ORIGINAL ARTICLE

The pulmonary artery wedge pressure response to sustained exercise is time-variant in healthy adults

Stephen P Wright,[1,2] Sam Esfandiari,[1,2] Taylor Gray,[3] Felipe C Fuchs,[2] Anjala Chelvanathan,[2] William Chan,[2] Zion Sasson,[2] John T Granton,[1,4] Jack M Goodman,[1,2,3] Susanna Mak[1,2]

▶ Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/heartjnl-2015-308592).

[1]Institute of Medical Science, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[2]Division of Cardiology, Mount Sinai Hospital/University Health Network, Toronto, Ontario, Canada
[3]Department of Exercise Sciences, University of Toronto, Toronto, Ontario, Canada
[4]Division of Respirology, University Health Network, Toronto, Ontario, Canada

Correspondence to
Dr Susanna Mak, Division of Cardiology, Mount Sinai Hospital, 600 University Avenue, Rm 18-365, Toronto, ON M5G 1X5, Canada; smak@mtsinai.on.ca

Received 24 August 2015
Revised 14 December 2015
Accepted 15 December 2015
Published Online First 13 January 2016

ABSTRACT

Objectives The clinical and prognostic significance of 'exaggerated' elevations in pulmonary artery wedge pressure (PAWP) during symptom-limited exercise testing is increasingly recognised. However, the paucity of normative data makes the identification of abnormal responses challenging. Our objectives was to describe haemodynamic responses that reflect normal adaptation to submaximal exercise in a group of community-dwelling, older, non-dyspnoeic adults.

Methods Twenty-eight healthy volunteers (16 men/12 women; 55±6 years) were studied during rest and two consecutive stages of cycle ergometry, at targeted heart rates of 100 bpm (light exercise) and 120 bpm (moderate exercise). Right-heart catheterisation was performed to measure pulmonary artery pressures, both early (2 min) and after sustained (7 min) exercise at each intensity.

Results End-expiratory PAWP at baseline was 11 ±3 mm Hg and increased to 22±5 mm Hg at early-light exercise ($p<0.01$). At sustained-light exercise, PAWP declined to 17±5 mm Hg, remaining elevated versus baseline ($p<0.01$). PAWP increased again at early-moderate exercise to 20±6 mm Hg but did not exceed the values observed at early-light exercise, and declined further to 15±5 mm Hg at sustained-moderate exercise ($p<0.01$ vs baseline). When analysed at 30 s intervals, mean and diastolic pulmonary artery pressures peaked at 180 (IQR=30) s and 130 (IQR=90) s, respectively, and both declined significantly by 420 (IQR=30) s (both $p<0.01$) of light exercise. Similar temporal patterns were observed at moderate exercise.

Conclusions The range of PAWP responses to submaximal exercise is broad in health, but also time-variant. PAWP may routinely exceed 20 mm Hg early in exercise. Initial increases in PAWP and mean pulmonary artery pressures do not necessarily reflect abnormal cardiopulmonary physiology, as pressures may normalise within a period of minutes.

INTRODUCTION

Exercise capacity is an important determinant of health and well-being during normal aging as well as in diseases of cardiopulmonary function.[1] Haemodynamic evaluation during exercise stress can be a valuable diagnostic tool for patients presenting with dyspnoea and otherwise unremarkable cardiac and respiratory testing performed at rest.[2] The extent to which the pulmonary artery wedge pressure (PAWP) is elevated during symptom-limited exercise testing is increasingly recognised as an important pathophysiological response indicative of latent heart failure with preserved ejection fraction (HFpEF) and is associated with an adverse prognosis.[3 4] However, the paucity of normative data derived from healthy, non-dyspnoeic older adults currently makes the identification of abnormal responses challenging. Further exploration and characterisation of both the physiologic and pathophysiological determinants of the PAWP response to exercise may help refine methodology and interpretation of the haemodynamic exercise challenge.

Previous work suggests that in otherwise healthy adults aged over 50 years, pulmonary artery (PA) pressures and PAWP may increase markedly even with 'slight' exercise,[5] and the decrease in total pulmonary resistance may be delayed by several minutes after exercise onset,[6] potentially indicative of age-related changes in cardiopulmonary accommodation to exercise-related increases in cardiac output (CO). Data from earlier studies suggested that PA pressures may demonstrate a marked initial increase in pressure followed by attenuation over a period of minutes when exercise is sustained;[7 8] however, these observations were limited as measurements of the PAWP were not available. Accordingly, this study aimed to describe central cardiopulmonary haemodynamic responses that reflect a normal adaptation to exercise in a group of healthy, community-dwelling, older, non-athletic, non-dyspnoeic adults. We hypothesised that older, non-dyspnoeic adults would demonstrate a biphasic response to exercise, wherein PAWP increases in the early phase of exercise, followed by decay as submaximal exercise is sustained.

METHODS

Participants

We recruited healthy, non-athletic volunteers aged ≥45 years from the community. All participants underwent screening including a medical history, blood pressure measurement, 12-lead ECG and a clinical echocardiogram. Exclusion criteria comprised a history of any cardiovascular disease or cardioactive drug use, recent smoking, diabetes, premenopausal status and any other chronic systemic illness. A seated blood pressure >140/90 mm Hg, body mass index >30 kg/m^2, non-sinus rhythm and significant left ventricular (LV) hypertrophy or valvular abnormalities were further exclusion criteria. The study was approved by the

To cite: Wright SP, Esfandiari S, Gray T, *et al*. *Heart* 2016;**102**:438–443.

Mount Sinai Hospital research ethics board, and all participants provided informed, written consent.

Experimental design and cardiac catheterisation

Simultaneous right-heart catheterisation and echocardiography were performed at rest and during exercise. Ultrasound-guided peripheral vein cannulation allowed positioning of a 7Fr multi-lumen PA catheter (Edwards Lifesciences) in a main branch of a PA. Baseline right atrial (RA) pressure, right ventricular pressure, PA pressure and PAWP were measured in the supine position. Heart rate (HR) was monitored with three-lead electrocardiography, and non-invasive brachial blood pressure was measured intermittently (Tango+, SunTech Medical).

After instrumentation, the participant was transferred to a cycle ergometer (Ergoselect 1200E, Ergoline), and inclined to a semi-upright position. The proximal and distal catheter ports were transduced on two channels, and zeroed at the level of the midaxillary line.[9] RA and PA pressures were recorded continuously, and PAWP was acquired intermittently for offline analysis (MacLab V.6.5, GE Healthcare; 300 Hz). Mixed venous oxygen saturation (SvO_2) was determined throughout each condition. Measurements were acquired in the following sequential conditions: *baseline*, resting semi-upright; *light exercise*, at a work rate eliciting an HR of 100 bpm for 8–10 min and *moderate exercise*, at a work rate eliciting an HR of 120 bpm for 8–10 min. Haemodynamic measurements were captured 1 min prior to the onset of cycling (*baseline*), and at 2 min (*early*) and 7 min (*sustained*) after the onset of each exercise condition. Wherever possible, thermodilution CO measurements were made at baseline and during the sustained phase of each exercise condition, averaged from triplicate measurements with ≤10% variation. Sonographic images were acquired at similar time points. In eight subjects, bolus thermodilution was not obtained and CO was determined from pulse-wave Doppler interrogation of the LV outflow tract.[10]

Data analysis

At each measurement, RA pressure, systolic/diastolic/mean PA pressure (PASP/PADP/mPAP) and PAWP were determined from digital recordings inspected by a single investigator blinded to participant characteristics and other haemodynamic data. All analysis intervals were confirmed to consist of at least 10 consecutive beats free from extrasystoles over two to three respiratory cycles.

Given increasing respiratory effort with exercise, PAWP was reported as the automated digital mean,[9] as well as by visual determination of the mean PAWP at end-expiration.[11] Calculated variables are reported using the end-expiratory PAWP. The digital acquisitions of PASP and PADP were inspected beat-by-beat and the digital automated mPAP measurement was recorded.

To describe a temporal pattern of PA pressure during exercise, the continuous recording of PA pressure was also analysed continuously from the onset of each exercise condition (light and moderate) until completion of the protocol. Recordings were divided into sequential 30 s intervals and the last 10 beats of each interval were analysed for PASP and PADP to determine mPAP. Through light and moderate exercise conditions, the 'peak' mPAP was identified from the 30 s interval containing the highest value for mPAP. Subsequent 30 s intervals were inspected and a 'nadir' mPAP was defined as the lowest mPAP response stable (≤1 mm Hg change) over three intervals. The time from the beginning of the condition to the 'peak' and 'nadir' intervals was also recorded. This analysis was repeated for PADP, blinded to the subject's PAWP results.

Echocardiographic image analysis was performed offline (EchoPAC 11, GE Healthcare) in accordance with current American Society of Echocardiography guidelines. Stroke volume (SV) was calculated as (LV outflow tract cross-sectional area)×(pulse-Doppler velocity–time integral), averaged over at least five beats. The LV outflow tract area was derived from the subannular aortic valve diameter in the parasternal long-axis view. CO was calculated as (SV×HR).

Statistical analysis

Statistical analyses were performed using SPSS Statistics V.20 (IBM). Normality was assessed using the Shapiro–Wilk test. Normally distributed data are presented as mean±SD; non-normally distributed data are presented as median (IQR). The agreement between the digital acquisition of the mean PAWP and the individually interpreted end-expiratory value was assessed using Bland–Altman plots. Similarly, the agreement between PAWP measurements and the PADP was also assessed (see online supplementary material). Comparisons of continuous variables between conditions were analysed using one-way repeated measures analysis of variance or Friedman's test as appropriate. Significant main effects were analysed post hoc using Bonferonni-corrected t tests or Wilcoxon signed-rank tests. An α level of 0.05 was considered significant.

RESULTS

Subject characteristics

A total of 28 subjects completed the exercise study. Subject characteristics are presented in table 1. Echocardiographic data indicate that subjects were within normal ranges for LV size and function. Haemodynamic measurements during supine rest were within acceptable normal limits (see online supplementary e-Table 1).[5]

Table 1 Subject characteristics

General	
Sex (M/F)	16 /12
Age (years)	55±6
Height (m)	1.7±0.9
Mass (kg)	73±13
BSA (m^2)	1.8±0.2
BMI (kg/m^2)	25.1±3.3
Resting HR (bpm)	61±8
HgB (g/L)	137±13
Echocardiography	
LV IDd (cm)	4.2±0.5
LV IDs (cm)	2.9±0.3
LV IVSd (cm)	0.9±0.2
LA ESD (cm)	3.0±0.3
LV mass index (g/m^2)	60±18
Ejection fraction (%)	59±4
E:A ratio	1.1±0.2
IVRT	90±7

Mean±SD.
BMI, body mass index; BSA, body surface area; E:A ratio, ratio of early to late mitral inflow velocity; ESD, end-systolic dimension; HgB, haemoglobin; HR, heart rate; IDd, internal dimension at end-diastole; IDs, internal dimension at end-systole; IVRT, isovolumetric relaxation time; IVSd, interventricular septum dimension; LA, left atrium; LV, left ventricle; M/F, male/female.

Haemodynamic responses to exercise study protocol

Exercise haemodynamic data are presented in table 2. By design, at early-light exercise, HR increased to 100 (5) bpm, remaining stable at sustained-light exercise (43±18 W). CO was determined using thermodilution in 20 subjects, and by Doppler echocardiography in eight subjects. CO increased at sustained-light exercise compared with baseline. With escalation of work rate, HR increased to 122 (4) bpm at early-moderate exercise, remaining stable at sustained-moderate exercise (70 ±26 W). CO increased further at sustained-moderate exercise compared with baseline and light exercise. Systemic systolic and mean blood pressure increased with each successive exercise stage. The SvO_2 decreased at early-light and remained stable at sustained-light exercise. Similarly, SvO_2 decreased again with early-moderate and remained stable at sustained-moderate exercise.

The changes in PAWP, PASP, PADP and mPAP are illustrated in figure 1 and the individual PAWP responses to light and moderate exercise are illustrated in figure 2. A consistent pattern was observed in the PAWP and PA pressure responses to the exercise protocol. PAWP at rest was 11±3 mm Hg and increased at early-light exercise. At the sustained-light exercise condition, PAWP declined significantly, while remaining elevated above baseline. With the increase in work rate, at early-moderate exercise, PAWP increased again but did not exceed the values observed at early-light exercise, then declined again. PASP, PADP and mPAP demonstrated a similar pattern, increasing significantly at early-light exercise and declining at sustained-light exercise, subsequently increasing at early-moderate exercise and declining at sustained-moderate exercise.

Temporal variability of pulmonary pressures

The continuous recording of PA pressures allowed increased temporal precision of the analysis at each work rate (table 3), describing the early increase and decay of pressures in detail. We examined both mPAP and PADP, as a potential surrogate of the PAWP, considering the small bias between PAWP and PADP at the work rates studied (see online supplementary material). This analysis demonstrated that at both light and moderate exercise, peak mPAP was similar though slightly higher than the value measured at 2 min of the condition. The actual peak mPAP occurred at 180 (30) s after exercise onset, with the nadir value measured at 420 (30) s. After exercise intensity was increased at moderate exercise, peak mPAP was reached at 120 (60) s. Peak PADP was measured at 135 (90) s after light exercise onset, with the nadir value at 420 (30) s. After exercise intensity was increased at moderate exercise, peak PADP was reached at 120 (53) s.

DISCUSSION

The study of invasively measured haemodynamics during exercise in humans extends back over 60 years. Recent investigations have identified excessive elevations of mPAP or PAWP during symptom-limited exercise testing as a pathophysiological response indicative of more severe left-heart disease[3] or latent HFpEF.[4 12] However, recent reviews[5 13] have pointed to an incomplete understanding of normal physiology.[14] In two systematic reviews, Kovacs *et al*[5] observed marked elevations in mPAP during 'slight' exercise in healthy adults aged >50 years compared with aged <50 years; these investigators further documented in older adults that initial increases in total pulmonary vascular resistance during exercise appeared to attenuate with sustained exercise duration.[6] Earlier studies from the 1950s made similar but more temporally detailed observations of the time course of PA pressure attenuation after initial elevations with exercise onset.[7 8] These studies were limited by relatively small sample sizes (<10) and did not report PAWP. Although PAWP and PA pressures are understood to be closely linked in the absence of pulmonary vascular disease,[12 15] the

Table 2 Exercise haemodynamic data

		Light		Moderate		
	Baseline	Early	Sustained	Early	Sustained	ANOVA
HR (bpm)	64 (11)	100 (5)*	103 (4)*	122 (4)*,‡,¶¶	122 (3)*,‡,¶¶	<0.001
CO (L/min)	4.8±0.8	–	9.5±2.2*	–	11.1±2.8 *,¶¶	<0.001
SV (mL)	77±17	–	93±22*	–	92±24*	<0.001
SvO_2 (%)	75±3	50±7*	53±6*	45±9*,‡,¶¶	48±6*,¶¶	<0.001
SBP (mm Hg)	128±14	149±11*	154±14*	167±15*,‡,¶¶	168±16*,‡,¶¶	<0.001
DBP (mm Hg)	80±8	83±9	85±10	83±10	80±8	0.028
MAP (mm Hg)	96±9	105±9*	108±10*	111±9*,‡	110±8*,‡	<0.001
RAP (mm Hg)	6±3	9±3*	7±3*,‡	8±3*,‡,¶	6±3 ‡,§,¶¶	<0.001
mPAP (mmHg)	17±3	30±5*	27±5*,‡	30±6*,¶¶	25±6 ‡,§,¶¶	<0.001
PASP (mm Hg)	25±4	40±7*	39±8*	42±8*,¶¶	36±7*,†,§,¶	<0.001
PADP (mm Hg)	10±3	19±4*	16±4*,‡	19±5*,¶¶	15±4*,‡,§,¶	<0.001
PAWP (EE)	11±3	22±5*	17±5*,‡	20±6 *,¶¶	15±5 *,‡,§,¶¶	<0.001
PAWP (Dig)	10±3	20±5*	15±5*,‡	16±5 *,‡	12±5 ‡,§,¶¶	<0.001

Mean±SD or median (IQR).
*p<0.01 vs baseline.
†p<0.05 vs early-light.
‡ p<0.01 vs early-light.
§p<0.01 vs early-moderate.
¶p<0.05 vs sustained-light.
¶¶p<0.01 vs sustained-light.
bpm, beats per minute; CO, cardiac output; EE, end-expiratory; HR, heart rate; MAP, mean arterial pressure; mPAP, mean pulmonary artery pressure; PASP/PADP, pulmonary artery systolic/diastolic pressure; PAWP, pulmonary artery wedge pressure; RAP, right atrial pressure; SBP/DBP, systolic/diastolic blood pressure; SV, stroke volume; SvO_2, mixed venous oxygen saturation.

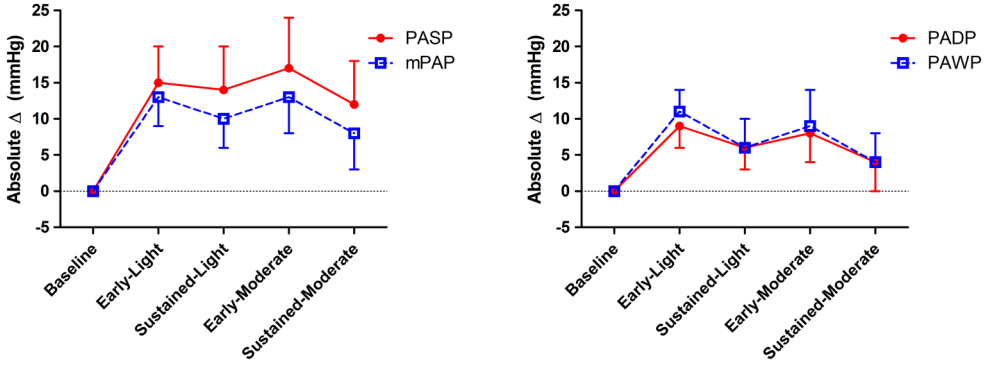

Figure 1 Absolute changes in pulmonary and pulmonary artery wedge pressures with exercise compared with baseline: mPAP and PASP (left), PAWP and PADP (right). See table 2 for significance levels. The changes in pulmonary and pulmonary artery wedge pressures exhibited a similar pattern at each exercise intensity between early and sustained phases. Data are presented as mean±SD. mPAP, mean pulmonary artery pressure; PASP, pulmonary artery systolic pressure; PAWP, pulmonary artery wedge pressure; PADP, pulmonary artery diastolic pressure.

literature to date includes a relatively small pool of exercise haemodynamic data from healthy non-dyspnoeic adults, particularly >50 years, and even fewer data on the response of the PAWP to exercise.

Accordingly, we performed a prospective, detailed study of the central haemodynamic response to sustained submaximal exercise in healthy, non-dyspnoeic, older individuals. Our key findings are that (1) the range of the PAWP and mPAP responses to 'slight' or 'early' exercise are broad and often exceed 20 and 30 mm Hg in health, respectively, and (2) the responses of both PAWP and PA pressure are time-variant during sustained submaximal exercise, decaying significantly over a period of minutes. Our observations reconcile with those of Kovacs *et al*,[5 6] and implicate the upstream transmission of changes in PAWP as a primary determinant of the temporal variation of the PA haemodynamic response to exercise. Collectively, these findings demonstrate that, in health, acute cardiovascular adaptations even to low-level submaximal exercise attenuate increases in PAWP in the face of sustained increases in CO. This adaptation may be fundamental in limiting the peak PAWP and PA pressures reached, despite a high CO during exercise. Interestingly, while the majority of our healthy study group demonstrated the phenotype of initial pressure rise followed by decay, a few did not. We speculate that such a response may represent subclinical abnormalities of LV diastolic adaptation, analogous to sonographic evidence of diastolic dysfunction identified in otherwise healthy older subjects.[16] Whether the apparent transient early peak in pressures in older adults contributes to effort intolerance at the initiation of exercise is unclear; however, our findings may provide additional support for the recognised benefits of warming-up prior to exertion.[17]

The net result of the haemodynamic behaviour observed was that even marked initial increases in PAWP and PA pressures were not sustained throughout exercise in healthy older subjects. Early increases in pressure have been attributed in part to an initial mobilisation of venous return,[18] driven by sympathetic activation and the activity of the skeletal muscle pump at the onset of exercise.[19] The mechanisms by which PAWP and mPAP subsequently decayed during sustained exercise were not elucidated in this study, but a time-varying accommodation via augmented LV diastolic function, such as enhanced relaxation and early diastolic suction,[20] may contribute. The current study recorded a measurable interval over which both PAWP and PA pressures declined, suggesting there may be a delay in recruitment of LV diastolic reserve[21] in response to exercise within this age group.

PA catheterisation is performed in select centres for the clinical evaluation of unexplained dyspnoea.[3 12] A growing number

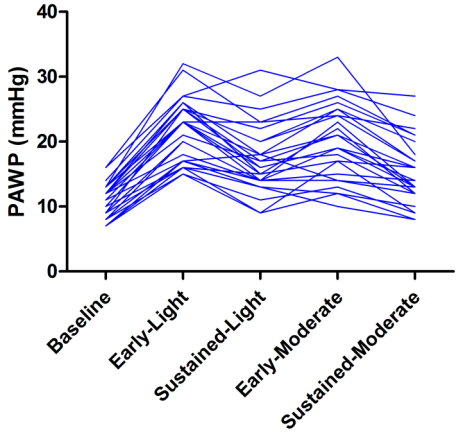

Figure 2 Individual changes in pulmonary artery wedge pressure during exercise. The overall trend was an increase in PAWP from baseline to early-light measurements, with a subsequent decay in pressure at sustained-light measurements. At early-moderate exercise, individual PAWP increased or remained relatively stable, with subsequent further decay in PAWP at sustained-moderate exercise. PAWP, pulmonary artery wedge pressure.

Table 3 Time to peak and nadir mean and diastolic pulmonary artery pressures during light and moderate exercise

		Light exercise		Moderate exercise	
	Baseline	Peak	Nadir	Peak	Nadir
mPAP (mm Hg)	17±3	32±5*	27±5*,‡	31±6*	25±5*,§,¶¶
Time interval (s)	–	180 (30)	420 (30)	120 (60)	390 (83)
PADP (mm Hg)	10±2	21±4*	16±4*,‡	20±5*	15±4*,§,¶
Time interval (s)	–	135 (90)	420 (30)	120 (53)	375 (120)

Mean±SD or median (IQR).
*p<0.01 vs baseline.
‡p<0.01 vs light peak.
§p<0.01 vs moderate peak.
¶p<0.05 vs light nadir.
¶¶p<0.01 vs light nadir.
mPAP, mean pulmonary artery pressure; PADP, pulmonary artery diastolic pressure.

of studies have demonstrated the adverse prognostic implications of 'exaggerated' exercise-associated increases in PAWP.[3 4 12] When resting haemodynamics are normal, exaggerated PAWP responses to exercise are thought to be indicative of latent HFpEF. The current study addresses the relative absence of normative comparison data and yields novel insights that should impact the conduct and diagnostic interpretation of haemodynamic exercise testing. Our data support the contention that in health, increases in PAWP and mPAP are ultimately limited in response to exercise. In previous studies, exercise intensity was ramped or escalated progressively in short intervals with important variability in total exercise duration. Measurements of mPAP and PAWP then were typically reported at peak exercise.[22] Our findings demonstrate that when submaximal exercise is sustained over a period of minutes, PAWP and mPAP decline after the initial rise at onset. As such, the lowest PAWP and mPAP after exercise onset occurred with sustained moderate exertion, when CO was at its highest. An important corollary of this observation is that the highest PAWP and mPAP do not necessarily occur at peak work rate or CO achieved, and reported values of both are dependent on the nature of the exercise stress used and the timing of haemodynamic measurements. Particularly in subjects aged >50 years,[5] early elevation PA pressures and PAWP are therefore not necessarily indicative of disease. Such knowledge should refine the timing of measurements during exercise protocols to prevent false positives and overdiagnosis of pathologic responses.

Our data highlight the importance of approaching haemodynamic exercise interventions systematically, with the ability to measure work rate and duration in addition to pressure and CO. For subjects with limited exercise tolerance, submaximal exercise testing may offer an alternative diagnostic probe based on acquisition of multiple haemodynamic data points to establish patterns of response. Compared with single-point measurements obtained at peak exertion, submaximal testing may lessen the impact of measurement artefacts and mitigate the effects of poor exercise capacity of non-cardiovascular aetiology. Further examination regarding the upper limits of these responses from a large cohort of healthy humans stratified by age and sex would be required.

There were still limitations to our methods that merit discussion. Haemodynamic responses were not examined at peak, fatigue-limited exertion. Submaximal exercise intensities were selected as to be sustainable by all subjects to minimise variability. Submaximal exercise was also employed given the well-understood frequency response limitations of fluid-filled catheters, and analysis of haemodynamic recordings during exercise can be further confounded by both motion and respiratory artefact. Multiple CO measurements by thermodilution in triplicate were not timed feasibly to allow repeated measures within an exercise stage, nor did we employ expired gas analysis for direct Fick analysis.

CONCLUSIONS

This study advances our understanding of the haemodynamic response to submaximal exercise in healthy, older adults. The range of PAWP responses to submaximal exercise is broad in health, but also time-variant. PAWP may routinely exceed 20 mm Hg early in exercise, but decline significantly within minutes. Initial increases in PA pressures may not reflect abnormal cardiopulmonary physiology.

Key messages

What is already known on this subject?
The pulmonary artery wedge pressure (PAWP) and the mean pulmonary artery pressure (mPAP) responses to exercise have garnered increasing attention as a diagnostic modality for patients limited by dyspnoea. However, the paucity of normative data makes the identification of abnormal responses challenging.

What might this study add?
Healthy older adults may demonstrate marked initial increases in PAWP and mPAP, routinely exceeding 20 and 30 mm Hg, respectively. However, these responses are time-variant and normalise as exercise continues.

How might this impact on clinical practice?
This study should improve the interpretation of the invasive haemodynamic exercise test. Understanding the time course of PAWP and mPAP responses will prevent inappropriate overdiagnosis of latent haemodynamic abnormalities in older adults.

Correction notice Since this paper was published some of the units in table 1 have been updated.

Acknowledgements We thank Joan Persaud, Dr Sarah Armstrong, Dr John Dimitry and the research staff of the Mecklinger Family and Posluns Family Cardiac Catheterisation Research Lab for their support.

Contributors SPW and SE contributed to study design, data collection and analysis, writing and provided revision and final approval of the manuscript. TG, FCF, AC and WC contributed to data collection, and revision and final approval of the manuscript. ZS, JTG and JMG contributed to the study design, supervision, interpretation of results and provided revision and final approval of the manuscript. SM contributed to the study design, supervision, data collection, interpretation of results, writing and provided revision and final approval of the manuscript.

Funding SPW Ontario Graduate Scholarship. SM, Heart and Stroke Foundation of Ontario Grant-in-aid (no. T7336).

Competing interests None declared.

Ethics approval Mount Sinai Hospital Research Ethics Board.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1 Fletcher GF, Ades PA, Kligfield P, *et al*. Exercise standards for testing and training a scientific statement from the American Heart Association. *Circulation* 2013;128:873–934.
2 Andersen MJ, Olson TP, Melenovsky V, *et al*. Differential hemodynamic effects of exercise and volume expansion in people with and without heart failure. *Circ Heart Fail* 2015;8:41–8.
3 Lewis GD, Murphy RM, Shah RV, *et al*. Pulmonary vascular response patterns during exercise in left ventricular systolic dysfunction predict exercise capacity and outcomes. *Circ Heart Fail* 2011;4:276–85.
4 Dorfs S, Zeh W, Hochholzer W, *et al*. Pulmonary capillary wedge pressure during exercise and long-term mortality in patients with suspected heart failure with preserved ejection fraction. *Eur Heart J* 2014;35:3103–12.
5 Kovacs G, Berghold A, Scheidl S, *et al*. Pulmonary arterial pressure during rest and exercise in healthy subjects: a systematic review. *Eur Respir J* 2009;34:888–94.
6 Kovacs G, Olschewski A, Berghold A, *et al*. Pulmonary vascular resistances during exercise in normal subjects: a systematic review. *Eur Respir J* 2012;39:319–28.
7 Sancetta SM, Rakita L. Response of pulmonary artery pressure and total pulmonary resistance of untrained, convalescent man to prolonged mild steady state exercise. *J Clin Invest* 1957;36:1138.
8 Slonim NB, Ravin A, Balchum OJ, *et al*. The effect of mild exercise in the supine position on the pulmonary arterial pressure of five normal human subjects. *J Clin Invest* 1954;33:1022–30.
9 Kovacs G, Avian A, Pienn M, *et al*. Reading pulmonary vascular pressure tracings. How to handle the problems of zero leveling and respiratory swings. *Am J Respir Crit Care Med* 2014;190:252–7.

10 Quiñones MA, Otto CM, Stoddard M, *et al*. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. *J Am Soc Echocardiogr* 2002;15:167–84.
11 Ryan JJ, Rich JD, Thiruvoipati T, *et al*. Current practice for determining pulmonary capillary wedge pressure predisposes to serious errors in the classification of patients with pulmonary hypertension. *Am Heart J* 2012;163:589–94.
12 Borlaug BA, Nishimura RA, Sorajja P, *et al*. Exercise hemodynamics enhance diagnosis of early heart failure with preserved ejection fraction. *Circ Heart Fail* 2010;3:588–95.
13 Naeije R, Vanderpool R, Dhakal BP, *et al*. Exercise-induced pulmonary hypertension: physiological basis and methodological concerns. *Am J Respir Crit Care Med* 2013;187:576–83.
14 West JB. Left ventricular filling pressures during exercise. *CHEST J* 1998;113:1695–7.
15 Reeves JT, Taylor AE. Pulmonary hemodynamics and fluid exchange in the lungs during exercise. Handbook of Physiology. Exercise: Regulation and Integration of Multiple Systems. Bethesda, MD. *Am Physiol Soc* 1996;585–613.
16 Fischer M, Baessler A, Hense HW, *et al*. Prevalence of left ventricular diastolic dysfunction in the community. Results from a Doppler echocardiographic-based survey of a population sample. *Eur Heart J* 2003;24:320–8.
17 Fradkin AJ, Zazryn TR, Smoliga JM. Effects of warming-up on physical performance: a systematic review with meta-analysis. *J Strength Cond Res* 2010;24:140–8.
18 Naeije R, Chesler N. Pulmonary circulation at exercise. *Compr Physiol* 2012;2:711–41.
19 Notarius CF, Magder S. Central venous pressure during exercise: role of muscle pump. *Can J Physiol Pharmacol* 1996;74:647–51.
20 Little WC. Diastolic dysfunction beyond distensibility adverse effects of ventricular dilatation. *Circulation* 2005;112:2888–90.
21 Borlaug BA, Jaber WA, Ommen SR, *et al*. Diastolic relaxation and compliance reserve during dynamic exercise in heart failure with preserved ejection fraction. *Heart* 2011;97:964–9.
22 Maron BA, Cockrill BA, Waxman AB, *et al*. The invasive cardiopulmonary exercise test. *Circulation* 2013;127:1157–64.

Heart

The pulmonary artery wedge pressure response to sustained exercise is time-variant in healthy adults

Stephen P Wright, Sam Esfandiari, Taylor Gray, Felipe C Fuchs, Anjala Chelvanathan, William Chan, Zion Sasson, John T Granton, Jack M Goodman and Susanna Mak

Heart 2016 102: 438-443 originally published online January 13, 2016
doi: 10.1136/heartjnl-2015-308592