end-systolic area[27,28] or tricuspid annular plane systolic excursion (TAPSE) and RVSP[29] have been proposed. The clinical relevance of exercise changes in echocardiographic estimates of RV-arterial coupling remains to be established.

Acute Changes in Right Heart Function after Extreme Exercise

The right ventricle is a high-volume pumping chamber facing a low-impedance circuit. With chronic endurance exercise challenges, the right-sided chambers remodel, resulting in significant ventricular enlargement (~20%), demonstrated by traditional two-dimensional (2D) as well as novel three-dimensional (3D) measures.[30] This increase in RV volume is associated with little, if any, change in parameters of RV systolic function, including RV ejection fraction and TAPSE. A decrease in 2D strain has been demonstrated in strength-trained but not in endurance-trained athletes, with both groups having preserved isovolemic acceleration and normal N-terminal pro–brain natriuretic peptide levels.[31]

Experimental data on racehorses have demonstrated that intense exercise can cause stress failure of pulmonary capillaries, resulting in exercise-induced pulmonary hemorrhage.[32] Elite human athletes