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● *Original Contribution*

THREE-DIMENSIONAL ECHOCARDIOGRAPHY-DERIVED NON-INVASIVE RIGHT VENTRICULAR PRESSURE-VOLUME ANALYSIS

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Abstract—In patients with pulmonary hypertension, repeated evaluations of right ventricular (RV) function are still required for clinical decision making, but the invasive nature of current pressure-volume analysis makes conducting regular follow-ups in a clinical setting infeasible. We enrolled 12 patients with pulmonary arterial hypertension (PAH) and 10 with pulmonary venous hypertension (PVH) May 2016–October 2016. All patients underwent a clinically indicated right heart catheterization (RHC), from which the yielded right ventricular pressure recordings were conjugated with RV volume by 3-D echocardiography to generate a pressure-volume loop. A continuous-wave Doppler envelope of tricuspid regurgitation was transformed into a pressure gradient recording by the simplified Bernoulli equation, and then a systolic pressure gradient-volume (PG-V) diagram was generated from similar methods. The area enclosed by the pressure-volume loop was calculated to represent semi-invasive right ventricular stroke work ($RVSW_{RHC}$). The area between the PG-V diagram and x-axis was calculated to estimate non-invasive RVSW ($RVSW_{echo}$). Patients with PAH have higher RV pressure, lower pulmonary arterial wedge pressure and larger RV volume that was contributed by the dilation of RV mid-cavity minor dimension. We found no significant difference of traditional parameters between these two groups, but RVSW values were significantly higher in PAH patients. The RVSW values of these two methods were *significantly* correlated by the equation $RVSW_{echo} = 0.8447\ RVSW_{RHC} + 129.38$ ($R^2 = 0.9151, p < 0.001$). The linearity remained satisfactory in both groups. We conclude that a PG-V diagram is a reliable method to estimate RVSW and to depict pathophysiological status. (E-mail: anniejou@ms28.hinet.net)

Key Words: **Pressure-volume loop, Pulmonary hypertension, Three-dimensional echocardiography.**

INTRODUCTION

In the mammalian cardiovascular system, the right ventricle (RV) performs the very first of the in-series double pumps. Its functioning reflects a composite result of fluid status, pulmonary vascular resistance and left heart function, and its failure to function properly is implicated in several cardiac diseases (Dandel et al. 2015; Gorcsan et al. 1996; Mohammed et al. 2014; Vachiéry et al. 2013). However, the parameters of RV function that can be measured non-invasively, such as right ventricular ejection fraction (RVEF), tricuspid annular plane systolic excursion (TAPSE), tricuspid regurgitation pressure gradient (TRPG), fractional area change, peak systolic longitudinal RV free wall strain, the RV index of myocardial performance and the load adaptation index, are considered to be only of modest predictive value in the prognosis of heart disease (Bleeker et al. 2006; Cameli et al. 2014; Guihaire et al. 2013; Ling et al. 2012). This is because the RV alters its shape continuously throughout its unique peristalsis-like contraction, but the above parameters only focus on static differences between the end-diastole and end-systole. As a result, the dynamic pumping process has been overlooked as has the individual contractive contribution made by each of the three parts of the RV, among which the infundibulum makes the last and longest contribution (Haddad et al. 2008).

The pressure-volume (PV) loop is the fundamental analytic tool of cardiac physiology. It is used to derive stroke work and elastance (Kass et al. 1986), which have played important roles in left ventricular (LV)

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evaluation beyond ejection fraction. A simultaneous high-quality recording of pressure and volume is the key for making use of the PV loop to analyze heart function. However, the complex geometry and abundant trabeculation of the right ventricle tend to hinder volumetric analysis. Geometric approximation of RV volume by two-dimensional echocardiography methods, such as fractional area change, totally overlook the contractive contribution of the infundibulum and cannot reflect the peristaltic bellows-like effect of RV contraction. A conductance catheter, being invasive in nature, makes conducting regular follow-ups in a clinical setting infeasible. Cardiac magnetic resonance imaging, the current gold standard for RV volume measurement, also requires an invasive technique to generate a PV loop (Kuehne 2004).

Echocardiography, the traditional tool of cardiac evaluation, has been widely used because of its good accessibility. Recently, multiple-beat reconstructed three-dimensional echocardiography (3-DE) and dedicated software for endocardial border tracking have brought volumetric analysis from theory into clinical practice. Not only does 3-DE show good consistency with cardiac magnetic resonance imaging in volume measurement (Medvedofsky et al. 2015), echocardiography also makes possible calculation of the pressure gradient, using the simplified Bernoulli equation. Because the diastolic pressure recording is in a low pulsatile pattern in the right heart (Ensing et al. 1994), the difference between its peak-to-peak pressure gradient and maximum pressure gradient diminishes to a negligible degree. As a result, we hypothesized that the tricuspid regurgitation pressure gradient (TRPG) recording calculated by spectral Doppler envelope tracing might have a similar curvilinear character to the right heart catheterization (RHC) pressure recording and should be applicable in estimating right ventricular stroke work (RVSW). The aim of this study is to examine the consistency between non-invasive RVSW derived from echocardiography ($RVSW_{echo}$) and semi-invasive RVSW yielded from RHC and 3-DE ($RVSW_{RHC}$) in terms of curvilinear character and stroke work values to provide a feasible method for clinical follow-ups.

MATERIALS AND METHODS

Patients

May 2016–October 2016 we enrolled twelve patients diagnosed with pulmonary arterial hypertension (PAH) and ten with pulmonary venous hypertension (PVH). Among the PAH patients, five were diagnosed with idiopathic pulmonary arterial hypertension (group 1) and seven were diagnosed with chronic thromboembolic pulmonary hypertension (group 4). The PVH patients all belonged to group 2 pulmonary hypertension. All of them underwent 3-DE, followed by a clinically indicated RHC. Informed consent was obtained and the institutional review board of National Taiwan University Hospital approved the collection protocol (201601071 RINC). Meeting the requirements for reimbursement of costs for PAH treatment and pre-operative evaluation for valvular heart disease were the only two indications for RHC in the present study. Patients with atrial fibrillation and other irregular heart beat arrhythmia were excluded because of the difficulty of performing the multiple-beat-reconstruction step of 3-DE in such patients.

Echocardiography

All echocardiographs were performed with the iE33 system equipped an X5-1 transducer (Philips Medical Systems, Andover, MA, USA). Two-dimensional RV parameters were measured as suggested by Rudski et al. (2010). Right ventricle 3-DE data sets were obtained from RV four chamber views adjusted to avoid a pulmonary shielding effect on the RV outflow tract (Lang et al. 2012). Continuous-wave Doppler recordings of the maximal tricuspid regurgitation (TR) envelope were obtained systematically from lower left parasternal long-axis RV inlet views, parasternal short axis views, apical long axis RV inlet views, apical four chamber views and subcostal transducer positions. The chosen TR envelope should have the highest velocity, the cleanest signal without envelope truncation in the whole spectral Doppler recording. When remarkable beat-to-beat variation occurred during respiration, TR velocity was acquired at the end-expiration, which is the most often used time frame for multiple-beat reconstruction of 3-DE. TR velocity recordings were transformed into TRPG tracings through the simplified Bernoulli's equation: $TRPG = 4 \times Vel^2$ (Vel = peak velocity of tricuspid regurgitation, m/s; TRPG calculated in mmHg). RV volumes and right ejection fraction (RVEF) were obtained from 3-D data sets that were analyzed offline with a module for RV volumetric analyses (4D RV-Function 2.0, Image-Arena v. 4.6, TOMTEC Imaging Systems, Unterschleissheim, Germany).

Pressure recording

A fluid-filled catheter was delivered into the apex of the right ventricle under fluoroscopy and RV pressure was measured with a calibrated pressure transducer. Catheterization pressure curves were recorded along with electrocardiography (ECG) signals using a commercially available hemodynamic recording system (Axiom Sensis XP Cath Lab Monitoring, Siemens Healthcare, Munich, Germany).