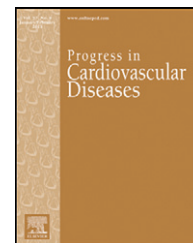


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Methods for evaluating right ventricular function and ventricular–arterial coupling

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ARTICLE INFO

Keywords:

Right ventricular function
Pulmonary hypertension
Reserve
Ventricular-arterial coupling

ABSTRACT

Right ventricular function (RVF) carries great prognostic significance in heart failure and pulmonary hypertension (PH). Although there is considerable focus on RVF in pulmonary arterial hypertension, RVF is also of great importance in group 2 PH. This article will discuss assessment of RVF and evaluation of the Right Ventricle-Pulmonary Artery (RV-PA) coupling relationship.

Cardiac imaging modalities allow direct visualization and assessment of RVF. Imaging modalities include the commonly utilized echo-Doppler imaging evaluating RV fractional area change, tricuspid annular plane systolic excursion and Tissue Doppler Imaging, in addition to the increasingly utilized cardiac magnetic resonance. Invasive hemodynamic assessment also plays an important role and can also be employed during exercise to help elucidate functional reserve. Cardiopulmonary exercise testing provides added insight into the mechanisms of cardiopulmonary disease. Cardiac imaging, invasive hemodynamics, and gas exchange stress testing can be combined to give a more sophisticated understanding of RVF. The RV-PA coupling relationship can be assessed using practical and clinically available metrics in order to gain clinically relevant understanding of the patients' physiologic state. RV-PA coupling assessments can be done using invasive, combined noninvasive–invasive, or non-invasive approaches. We also discuss our approaches in the assessment of the RV-PA coupling relationship.

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Introduction

Right ventricular function (RVF) assessment is integral to the understanding and evaluation of all forms of pulmonary hypertension (PH). In pulmonary arterial hypertension (PAH), the majority of the functional and prognostic significance of the condition relate either directly or indirectly to RVF.^{1,2}

Similarly in group 2 PH investigators have shown that RVF factors heavily into prognosis, and in fact PH in the setting of systolic left ventricular (LV) dysfunction only carries adverse prognostic significance in the presence of right ventricular (RV) dysfunction.³ Right ventricular ejection fraction (RVEF) has been proven to be an independent prognostic factor in patients with moderate to severe systolic heart failure (HF), moreover RVEF

Statement of Conflict of Interest: see page XX.

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<http://dx.doi.org/10.1016/j.pcad.2016.06.001>

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Please cite this article as: Kubba S, et al. Methods for evaluating right ventricular function and ventricular–arterial coupling. *Prog Cardiovasc Dis* (2016), <http://dx.doi.org/10.1016/j.pcad.2016.06.001>

Abbreviations and Acronyms

AT = acceleration time
CI = cardiac index
CMR = cardiac magnetic resonance
CPET = cardiopulmonary exercise testing
CTEPH = chronic thromboembolic pulmonary hypertension
DE = Doppler examination
Ea = arterial elastance
E _{max} = ventricular elastance
HF = heart failure
HFpEF = heart failure with preserved ejection fraction
HFREF = heart failure with reduced ejection fraction
LAP = left atrial pressure
LSN = late systolic notching
LV = left ventricle
MSN = mid-systolic notching
NN = no notch
PA = pulmonary artery
PAH = pulmonary arterial hypertension
PASP = pulmonary artery systolic pressure
PCWP = pulmonary capillary wedge pressure
PH = pulmonary hypertension
PVR = pulmonary vascular resistance
PVRI = pulmonary vascular resistance index
RA = right atrium
RAP = right atrial pressure
RHC = right heart catheterization
RV = right ventricle
RVF = right ventricular function
RVFAC = RV fractional area change
RVOT = right ventricular outflow tract

was the most important hemodynamic element of short-term survival when analyzing right heart catheterization data in patients with advanced HF.³⁻⁶ This follows as the functional and hemodynamic sequelae of PH are directly linked to the relationship between pulmonary vascular load and the adaptive response of the right heart coupled to that load. Since there is no single measure that accounts for both intrinsic RVF and RV afterload, assessment of RVF should always be taken as a composite of these two parameters. This can be done using a variety of relatively simple non-invasive and invasive approaches. Herein we will review the imaging, hemodynamic, and exercise modalities that measure or relate to RVF and its reserve. In addition, we will discuss concepts and practical methodologies to measure right ventricular-pulmonary arterial (RV-PA) coupling.

Cardiac imaging

Cardiac imaging modalities allow direct visualization of the right heart, including RV size and function, interventricular and interatrial septal position, reciprocal reduction of left heart size, tricuspid valve function and right atrial size.

Two dimensional-Doppler examination (DE) is by far the most common modality used to measure left and right sided heart function in all forms of PH.⁷ Echocardiography lends to this due to the fact that is practical, relatively inexpensive, and portable. In addition, when used properly, Doppler parameters provide insight into pulmonary artery pressure, flow dynamics, left heart filling pressures, cardiac output, and pulmonary arterial afterload.⁸ Like any imaging modality, it has its limitations. Two-dimensional echocardiography of the right heart can be limited by endocardial definition and difficulty in volumetric modeling of the RV when compared to the LV, which limits the reproducibility of RV fractional area change (RVFAC) and the ability to estimate RVEF.⁹⁻¹¹

Muscle fiber orientation within the RV lends to a greater proportion of longitudinal versus radial shortening as compared to the LV, which explains why measures of longitudinal shortening account for a larger proportion of overall RV function.^{12,13} This unique longitudinal contractile pattern can be exploited to measure RV function using relatively simple and reliable techniques without the need of precise endocardial definition or complex geometric assumptions. Tricuspid annular plane systolic excursion (TAPSE) quantifies the longitudinal displacement of the RV from base to apex during the cardiac cycle and has been shown to correlate strongly with RVEF measured by radionuclide angiography ($r = 0.92$), RVFAC ($r = 0.91$), and an impaired stroke volume index ($<29 \text{ ml/m}^2$) and cardiac index ($<2.2 \text{ l/min/m}^2$) by right heart catheterization.^{9,14-17}

TAPSE can easily be measured and reproduced from 2D echocardiography or M-mode (Fig 1). Ghio et al. showed in 140 consecutive patients with HF and reduced ejection fraction (HFREF), that a TAPSE $\leq 14 \text{ mm}$ was significantly associated with an increased likelihood of major events (death or emergent transplantation) in multivariate analysis over a mean follow up period of 24 months. Furthermore a significant correlation between TAPSE and thermodilution-derived RVEF was demonstrated ($r = 0.62$) by these investigators.¹⁸ Finally an inverse correlation between TAPSE and pulmonary artery systolic pressure ($r = -0.63$) was shown in 108 subjects with PH (mean PASP of $74 \pm 30 \text{ mmHg}$) including 33 patients with group 2 (HFREF) PH by Lopez-Candales et al., strengthening the importance and the usefulness of TAPSE in assessing RVF in patients with RV dysfunction secondary to left sided disease.¹⁹ Guazzi et al. have also employed TAPSE as a measure of RVF in HF and preserved ejection fraction (HFpEF), with subjects in the lowest TAPSE quartile demonstrating the highest mortality.^{20,21}

Tissue Doppler imaging (TDI) performed at the level of the RV base (approximately 1 cm apical of the tricuspid annulus) in the apical four chamber view is another reliable and reproducible modality to assess RVF. This determination is done using pulsed tissue Doppler to measure longitudinal peak tissue velocity, denoted S' (Fig 2). This measurement has been shown to be a highly sensitive and specific index of RV dysfunction and has been validated in a number of studies comparing S' with radionuclide angiography RVEF.²² A cut-off S' of $<11.5 \text{ cm/sec}$ predicts RV dysfunction (RVEF $<45\%$) with a sensitivity of 90% and a specificity of 85%.²³ TDI strongly correlates with TAPSE ($r = 0.90$), which is logical, as both are

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