JACC: CASE REPORTS VOL. 4, NO. 21, 2022

IMAGING VIGNETTE

INTERMEDIATE

CLINICAL VIGNETTE: SPORTS CARDIOLOGY

Right Ventricular Dysfunction During Endurance Exercise as Determined by Pressure-Volume Analysis

Justin A. Edward, MD,[a] Lukasz P. Cerbin, MD,[a] Daniel W. Groves, MD,[a,b] Robert A. Quaife, MD,[a,b] Kendall S. Hunter, PhD,[c] Benjamin D. Levine, MD,[d,e] William K. Cornwell III, MD, MSCS[a,f]

ABSTRACT

A 37-year-old athlete completed invasive endurance (90 km) bicycle exercise testing for right ventricular pressure-volume analysis. Increased right ventricular afterload caused declines in ventricular-arterial coupling and cardiac output, causing increased arteriovenous oxygen difference to maintain oxygen uptake. These findings demonstrate effects of changes in right ventricular performance on exercise capacity. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2022;4:1435–1438) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Invasive exercise testing with pressure-volume (PV) analysis demonstrates that the healthy right ventricle (RV) has substantial contractile reserve, with a 3- to 4-fold increase in metrics of contractility during short bouts of exercise.[1] That said, prolonged exercise may precipitate RV dysfunction caused by sustained increases in afterload.[2,3] However, there have not been any invasive hemodynamic assessments of RV performance during extended duration exercise. Herein, we present a first-ever analysis of RV function during prolonged exercise using conductance catheters to generate RV PV loops, a gold standard method of characterizing ventricular function (Cardiopulmonary and Right Ventricular Function in Health and Disease; NCT04147299).

CLINICAL VIGNETTE

A healthy 37-year-old male endurance athlete (187 cm, 78 kg) with maximal oxygen consumption ($\dot{V}O_2$ max) of 47.9 mL/kg/min and hemoglobin of 14.1 g/dL completed invasive hemodynamic testing during 90 km of exercise on upright stationary cycle ergometry. Immediately before exercise, hemodynamic evaluation was completed with pulmonary arterial (PA) catheterization and Fick cardiac output (Qc) was determined. Thereafter, the PA catheter was exchanged for a conductance catheter for RV PV analysis, which was left in

From the [a]Department of Medicine-Cardiology, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA; [b]Department of Radiology-Cardiothoracic Imaging, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA; [c]Department of Bioengineering, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA; [d]Division of Cardiology, Department of Medicine, University of Texas Southwestern Medical Campus, Dallas, Texas, USA; [e]Institute for Exercise and Environmental Medicine, Texas Health Presbyterian Hospital, Dallas, Texas, USA; and the [f]Clinical Translational Research Center, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA.
Mustafa Husaini, MD, served as Guest Associate Editor for this paper.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received March 13, 2022; revised manuscript received July 12, 2022, accepted August 4, 2022.

ISSN 2666-0849 https://doi.org/10.1016/j.jaccas.2022.08.006

JACC: CASE REPORTS, VOL. 4, NO. 21, 2022
NOVEMBER 2, 2022:1435-1438

ABBREVIATIONS AND ACRONYMS

CMR = cardiac magnetic resonance

E_A = effective arterial elastance

E_{ES} = end-systolic elastance

PA = pulmonary arterial

PV = pressure volume

Qc = cardiac output

RV = right ventricle

Vo_2 max = maximal oxygen consumption

place for the duration of testing. Cardiac magnetic resonance (CMR) was obtained 1 hour before invasive testing began and immediately following completion of exercise. RV PV loop volume was calibrated from CMR and loop width (ie, stroke volume) was calibrated from Fick Qc derived from PA catheterization. Single beat loop estimation was used to estimate end-systolic elastance (E_{ES}), obtained from determination of maximum isovolumic pressure, from which E_{ES} is derived.[4] End-systolic pressure is obtained from the second derivative of the pressure waveform (Figure 1).[3] Effective arterial elastance (E_A) was defined as the ratio of end-systolic pressure and stroke volume during exercise.[5] Peripheral oxygen extraction was directly measured by assessing arterial and mixed venous uptake throughout the study.

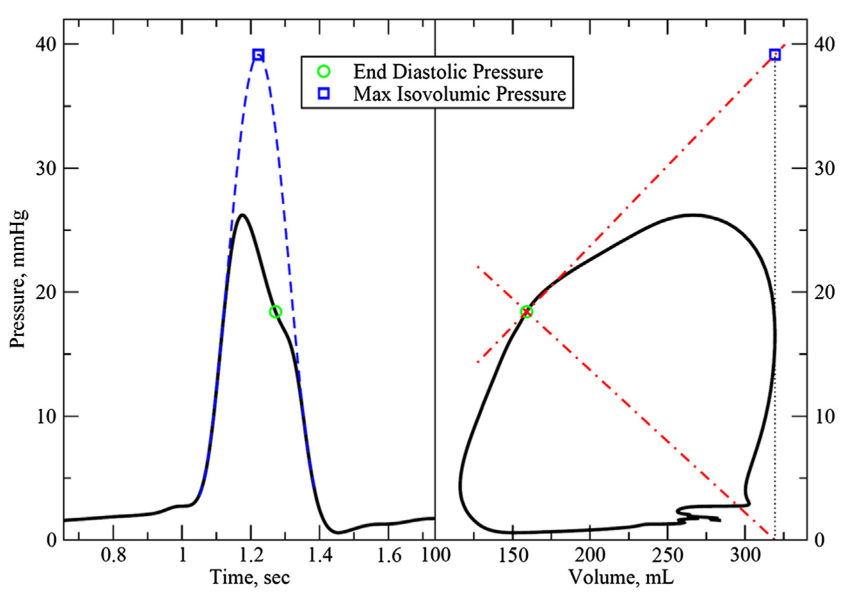
Supine resting hemodynamics were normal: heart rate, 54beats/min; blood pressure, 134/84 mm Hg; right atrial pressure, 5 mm Hg; systolic, diastolic, and mean PA pressure, 24, 10, and 15 mm Hg, respectively; pulmonary capillary wedge pressure, 9 mm Hg; PA saturation, 76%; Fick Qc, 6.5 L/min; and cardiac index, 3.25 L/min/m^2.

The participant maintained a cycling speed of ~21-23 km/h throughout the test and total exercise time was 4 hours, 20 minutes. RV PV analysis demonstrated an early initial increase in contractility and Qc (Figure 2A). Sustained increases in RV afterload (E_A) were associated with reductions in ventricular-arterial coupling (E_{ES}/E_A ratio), as well as reductions in Qc and contractility particularly during the final hours of exercise. CMR demonstrated an increase in RV end-systolic volume by 20 mL after exercise (Figure 2B). RV ejection fraction was preserved. Left ventricular ejection fraction and volumes were preserved.

DISCUSSION

This case represents the first invasive analysis of RV performance during endurance exercise. We found that after several hours of increased RV afterload in response to sustained exercise, RV contractility declined, and

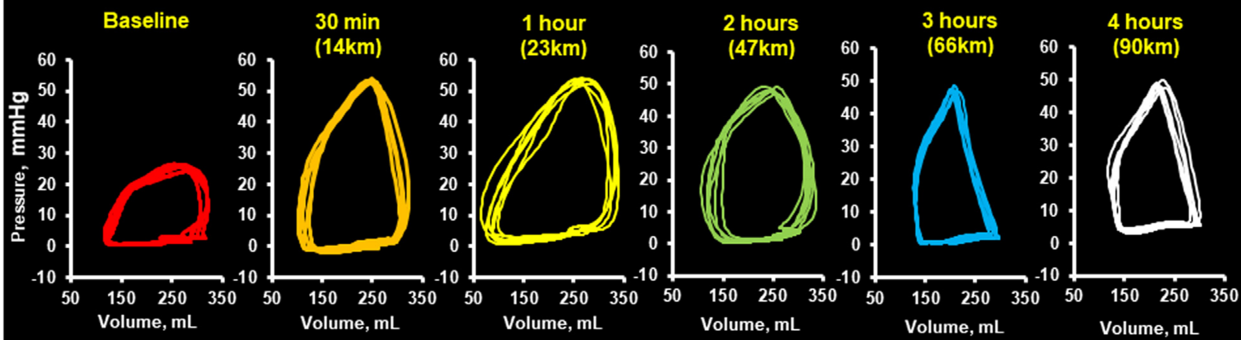
FIGURE 1 Schematic Overview of Single-Beat Modeling Technique for Determining E_{ES}



(Left) A sinusoid is fitted to the rising and falling isovolumic portions of the pressure waveform; the resulting peak of this sinusoid is known as the maximum isovolumic pressure. On the **right**, the line between maximum isovolumic pressure, at end-diastolic volume, and the end-diastolic pressure models the end-systolic pressure-volume relation, the slope of which is end-systolic elastance (E_{ES}). Effective arterial elastance is simply the slope of the line connecting end-diastolic pressure and no pressure (0) at end-diastolic volume.[6] The occurrence of end systole (and in turn, end-diastolic pressure) may be measured directly, or it may be inferred from waveform features of the second time derivative of pressure.

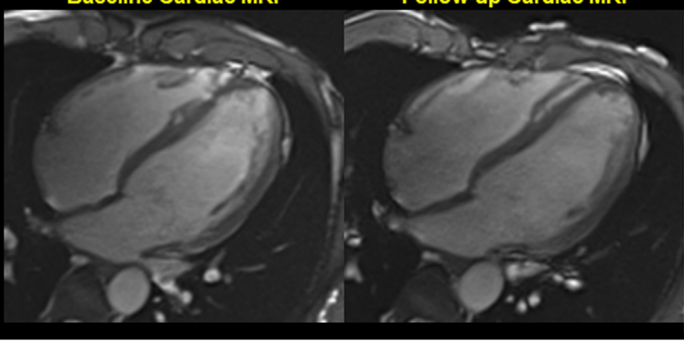
FIGURE 2 **Longitudinal Change in RV PV Analysis and Ventricular Structure and Function Derived From CMR**

A Pressure-Volume Analysis



	Baseline	30 min	1 hour	2 hours	3 hours	4 hours
VO_2, L/min, ml/kg/min	0.35, 4.8		2.03, 27.7	2.14, 29.2	1.90, 26.0	1.93, 26.3
$avO2_{diff}$, mL/100mL	5.79		7.29	9.28	13.51	11.37
Cardiac Output, L/min	6.1	22.8	27.8	23.1	14.1	16.9
HR, bpm	51	126	123	122	130	130
SV, ml/beat	119	180	226	190	108	130
PRSW, mmHg	14	28	30	25	16	17
$dpdt_{max}$, mmHg/sec	261	850	764	675	686	641
E_{ES}, mmHg/mL	0.11	0.14	0.11	0.14	0.22	0.16
E_A, mmHg/mL	0.08	0.16	0.12	0.13	0.23	0.20
E_{ES}/E_A	1.37	0.86	0.88	1.08	0.98	0.81

B Cardiac MRI data



MRI Data

	Before	After
LV mass, gm	172	160
LV EDV, mL	254	238
LV ESV, mL	126	114
LV SV, mL	129	124
LV EF(%)	50	52
RV EDV, mL	287	312
RV ESV, mL	168	183
RV SV, mL	119	129
RV EF (%)	41	42

(A) Longitudinal changes in the right ventricular (RV) pressure-volume (PV) analysis are shown. **(B)** Ventricular structure and function are derived from the cardiac magnetic resonance (CMR) data. $avO2_{diff}$ = peripheral oxygen extraction; E_A = end-arterial elastance; EDV = end-diastolic volume; E_{ES} = end-systolic elastance; EF = ejection fraction; ESV = end-systolic volume; HR = heart rate; LV = left ventricle; PRSW = preload recruitable stroke work; SV = stroke volume; Vo_2 = oxygen consumption.

despite an increase in heart rate, Qc declined. This reduction in Qc was partially offset by an increase in peripheral oxygen extraction to maintain V_{O_2} and overall workload throughout the duration of exercise. Preload recruitable stroke work (product of stroke work and end-diastolic volume), a marker of cardiac function that is independent of preload and afterload, initially increased but declined after several hours of exercise, which is also indicative of a decline in RV contractility and coinciding with the decline in stroke volume.

The RV historically has been referred to as a passive conduit and a mere bystander.[2,5] However, our findings demonstrate the impact of RV function on overall exercise capacity, as well as the body's attempt to compensate for reductions in RV cardiac output during prolonged exercise, such as by increases in HR and peripheral oxygen extraction as described. These observations describe the contributions of the RV to overall cardiac performance during prolonged exercise.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Cornwell has received funding by a National Institutes of Health/National Heart, Lung, and Blood Institute Mentored Patient-Oriented Research Career Development Award (1K23HLI32048), as well as the National Institutes of Health/National Center for Advancing Translational Sciences (UL1TR002535). All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr William K. Cornwell III, University of Colorado Anschutz Medical Campus, 12631 East 17th Avenue, B130, Office 7107, Aurora, Colorado 80045, USA. E-mail: William.cornwell@cuanschutz.edu.

REFERENCES

1. Cornwell WK, Tran T, Cerbin L, et al. New insights into resting and exertional right ventricular performance in the healthy heart through real-time pressure-volume analysis. *J Physiol*. 2020;598(13):2575–2587.

2. La Gerche A, Burns AT, Mooney DJ, et al. Exercise-induced right ventricular dysfunction and structural remodeling in endurance athletes. *Eur Heart J*. 2012;33(8):998–1006.

3. Edward J, Banchs J, Parker H, et al. Right ventricular function across the spectrum of health and disease. *Heart*. Published online May 31, 2022. https://doi.org/10.1136/heartjnl-2021-320526

4. Takeuchi M, Igarashi Y, Tomimoto S, et al. Single-beat estimation of the slope of the end-systolic pressure-volume relation in the human left ventricle. *Circulation*. 1991;83(1):202–212.

5. Dufva MJ, Ivy D, Campbell K, et al. Ventricular-vascular coupling is predictive of adverse clinical outcome in paediatric pulmonary arterial hypertension. *Open Heart*. 2021;8(2):e001611.

6. Kelly RP, Ting CT, Yang TM, et al. Effective arterial elastance as index of arterial vascular load in humans. *Circulation*. 1992;86(2):513–521.

KEY WORDS exercise, hemodynamics, right ventricle, sports