Almost 3 quarters of a century ago, an experimental dog model, involving the electrocautery ablation of the free wall of the right ventricle (RV), served as the basis for the contention that the RV serves functionally as a passive conduit. Clearly, our understanding of the RV has evolved over subsequent decades, and the prognostic significance of RV dysfunction is now recognized in a wide array of disorders including left heart dysfunction and pulmonary hypertension among others. Despite significant strides in elucidating the role of the RV in overall cardiac function on the one hand and in disease states on the other, both quantification and qualification of RV function remain challenging because of several inter-related factors. First, the RV has a complex geometry; second, the role of ventricular interaction in overall pump performance remains unclear; third, assessment of RV diastolic function is challenging and far from routine in a typical echocardiographic laboratory; and fourth, the role of the pericardium in pump performance, especially that of pericardial constraint during exercise, also influences the ability to both qualify and quantify RV function. The challenges in noninvasively assessing RV function at rest are only compounded when attempting to evaluate performance with exercise.

See Article by Kim et al

Exercise capacity is a robust prognostic variable that predicts total and cardiac mortality. In clinical practice exercise capacity is most commonly derived from the peak exercise workload and estimated in metabolic equivalents (METs) from published tables. However, the most accurate method of determining exercise capacity is directly measuring the amount of oxygen consumed during a graded maximal exercise test, referred to as maximal oxygen uptake ($VO_2$ max). The Fick equation states that the determinants of $VO_2$ max are cardiac output (CO), which represents the product of stroke volume (SV) x heart rate (HR), and arterial-venous oxygen difference (A-V$O_2$ diff): $VO_2$ max = CO x A-V$O_2$ diff = SV x HR x A-V$O_2$ diff. The average untrained middle aged adult is able to increase oxygen uptake approximately 10-fold during a maximal exercise effort (35-40 ml/kg/min, or 10 METs) over rest (3.5 ml/kg/min, or 1 MET). The 10-fold increase in $VO_2$ is achieved through a 5-fold increase in CO and a doubling of A-V$O_2$ diff. The increase in CO results from a 1.5-2.0-fold increase in SV and a 2-3-fold increase in HR.

Many cardiovascular conditions and cardiovascular medications can impact the individual variables that comprise the Fick equation and thereby influence exercise capacity. RV function can potentially influence left ventricular preload, subsequently modifying left ventricular systolic performance and exercise tolerance. The behavior of the RV at rest and during exercise in individuals with and without coronary artery disease (CAD) is complex. In a small study, including 14 subjects (7 with CAD and 7 without CAD), invasive parameters of RV function at rest and during supine bicycle exercise were measured. In this investigation, parameters, including tricuspid valve opening pressures, ventricular diastolic pressures, ventricular peak systolic pressures, ventricular filling rates, pressure–volume relationships, and chamber stiffness, were evaluated. In this study, hemodynamic factors that influenced RV function included systolic and diastolic function, chamber stiffness, ventricular interaction, and pericardial constraint, all of which may be negatively impacted in the setting of ischemia.

In the current issue of Circulation: Cardiovascular Imaging, Kim et al made a novel attempt at providing insight into the role of RV dysfunction on effort tolerance independent of left ventricular function in a cohort of 2051 subjects who underwent a clinically indicated resting echocardiogram and exercise single-photon emission computed tomography within a 1-month period. RV function on echocardiography was assessed both qualitatively by standard subjective visual assessment and quantitatively by measurement of tricuspid annular plane systolic excursion and peak tricuspid annular systolic velocity (S’). Both tricuspid annular plane systolic excursion and tissue Doppler imaging have been shown to be reliable measures of RV response to exercise. In the group studied by Kim et al, 6% of the population (n=123) had RV systolic dysfunction by quantitative parameters. In these patients, 19% had RV dilation and 40% had RV systolic dysfunction by qualitative assessment. The major finding of this study is that exercise duration in patients with RV dysfunction is significantly lower than that in patients without RV dysfunction (6.7±2.8 versus 7.9±2.9 minutes; P<0.001). In multivariable analysis, both LV ($P=0.002$) and RV ($P=0.02$) dysfunction were independently associated with exercise time. Patients with RV dysfunction had more severe left-sided heart disease, in particular, lower left ventricular ejection fraction and more extensive inferior and lateral ischemia.

The opinions expressed in this article are not necessarily those of the editors or of the American Heart Association.
As the authors note, several previous small studies performed in patient populations with heart failure or chronic lung disease have reported that RV dysfunction is associated with reduced exercise capacity.9–12 The unique contribution of the present study is the demonstration of the impact of RV dysfunction on exercise capacity independent of LV function or myocardial perfusion in a broad study population undergoing evaluation of CAD. As expected, LV dysfunction was also independently associated with reduced exercise capacity, with a reduction in magnitude similar to that associated with RV dysfunction (a reduction of 1 minute). An interesting finding is the association in univariable analysis of reversible and fixed inferior and lateral defects with RV dysfunction. Depending upon anatomic variation, the majority of the blood supply of the RV is the right coronary artery or the circumflex artery. Obstructive CAD involving these arteries likely partially explains the resting RV systolic dysfunction.

This study does not elucidate the mechanism by which RV dysfunction is associated with a reduction in exercise capacity. The reduction in exercise capacity in patients with RV dysfunction reported by Kim et al5 was statistically significant but modest in magnitude (an average of only one minute less during stage III of the Bruce protocol). Peak exercise heart rate, one of the components of the Fick equation, was 11 bpm lower in patients with RV dysfunction (128 versus 139; P<0.001). The percentages of patients with recorded exercise symptoms of chest pain (5%) and dyspnea (13%) were small without differences between patients with and without RV dysfunction. There was no difference in the prevalence of ischemic ECG responses for patients with and without ischemic LV dysfunction (19% versus 15%; P=0.21). Although single-photon emission computed tomography ischemia was more evident in patients with RV dysfunction, these results would not have been known while the exercise tests were being performed. Ischemia may have influenced exercise capacity, but clinically apparent ischemia at the time of test performance as a reason to terminate the test does not seem to explain the difference in exercise tolerance. A logical potential explanation by which RV dysfunction could lower exercise capacity is its impact on LV preload. No data are provided to investigate this possibility. Estimated RV systolic pressure  $\geq$ 35 mmHg at rest was more common in patients with RV dysfunction (32% versus 21%; P=0.006), but no information is available on RV pressure during exercise. Other conditions known to influence RV function apart from ischemic heart disease, such as chronic obstructive pulmonary disease,13 further limit the current technical ability to depict the mechanistic flow of aberrations in RV function leading to clinical symptoms. As indicated in the literature, the mechanism of purported RV dysfunction will be confounded by influence of concomitant hemodynamic alterations imposed by such factors as pericardial constraint and ventricular interaction.

The current study by Kim et al10 clearly highlights the following: (1) the importance of the RV in overall cardiovascular function; (2) the contribution of RV dysfunction to effort tolerance in the setting of ischemic heart disease; and (3) the current limitations of the noninvasive evaluation of RV function even when using a multimodality imaging strategy. The current investigation sets the precedent for further work in understanding not only the nuances of RV function but also the understanding of the evolution of the hemodynamic perturbations that contribute to RV dysfunction under different clinical settings.

Disclosures

None.

References


3. Mark DB, Lauer MS. Exercise capacity; the prognostic variable that doesn’t get enough respect. Circulation. 2003;108:1534–1536. doi: 10.1161/01.HER.0000094408.38603.7E.


Key Words: Editorial  ; coronary artery disease  ; diastole  ; dog  ; echocardiography  ; exercise tolerance
Right Ventricle and Exercise Capacity: More Than a Passive Conduit
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Circ Cardiovasc Imaging. 2016;9:
doi: 10.1161/CIRCIMAGING.116.005703
Circulation: Cardiovascular Imaging is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-9651. Online ISSN: 1942-0080

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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