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# Evidence of cardiac functional reserve upon exhaustion during incremental exercise to determine $\dot{V}O_{2\max}$

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## ABSTRACT

**Background** There remains considerable debate regarding the limiting factor(s) for maximal oxygen uptake ( $\dot{V}O_{2\max}$ ). Previous studies have shown that the central circulation can be the primary limiting factor for  $\dot{V}O_{2\max}$  and that cardiac work increases beyond  $\dot{V}O_{2\max}$ .

**Aim** We sought to evaluate whether the work of the heart limits  $\dot{V}O_{2\max}$  during upright incremental cycle exercise to exhaustion.

**Methods** Eight trained men completed two incremental exercise trials, each terminating with exercise at two different rates of work eliciting  $\dot{V}O_{2\max}$  (MAX and SUPRAMAX). During each exercise trial we continuously recorded cardiac output using pulse-contour analysis calibrated with a lithium dilution method. Intra-arterial pressure was recorded from the radial artery while pulmonary gas exchange was measured continuously for an assessment of oxygen uptake.

**Results** The workload during SUPRAMAX (mean $\pm$ SD: 346.5 $\pm$ 43.2 W) was 10% greater than that achieved during MAX (315 $\pm$ 39.3 W). There was no significant difference between MAX and SUPRAMAX for Q (28.7 vs 29.4 L/min) or  $\dot{V}O_2$  (4.3 vs 4.3 L/min). Mean arterial pressure was significantly higher during SUPRAMAX, corresponding to a higher cardiac power output (8.1 vs 8.5 W;  $p < 0.06$ ).

**Conclusions** Despite similar  $\dot{V}O_2$  and Q, the greater cardiac work during SUPRAMAX supports the view that the heart is working submaximally at exhaustion during an incremental exercise test (MAX).

## INTRODUCTION

Maximal oxygen uptake ( $\dot{V}O_{2\max}$ ) is arguably the most researched parameter in exercise physiology. Its relationship with performance has been recognised since the pioneering work of Hill and Lupton<sup>1</sup> who concluded that oxygen uptake ( $\dot{V}O_2$ ) reached a maximum level during peak physical work, since interpreted as a plateau in the  $\dot{V}O_2$  response. Significant debate has surrounded the plateau phenomenon<sup>2</sup> although the concept of a truly maximal  $\dot{V}O_2$ , established by supramaximal testing to verify that obtained from incremental exercise, is generally accepted.<sup>3–5</sup> However, there remains considerable debate regarding the factor(s) limiting  $\dot{V}O_{2\max}$ .<sup>6–9</sup> Broadly, the most commonly suggested mechanisms are that either a circulatory (cardiac) limitation or a neural (central) regulation determines the  $\dot{V}O_{2\max}$ .

It is established that skeletal muscle perfusion capacity exceeds the pumping capacity of the heart.<sup>10–11</sup> Secher *et al*<sup>12</sup> showed a reduction in leg blood flow when arm exercise is superimposed on maximal two-leg exercise, supporting the theory

that the capacity to supply  $O_2$  during maximal exercise is limited thereby constraining oxidative metabolism and, consequently, exercise capacity. Recently, a plateau in cardiac output (Q) close to exhaustion during both incremental and constant load maximal exercise<sup>13–14</sup> has been demonstrated. This has been interpreted as further evidence that the circulation limits  $\dot{V}O_{2\max}$ .

Opponents to the cardiac limitation theory propose that skeletal muscle recruitment is regulated through a central, neurally mediated mechanism during exhaustive exercise.<sup>8–15–18</sup> Proponents of this theory argue that this ensures myocardial ischaemia is avoided by moderating the demand placed on the heart, thereby preventing the attainment of an absolute maximum. This theory is supported by the findings that, in trained athletes, Q continues to increase linearly up until exhaustion without a plateau.<sup>19–21</sup>

Cardiac power output (CPO) is a measurement of cardiac function that incorporates both flow and pressure domains of the cardiovascular system and is measured as the product of Q and mean arterial pressure.<sup>22</sup> By measurement of CPO during maximal and supramaximal exercise, it becomes feasible to study the heart's ability to maintain circulation in the presence of increasing arterial pressure. During exercise at  $\dot{V}O_{2\max}$ , the measurement of CPO allows the exercise physiologist to determine whether the work of the heart continues to increase at the exercise intensity resulting in exhaustion. Should an increase in CPO be observed during exercise above that achieved at  $\dot{V}O_{2\max}$ , one might make one of two conclusions; that the heart is working submaximally during exercise at  $\dot{V}O_{2\max}$ <sup>8</sup> or, alternatively, that the circulation is absolutely maximal during exercise at  $\dot{V}O_{2\max}$  despite an increase in cardiac work.<sup>23</sup>

To differentiate between the theories explaining the limitation to maximal exercise, Brink-Elfegou *et al*<sup>23</sup> designed an experiment in which two levels (100% and 110%  $\dot{V}O_{2\max}$ ) of whole-body exercise were performed.  $\dot{V}O_2$  and Q were similar between workloads but blood pressure was significantly higher during exercise at 110%  $\dot{V}O_{2\max}$ , resulting in increased cardiac work.<sup>22</sup> The authors concluded that the greater cardiac work during supramaximal exercise indicates the absence of a central 'governor'. This conclusion was questioned by Noakes and Marino<sup>8</sup> who argued that these findings show the heart to be working submaximally at  $\dot{V}O_{2\max}$  and that the higher work rate achieved during a supramaximal bout indicates dissociation between Q and work rate, disproving the theory that Q regulates peak work rate and, consequently,  $\dot{V}O_{2\max}$ .

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Despite the extensive discussion on cardiac function and limitations during maximal exercise, CPO has not been measured continuously during maximal and supramaximal exercise, even in studies in which a plateau in  $\text{VO}_2^3$  and  $\text{Q}^{13-14}$  have been observed. The aims of this study were to evaluate the work of the heart during cycling exercise at maximal and supramaximal workloads. We hypothesised that the greater exercise workload would induce a greater circulatory and myocardial work demand, thus showing that the heart works submaximally at  $\text{VO}_{2\text{max}}$ , confirming the finding of Brink-Elfegoun *et al.*<sup>23</sup>

## MATERIALS AND METHODS

### Subjects

Eight recreationally trained male cyclists, age  $40.5 \pm 9.2$  years, body mass  $80.5 \pm 10.9$  kg, height  $178.8 \pm 4.7$  cm,  $\text{VO}_{2\text{max}}$   $53.7 \pm 6.5$  ml/kg/min, volunteered to participate in the study. All participants were training for  $>5$  h/week. Exclusion criteria for participation included a history of cardiopulmonary disease, lithium allergy and current therapy with lithium or muscle relaxants. The protocol was explained to the participants before they gave written informed consent. The research ethics committees at Northumbria University and Kingston University approved the study. All procedures were performed in accordance with national<sup>24</sup> and international (Declaration of Helsinki, 1964) guidelines.

### Exercise protocol

Participants reported to the laboratory on a single occasion after abstaining from caffeine, alcohol and heavy exercise in the preceding 24 h. Participants performed two exercise trials during their visit, each separated by 1 h. Each trial, consisting of exercise conducted on an electromagnetically braked cycle ergometer (Velotron, Racermate Inc, Seattle, WA, USA), took place within an air-conditioned laboratory controlled to  $22\text{--}23^\circ\text{C}$ . The cycle ergometer was set up to each participant's specifications. Participants were allowed to self-select their cadence while remaining seated throughout each trial. The investigators provided consistent verbal encouragement throughout.

The first exercise trial (T1) consisted of an incremental protocol to exhaustion starting with 6 min at a power output of 120 W, increasing by 30 W every 3 min until the participant reached volitional exhaustion (MAX). Ventilatory threshold (VT) was determined according to the method of Beaver *et al.*,<sup>25</sup> the workload for the second trial (T2) was derived from VT. During T2, participants each completed four exercise stages, each being separated by a 2 min recovery period at 100W. The first three stages consisted of 6 min at 120 W followed by 8 min each at 80% of VT, and 30% of the difference between power at VT and power at MAX. The final stage was performed at a power output 10% greater than that achieved during T1, until volitional fatigue (SUPRAMAX). The structure of T2 was designed so that the total exercise time was approximately similar to T1.

### Measurements

Throughout each trial, pulmonary gas exchange was recorded continuously with an online gas analyser (Oxycon Pro, Jaeger, Germany). Participants wore a close-fitting facemask connected to a tripe-V sensor (Jaeger, Germany) consisting of a flow turbine and gas sampling tube. Prior to each trial, the gas analyser was calibrated using gas of a known composition (16%  $\text{O}_2$ ; 4%  $\text{CO}_2$ ; balance nitrogen). Volume calibration of the flow turbine was performed using a 3 l syringe over a range of flow rates.

Q was assessed continuously throughout each exercise by pulse contour analysis calibrated by an incorporated lithium

dilution method (LiDCO, Cambridge, UK). The LiDCO device permits continuous haemodynamic recording by analysis of the radial artery pressure waveform (PulseCO, Cambridge, UK), calibrated by lithium dilution (LiDCO). Lithium dilution shows good agreement with thermodilution,<sup>26-27</sup> while continuous measurements have reported clinically acceptable accuracy and precision in critically ill patients.<sup>26-28-29</sup> During exercise, the LiDCO device compares favourably with direct Fick measurements during constant load and incremental exercise<sup>30</sup> and performs well during high-intensity exercise in trained cyclists.<sup>31</sup>

Prior to T1, a 21-gauge cannula was placed into a peripheral vein mid-way between the wrist and elbow of the right arm. A 20-gauge arterial cannula was then placed into the radial artery of the left arm under local anaesthesia (2% Lidocaine) and connected to an intensive care unit monitor (Hewlett Packard, Palo Alto, CA, USA) via a disposable pressure transducer (Philips M1567A, Philips, Germany), zeroed to ambient pressure. The pressure monitor provides continuous arterial pressure waveform data to the LiDCO monitor. The LiDCO system calculates a nominal stroke volume from a pressure-volume transformation of the arterial pressure waveform, which is then converted to absolute stroke volume using the incorporated lithium dilution method.

Lithium dilution calibration involved the administration of a lithium chloride bolus (0.3–0.45 mM) into the peripheral vein. The bolus was immediately followed by a 20 ml saline flush. A lithium dilution curve was subsequently derived by drawing arterial blood past a lithium sensor connected to the arterial cannula, at a constant flow rate using a flow pump. Q was calculated according to the following equation:<sup>32</sup>

$$Q = [\text{LiCl dose (mM)} \times 60] / [\text{area under dilution curve (mM/L/s)} \times (1 - \text{PCV})]$$

where  $\text{PCV} = \text{haemoglobin (g/dl)} / 33$

Heart rate (HR) was calculated by the duration between subsequent pressure waveforms. Arterial pressure was recorded directly by the LiDCO monitor from the arterial pressure trace. LiDCO calibrations were performed during the SUPRAMAX workload of T2 and applied to all Q data. Calibration procedures began 1 min into the SUPRAMAX stage. The pulse contour analysis data required for calibration with the lithium dilution method was obtained by interpolation of the mean values in the 10 s preceding and succeeding the calibration period to ensure that all data were time-matched. This calibration factor was applied retrospectively to all data obtained during the study.

CPO and rate-pressure product (RPP) were calculated according to the following equations:<sup>22</sup>

$$\text{CPO(W)} = Q \times \text{MAP} \times k$$

where  $k = 2.22 \times 10^{-3}$  and  $\text{MAP} = \text{mean arterial pressure (mm Hg)}$ .<sup>33</sup>

$$\text{RPP (beats/min} \times \text{mm Hg)} = \text{HR} \times \text{SBP}$$

where  $\text{SBP} = \text{systolic blood pressure (mm Hg)}$

$$\text{MAP (mm Hg)} = \text{DBP} + 1/3(\text{SBP} - \text{DBP})$$

where  $\text{DBP} = \text{diastolic blood pressure (mm Hg)}$ .

## Data analysis

Haemodynamic and pulmonary gas exchange data were averaged over 10 s epochs throughout both T1 and T2. Data for MAX and SUPRAMAX were taken at the time point of maximal Q. Data analysis was performed with GraphPad Prism V.5. A paired t test was performed to compare MAX and SUPRAMAX data. Statistical significance was determined at  $p < 0.05$ . All data are presented as means  $\pm$  SD unless otherwise stated.

## RESULTS

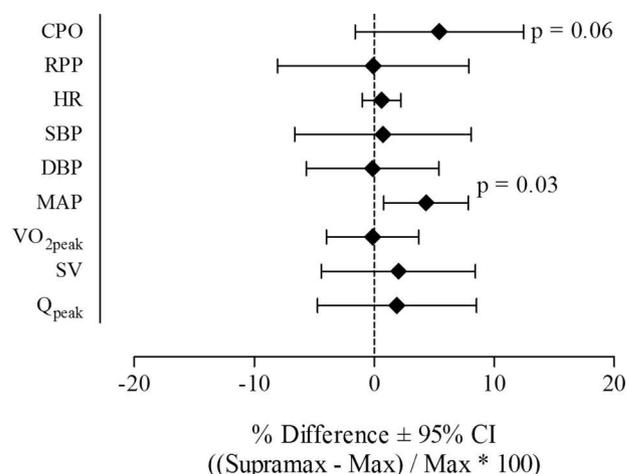
The workloads for MAX and SUPRAMAX were  $315 \pm 39.3$  W and  $346.5 \pm 43.2$  W, respectively. Time to exhaustion was not significantly different between MAX and SUPRAMAX trials ( $176 \pm 12.6$  vs  $170 \pm 40.7$  s).

Peak exercise data are shown in table 1. There was no significant difference between MAX and SUPRAMAX (figure 1) for Q ( $28.7$  vs  $29.4$  l/min, 95% CI  $-2.6$  to  $1.4$ ;  $p = 0.48$ ),  $VO_2$  ( $4.26$  vs  $4.26$  l/min, 95% CI  $-0.18$  to  $0.17$ ;  $p = 0.96$ ), stroke volume ( $154.1$  vs  $157.3$  ml, 95% CI  $-13.5$  to  $7.1$ ;  $p = 0.49$ ) or HR ( $188.9$  vs  $190.1$  beats/min, 95% CI  $-4.3$  to  $1.8$ ;  $p = 0.36$ ), respectively. MAP was significantly higher at peak exercise during the SUPRAMAX stage ( $129.1$  vs  $134.6$  mm Hg, 95% CI  $-10.1$  to  $-0.9$ ;  $p = 0.03$ ), although both systolic and diastolic blood pressure remained unchanged between workloads. In addition, no significant differences were observed for Q, SV, HR, MAP or  $VO_2$  between peak values and exhaustion during either exercise stage. Both Q (Q/W;  $91.6 \pm 18.4$  vs  $85.3 \pm 21.4$  ml/W; 95% CI  $1.24$  to  $11.31$ ;  $p = 0.02$ ) and  $VO_2$  ( $VO_2$ /W;  $13.5 \pm 1.1$  vs  $12.3 \pm 1.5$  ml/W; 95% CI  $0.71$  to  $1.69$ ;  $p = 0.0007$ ) expressed per unit of power output, were significantly greater during the MAX stage.

The significantly greater MAP at the SUPRAMAX workload led to a tendency for a greater CPO ( $8.1$  vs  $8.5$  W, 95% CI  $-0.92$  to  $0.02$ ), although this did not reach statistical significance ( $p = 0.06$ ). RPP was not significantly different between MAX and SUPRAMAX ( $41, 625$  vs  $41, 546$  beats/min/mm Hg, 95% CI  $-3222$  to  $3378$ ;  $p = 0.96$ ).

## DISCUSSION

The most significant finding from this study was that although Q was similar, the work performed by the heart, assessed by CPO, was increased during supramaximal exercise compared with maximal exercise due to higher mean arterial pressure. Although this did not reach statistical significance, the 95% CIs



**Figure 1** Forrest plot displaying mean percentage differences ( $\pm 95\%$  CI) of measurements between SUPRAMAX and MAX exercise. All data are time aligned to measurement of peak cardiac output.

indicate a substantial increase that is likely to be of biological significance. This confirms previous findings<sup>23</sup> during combined arm and leg exercise. These findings indicate an increase in the work performed by the heart during supramaximal exercise with a greater myocardial  $VO_2$ .<sup>22</sup>

The observation that, at maximal exercise, further elevations in workload occur without any additional increase in Q and  $VO_2$  suggests that, in health, the attainment of  $VO_{2max}$  is accompanied by an attenuated increase in systemic blood flow, as frequently argued.<sup>6 11 14 34–36</sup> It is known that the maximally vasodilated skeletal muscle in humans can accept a greater blood flow than the heart can supply (ie, greater than  $Q_{max}$ ).<sup>10–12</sup> Furthermore, a number of experimental manipulations of  $O_2$  delivery have resulted in the reduction of  $VO_{2max}$ ,<sup>35 37 38</sup> supporting the theory that  $O_2$  delivery constrains  $VO_{2max}$  during exercise. However, the findings that the heart is able to increase its work output beyond that achieved during  $VO_{2max}$  testing, as previously shown,<sup>23</sup> confirms that typical incremental exercise to  $VO_{2max}$ , as observed during the MAX trial, terminates with some degree of cardiac functional reserve.

Our findings of a similar  $VO_{2max}$  between MAX and SUPRAMAX support the concept of a true maximal  $VO_2$  observed by a number of groups comparing maximal and supramaximal exercise<sup>3–5</sup> although alternative testing methods, such as a decremental test in which exercise intensity starts high and decreases, may yield higher  $VO_{2max}$  values.<sup>39</sup> By the same principle, the absence of any increase in Q despite a greater workload during SUPRAMAX indicates that a maximal Q is achieved at the termination of incremental and constant-load exhaustive exercise, although the Q response to alternative testing methods producing higher  $VO_{2max}$  have not been investigated. The observation that Q fails to increase at or near maximal exercise has been demonstrated previously.<sup>13 14 23 36 40–42</sup>

The theory of a central, neurally mediated limitation<sup>15</sup> predicts that the loss of homeostasis during exhaustive exercise is avoided by the actions of a centrally located ‘governor’ that limits skeletal muscle recruitment, thus reducing the likelihood of any homeostatic disturbances, including both metabolic and/or thermoregulatory regulation.<sup>17</sup> Our findings that circulation appears maximal during exercise to exhaustion do not exclude the existence of a governor within the central nervous system that anticipates significant homeostatic disturbance(s), therefore limiting any further increase in myocardial  $VO_2$  and risking the

**Table 1** Mean (SD) exercise data obtained from MAX and SUPRAMAX trials

Variable	MAX (n=8)	SUPRAMAX (n=8)
Power output (W)	315 (39.3)	346.5 (34.2)
Q (l/min)	28.7 (5.9)	29.4 (7.0)
$VO_2$ (l/min)	4.26 (0.61)	4.26 (0.7)
SV (ml)	154.1 (30.9)	157.3 (34.4)
HR (bpm)	189 (10)	190 (13)
MAP (mm Hg)	129 (11)	135 (12)
SBP (mm Hg)	222 (28)	224 (33)
DBP (mm Hg)	78 (6)	81 (8)
CPO (W)	8.05 (1.9)	8.5 (2.1)
RPP (beats/min/mm Hg)	41, 625 (4347)	41, 546 (5489)

CPO, cardiac power output; DBP, diastolic blood pressure; HR, heart rate; MAP, mean arterial pressure; RPP, rate-pressure product; SBP, systolic blood pressure; SV, stroke volume; Q, cardiac output;  $VO_2$ , oxygen uptake.

onset of myocardial ischaemia. The observation that the heart appears to be work submaximally during exercise eliciting  $\text{VO}_{2\text{max}}^{23}$  supports a central limitation theory by posing the question of why the heart does not work harder at  $\text{VO}_{2\text{max}}$  despite its apparent capacity to do so.<sup>8</sup> One interpretation is that a central regulator may limit myocardial oxygen demand by preventing additional skeletal muscle recruitment at the point of exhaustion during maximal exercise.

However, the greater workload during SUPRAMAX would require additional motor unit recruitment<sup>43 44</sup> that, in the view of the central limitation theory, should be regulated to constrain Q.<sup>8</sup> It has been argued that it remains unclear as to how a central 'governor' would terminate exercise at  $\text{VO}_{2\text{max}}$  when there is evidence that greater skeletal muscle recruitment<sup>43</sup> and workloads<sup>5</sup> are achievable in the absence of significant homeostatic disturbances or myocardial ischaemia. However, there are several points worth noting; First, the central theory proposes that exercise terminates *before* there is maximal skeletal muscle activation,<sup>17</sup> as shown elsewhere.<sup>43 45</sup> Second, a dissociation between Q and exercise power output appears during SUPRAMAX such that Q/W is significantly lower than that measured during MAX, suggestive of an uncoupling between workload and cardiovascular function. This finding confirms that Q does not determine skeletal muscle work. Finally, one should consider how supramaximal exercise as a separate effort, as conducted here and elsewhere<sup>3 5 23</sup> influences this discussion. It is plausible that the degree of 'homeostatic disturbance' differs during a separate supramaximal bout. Indeed, Mortensen *et al*,<sup>14</sup> with a similar experimental model, observed greater disturbances to blood pH, lactate and body temperature during incremental exercise to  $\text{VO}_{2\text{max}}$  as compared with constant-load supramaximal exercise. One could postulate that supramaximal exercise performed separately provides no greater metabolic/homeostatic challenge than maximal exercise performed at the end of incremental exercise, with the consequence that constant-load supramaximal exercise requires little constraint from a central 'governor' in the initial stages.

While it is agreed that a maximal  $\text{VO}_2$  exists, this study and others<sup>39</sup> suggest that neither Q nor  $\text{VO}_2$  are maximal during incremental exercise to exhaustion. Despite efforts to portray the  $\text{VO}_{2\text{max}}$  measured during incremental exercise as being limited by the circulation,<sup>44</sup> the submaximal cardiac function observed during 'maximal' exercise in this study and others<sup>23</sup> suggests that this form of exercise testing may not be a useful evaluation of exercise performance<sup>46</sup> or for the evaluation of maximal cardiac function in healthy humans.

Direct Fick and/or thermodilution are typically considered 'gold standard' methods for Q measurement during exercise. However, the technical difficulties and risk<sup>47</sup> associated with these methodologies renders them unsuitable for most exercise studies. Furthermore, previous studies employing these methods, and others, are typically only able to assess Q at one or two timepoints during maximal exercise, thus potentially recording submaximal values. Our method of assessment provides continuous measurements throughout exercise up until exhaustion,<sup>31</sup> with only minimal risk and invasiveness. Therefore, we were able to be absolutely sure that we obtained a maximal measure for Q. Lithium dilution has proven accuracy in the clinical setting in critically ill patients<sup>27 48 49</sup> patients with hyperdynamic circulation<sup>50</sup> and exercising heart failure patients.<sup>30</sup> In this study, we were able to successfully calibrate the device during the SUPRAMAX exercise stage, with this calibration factor being applied to all exercise data. Importantly, we were also able to obtain true peak Q and arterial pressure

### What are the new findings

- ▶ This study shows that cardiac power output is submaximal during an incremental cycle exercise test to exhaustion.
- ▶ Using a novel approach to measuring cardiac output during exercise, both oxygen uptake and cardiac output do not increase with a subsequent supramaximal exercise bout.
- ▶ This study supports the theory of a central governor that constrains  $\text{VO}_{2\text{max}}$  despite an apparent cardiovascular reserve upon exhaustion.

### How might it impact on clinical practice in the near future

- ▶ The potential clinical relevance of this study is that a typical incremental exercise test to determine  $\text{VO}_{2\text{max}}$  may not provide an accurate reflection of full cardiac pumping capacity.
- ▶ Clinicians and/or exercise physiologists should consider the potential use of a supramaximal exercise protocol to establish a more accurate assessment of cardiac pumping capacity.
- ▶ Additionally, this study provides evidence of a practical, continuous method for the measurement of cardiac output during exercise testing.

measurements, regardless of the timepoint at which they occurred. We believe this provides significant benefit when assessing the haemodynamic response to maximal exercise, which is typically of short duration.

Our study is not without limitations. First, we chose to perform all testing in one session for practical reasons relating to the procedures associated with Q measurement. Likewise, we did not counterbalance the order of trials. This was to allow us to ensure that the SUPRAMAX exercise trial did not impact upon data obtained from a subsequent MAX trial. Both of these limitations mirror those relevant to the Brink-Elfegoun *et al*<sup>23</sup> study therefore permitting comparisons between the two studies. Additionally, we chose upright cycling as our testing modality. Incremental cycle exercise is the common modality of maximal exercise testing for the determination of  $\text{VO}_{2\text{max}}$  and has been shown to elicit a plateau in  $\text{VO}_2$  suggestive of the true attainment of  $\text{VO}_{2\text{max}}$ . Future studies should attempt to determine the cardiovascular responses to exercise in trials where recent evidence has shown the potential for increased  $\text{VO}_2$  during alternative protocols to those used in this study.<sup>39</sup> We also acknowledge the limitations of Q measurement. We chose a method that permitted continuous measurements of Q throughout maximal exercise and therefore measurements in the period immediately preceding exhaustion. Pulse-contour analysis with lithium dilution calibration has shown close agreement with gold standard methods during exercise.<sup>30</sup> Finally, this study's small sample size increased the chances of a type II error due to insufficient statistical power. Sample size was largely dictated by the requirement to perform invasive procedures of healthy participants during strenuous exercise. Future studies attempting to address this research question should consider a statistical power

analysis to determine the required sample size to detect the differences observed during this study and others.

In conclusion, this study shows that during two levels of maximal cycling exercise, differing by a workload of 10% and eliciting identical  $\dot{V}O_{2\max}$ , cardiac work continues to increase despite Q remaining the same. These findings suggest that cycling exercise to  $\dot{V}O_{2\max}$  terminate with cardiac functional reserve, yet maximal Q.

**Contributors** All authors were involved with the planning and design of the study. AE, JS, MP and LA were responsible for data collection. All authors contributed to analysis and interpretation of the data. AE was responsible for the first draft of the manuscript, which was subsequently revised by all authors. All authors agreed the final version of the manuscript.

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## Evidence of cardiac functional reserve upon exhaustion during incremental exercise to determine $VO_2\text{max}$

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