International Journal of Sports Medicine
Thieme

Reliability and validity of a self-paced cardiopulmonary exercise test in post-MI patients

Journal:	*International Journal of Sports Medicine*
Manuscript ID	IJSM-06-2016-5715-tt.R1
Manuscript Type:	Training & Testing
Key word:	cardiology, RPE, Aerobic Capacity, Pacing
Abstract:	A self-paced peak oxygen uptake (VO2peak) test (SPV) has been shown to produce higher VO2peak values compared to standard cardiopulmonary exercise tests (sCPET), but has not been tested on any clinical population. This study aimed to assess the reliability of the SPV in a healthy population (study 1), and the validity and reliability of the SPV in post Myocardial Infarction (post-MI) patients (study 2). For study 1, twenty-five healthy participants completed three SPV's. For study 2, twenty-eight post-MI patients completed one sCPET and two SPV's. The SPV consisted of 5 x 2-min stages where participants were able to self-regulate their effort by using incremental 'clamps' in ratings of perceived exertion. The sCPET consisted of a 20 W/min ramp. Results demonstrated the SPV to have a coefficient of variation for VO2peak of 4.7% for the healthy population, and 8.2% for the post-MI patients. Limits of agreement ranged between ± 4.22-5.86 $ml \cdot kg^{-1} \cdot min^{-1}$, with the intraclass correlation coefficient ranging between 0.89-0.95. In study 2, there was a significantly higher VO2peak achieved in the SPV (23.07 ± 4.90 $ml \cdot kg^{-1} \cdot min^{-1}$) against the sCPET (21.29 ± 4.93 $ml \cdot kg^{-1} \cdot min^{-1}$). It is concluded that these results provide initial evidence that the SPV may be a safe, valid and reliable method for determining exercise capacity in post-MI patients.

Title: Reliability and validity of a self-paced cardiopulmonary exercise test in post-MI patients

Abstract

A self-paced peak oxygen uptake ($\dot{V}O_{2peak}$) test (SPV) has been shown to produce higher $\dot{V}O_{2peak}$ values compared to standard cardiopulmonary exercise tests (sCPET), but has not been tested on any clinical population. This study aimed to assess the reliability of the SPV in a healthy population (study 1), and the validity and reliability of the SPV in post Myocardial Infarction (post-MI) patients (study 2). For study 1, twenty-five healthy participants completed three SPV's. For study 2, twenty-eight post-MI patients completed one sCPET and two SPV's. The SPV consisted of 5 x 2-min stages where participants were able to self-regulate their effort by using incremental 'clamps' in ratings of perceived exertion. The sCPET consisted of a 20 W/min ramp. Results demonstrated the SPV to have a coefficient of variation for $\dot{V}O_{2peak}$ of 4.7% for the healthy population, and 8.2% for the post-MI patients. Limits of agreement ranged between ± 4.22-5.86 $ml \cdot kg^{-1} \cdot min^{-1}$, with the intraclass correlation coefficient ranging between 0.89-0.95. In study 2, there was a significantly higher $\dot{V}O_{2peak}$ achieved in the SPV (23.07 ± 4.90 $ml \cdot kg^{-1} \cdot min^{-1}$) against the sCPET (21.29 ± 4.93 $ml \cdot kg^{-1} \cdot min^{-1}$). ~~We conclude~~It is concluded that these results provide initial evidence that the SPV ~~is~~may be a safe, valid and reliable method for determining exercise capacity in post-MI patients.

Key words: cardiology, RPE, aerobic capacity, pacing

Introduction

Cardiopulmonary exercise testing (CPET) is an increasingly popular tool that allows clinicians to objectively assess the integrated response to exercise [29,48][~~27,41~~]. Moreover, CPET derived exercise tolerance and capacity have been strongly correlated with overall health status and mortality, and can therefore provide valuable diagnostic and prognostic information for various patient populations [1,12,29,39][~~1,10,27,35~~]. One of the key measures obtained from CPET is peak oxygen uptake ($\dot{V}O_{2peak}$), which is defined as the highest amount of oxygen a person can utilise during dynamic exercise [7][~~5~~]. The identification of $\dot{V}O_{2peak}$ has become a fundamental procedure when assessing cardiorespiratory fitness, monitoring exercise intensity [7][~~5~~] and when risk stratifying individuals prior to major surgical procedures [8][~~6~~]. Exercise testing soon after a Myocardial Infarction (MI) is beneficial as it can provide information on a patient's future risk of a subsequent cardiac event [15][~~13~~] and can be used in individualising exercise rehabilitation programmes [32][~~29~~].

Traditionally, CPET is completed on a stationary bike or a treadmill using a maximal incremental exercise test (MIE), whereby the intensity (speed or power output (PO)) increases by a set amount, for a given period of time, until volitional exhaustion is reached [44][~~38~~]. For optimum values to be achieved it is suggested that participants reach volitional exhaustion between 8-12 minutes [11][~~9~~]. Clinicians are therefore required to estimate the most suitable starting intensity and work rate increments to ensure test validity. This increases the risk of a test being unsuccessful due to participants either exceeding 12 minutes, or worse, not lasting long enough for $\dot{V}O_{2peak}$ to be accurately measured. There has also been

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a number of other limitations that have been brought to light regarding the general nature of the current CPET protocol [41], in particular the patient is unaware of the test duration and previous work suggests that knowledge of exercise duration can facilitate performance [33]. In addition the patient only has control over when they stop the test which adds a psychological aspect to the test i.e. low motivation [41]. Recently, a novel self-paced CPET protocol (SPV) was developed [36]~~[32]~~ to address the some of the aforementioned problems with the traditional CPET protocol. The SPV uses a closed-loop self-paced design, consisting of 5 x 2-min stages, where participants are able to regulate their work rate according to specific ~~their~~ ratings of perceived exertion (RPE). Previous studies have concluded that the SPV is able to produce significantly higher $\dot{V}O_{2peak}$ values when compared against traditional CPET protocols [3,34,36], although not all studies have found this [13,47]. In recent years the SPV protocol has raised a lot of discussion points [2,17,35,43] with some researchers criticising the test [13,17,43]. Although, there is now a body of research which supports the validity of the SPV, with all studies demonstrating it to produce at least similar $\dot{V}O_{2peak}$ values [3,13,34,36,47]. This type of test may be beneficial in clinical practice as it will reduce the risk of acquiring unusable data, this is because all patient will have the opportunity to complete the test at their own ability whilst meeting the recommended test time requirements.

A number of studies have assessed the use ~~validity~~ of the SPV in 'healthy populations' [13,34,36,47]~~[11,31,32,40]~~, however the reliability of this protocol has yet to be determined. Moreover, no research has investigated ~~the reliability or validity of~~ the use of the SPV in a clinical population. There are a number of important benefits associated with completing CPET in post-MI patients [15,32], therefore any test which may improve the validity and reliability of this process should be of interest. Therefore two separate studies were~~we~~ conducted~~ two separate studies~~; 1. To investigate the reliability of the SPV in an apparent

"healthy" population, and; 2. To investigate the reliability and validity of the SPV in early post-MI patients. The hypotheses for the current study are that the SPV will be a reliable indicator of key CPET derived variables in the healthy and clinical populations. The SPV will also produce higher $\dot{V}O_{2peak}$ values compared to a traditional CPET protocol in the post-MI patients.

Materials & Methods

Twenty-five (12 females, 13 males) healthy participants (age = 26 ± 6 yr, weight = 68 ± 10 kg, height = 172 ± 9 cm) volunteered to participate in study 1. Study 1 was conducted following institutional ethical approval of the researcher's own University. For study 2, thirty-seven patients undergoing phase III cardiac rehabilitation were asked to participate, out of those, thirty agreed to take part. Two patients withdrew from the study, therefore twenty-eight post-MI patients (2 females, 26 males) ~~undergoing cardiac rehabilitation volunteered to participate~~ took park in study 2 (age = 58 ± 8 yr, weight = 89.5 ± 12 kg, height = 178 ± 8 cm, days from MI event 57 ± 35). All participants recruited for study 2 already had their coronary angiography and any interventions needed following their MI, and were thought to require no further intervention or revascularisation. Study 2 was conducted following NHS ethical approval (Brighton and Sussex REC**:** 12/LO/1737). Both studies met the ethical standards outlined by Harris and Atkinson for the IJSM [21]~~[18]~~. All participants gave their written informed consent.

For study 1 each participant visited the exercise-testing laboratory on three separate occasions. During each visit participants were required to complete an SPV test. For study 2 each patient was required to complete three exercise tests (a standard CPET protocol (sCPET) and two SPV tests) in order to determine the tests' validity and reliability. An

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overview of the experimental procedures for both studies are provided in figure 1.The order in which participants completed the tests was in a randomised, counterbalanced crossover design. For both studies, each test was separated by at least 24 h and all tests were completed at the same time of the day (± 2 h). Participants were asked to refrain from drinking alcohol (24 h abstinence), eating (2 h abstinence), smoking (2 h abstinence), and not to perform any exercise in the 24 h prior to each test. In both studies, participants were required to complete a 5-min warm-up at a self-selected intensity during which they were also familiarised with the process of freely adjusting their PO on the cycle ergometer.

INSERT FIGURE 1 HERE

The SPV was completed on an air-braked cycle ergometer (Wattbike Trainer, UK), which allowed participants to continually vary their PO throughout the test. The SPV was conducted in accordance with the procedures previously outlined by Mauger and Sculthorpe [36]~~[32]~~ and consisted of 5 x 2-min stages (total test time of 10-min), where for each stage participants were able to continuously vary their PO, but with RPE (Borg's 6-20 scale) fixed to a level for each stage (RPE 11, 13, 15, 17 and 20), following an incremental format. Changes in PO were facilitated by the participants manually adjusting the cycle ergometer air brake and cadence at their own free will in order to produce a level of resistance that allowed them to match the target RPE for each stage of the SPV.

The sCPET from study 2 was completed on an electro-magnetically braked cycle ergometer (Lode Corival), so that PO for each stage could be fixed according to the test requirements. The test followed a standard incremental ramp design. As previously used with other clinical populations, the test commenced with no resistance and gradually increased by 20 W per

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minute, standardized across all patients [10,16,20,26]~~[8,14,17,24]~~. The test was stopped when the patient felt like they could no longer continue or if they could no longer maintain more than 60 RPM, despite verbal encouragement.

During all exercise tests, expired gases were measured via the use of an online breath-by-breath analysis system (Cortex Metalyzer, Cortex, NL). Expired gases, heart rate (HR), PO and cadence were continuously recorded during the tests. A 12-lead ECG was used when exercising the post-MI patients in study 2. After the test, $\dot{V}O_{2peak}$ was calculated as the highest 30 second average $\dot{V}O_2$ (L/min^{-1} and $ml \cdot kg^{-1} \cdot min^{-1}$). ~~We did not assess for a~~A $\dot{V}O_2$ plateau was not assessed which is why ~~we use~~ the term $\dot{V}O_{2peak}$ is used, rather than $\dot{V}O_{2max}$. Peak cycling PO and minute ventilation ($\dot{V}E$) were also both calculated as the highest 30 second average value. The anaerobic threshold (AT) was determined using the V-slope method with confirmation via the ventilatory equivalents ($\dot{V}E/\dot{V}O_2$ and $VE/\dot{V}CO_2$) and the partial end-tidal ($P_{ET}O_2$ and $P_{ET}CO_2$) methods [23]~~[20]~~. All AT's were independently assessed by two experienced researchers.

All data was analysed using IBM SPSS Statistics version 21. Descriptive data is presented as mean ± standard deviation (SD). Statistical significance was set at 95% ($p < 0.05$). A sample size calculation was completed based upon the findings from the study by Mauger and Sculthorpe [36]. The SD of the differences in $\dot{V}O_{2peak}$ between the two tests was 8.5 $ml \cdot kg^{-1} \cdot min^{-1}$ [36] and if it is assumed that the minimal clinically worthwhile differences between the two tests is 5 $ml \cdot kg^{-1} \cdot min^{-1}$, this equals to an effect size of 0.58. With this information it was therefore estimated that a minimim sample size of 25 was needed to achieve a statistical power 80% and an alpha level of 0.05. Test-retest reliability was assessed via the use of 95%

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Limits of Agreement (LOA) using Bland-Altman plots [9][7], Confidence intervals (95% CI) of the coefficient of variation (CV), and intraclass correlation coefficients (ICC) were calculated to assess the variability of the repeated tests (Hopkins, A New View of Statistics. Internet Society for Sports Science: http://www.sportsci.org/resource/stats/index.html (2015)). It has been suggested that a CV of < 5% [24][21], and an ICC close to 1 both indicate good test-retest reliability [5][3], with classifications for ICC ranging from 'questionable' (0.7 to 0.8) to 'high' (> 0.9) [5][3]. For study 1 differences in $\dot{V}O_{2peak}$, peak PO, AT, peak HR and peak $\dot{V}E$ were assessed using a one-way repeated measures ANOVA. For study 2, physiological responses from the 1st SPV test were compared to those obtained from the sCPET, using a paired-samples t-test. Complete 2nd SPV test data was not achieved for three of the patients in study 2, and so data from only SPV1 has been used in these cases. The reasons for these three missing tests were; one patient had an unrelated illness and was unable to attend their final test within the required timeframe; the other two miscalculated their work rate during the RPE 17 stage causing a premature end to the test. The data of these two patients who did not meet the test requirements for SPV2 has been excluded from the main analysis, but complete data is also presented within the results section.

Results

Study 1:

Table 1 represents a summary of the mean peak values for all the physiological variables recorded during the three repeated SPVs.

INSERT TABLE 1 HERE

The CV for $\dot{V}O_{2peak}$ (ml·kg^{-1}·min^{-1}) was 4.2% (95% CI: 3.4-5.6%) for trials 2-1 and 5.1% (95% CI: 4.2-6.8%) for trials 3-2. The mean CV for all three tests was 4.7% (95% CI: 3.8-6.2%). A high level of agreement was found between trials 2-1 (ICC = 0.95) and trials 3-2 (ICC = 0.94). The LOA were ± 5.59 ml·kg^{-1}·min^{-1} for trials 2-1 (Figure 2~~1~~a) and ± 5.86 ml·kg^{-1}·min^{-1} for trials 3-2 (Figure 2~~1~~b).

Participants demonstrated a mean CV of 5.5% (95% CI: 4.4-7.3%) for AT, 7.9% (95% CI: 6.3-10.6%) for peak PO, 1.7% (95% CI: 1.4-2.3%) for peak HR, and 7.2% (95% CI: 5.8-9.6%) for peak $\dot{V}E$. The ICC for these three variables ranged between 0.91-0.97.

Study 2

The CV for $\dot{V}O_{2peak}$ between SPV1 and SPV2 was 8.2% (95% CI: 6.6-10.9%). Therefore, if a patient achieved a $\dot{V}O_{2peak}$ of 23 ml·kg^{-1}·min^{-1} a typical variation of 1.9 ml·kg^{-1}·min^{-1} would be expected. The ICC was 0.89 which represents a high level of agreement. The LOA was ± 4.22 ml·kg^{-1}·min^{-1} for the measure of SPV1 and SPV2 (Figure 2~~1~~c). ~~If we include~~ When the SPV2 data for the two patients who were excluded from the main analysis are included, the CV becomes 8.4% (95% CI: 6.8-11%), the ICC is unchanged, and the LOA become ± 4.52 ml·kg^{-1}·min^{-1}.

INSERT FIGURE 2~~1~~ HERE

The CV for AT between SPV1 and SPV2 was 8.4% (95% CI: 6.8-11.2%). The ICC was 0.86 which suggests an 'acceptable' agreement [5]~~[3]~~. The LOA was ± 3 ml·kg^{-1}·min^{-1} for the measure of SPV1 and SPV2 (Figure 2~~1~~d). If ~~we include~~ the SPV2 data for the two patients

who were excluded from the main analysis are included, the CV for AT becomes 8.6% (95% CI: 7-11.4%), the ICC is 0.84, and the LOA remain unchanged. There was a CV of 15.1% (95% CI: 12.1-20.4%) for peak PO, 4.7% (95% CI: 3.8-6.5%) for peak HR, and 11.5% (95% CI: 9.2-15.4%) for peak $\dot{V}E$. The ICC for these three variables ranged between 0.83-0.97, demonstrating a high level of agreement [5]~~[3]~~.

As shown in Table 2, patients achieved a significantly higher $\dot{V}O_{2peak}$ ($p < 0.01$) in the SPV compared with the sCPET. Patients also achieved a significantly higher peak PO, peak HR and peak $\dot{V}E$ in the SPV than in the sCPET ($p < 0.01$). There were no significant differences in AT between the SPV and the sCPET ($p > 0.05$).

INSERT TABLE 2 HERE

Discussion

This is the first study to assess the SPV on a clinical population. The results of the current study demonstrated the SPV to be a reliable indicator of $\dot{V}O_{2peak}$ in a healthy population; which is mirrored by the post-MI patient population. The CV for $\dot{V}O_{2peak}$ ($ml \cdot kg^{-1} \cdot min^{-1}$) in the healthy population was 4.7% and 8.2% for the post-MI patients. Post-MI patients achieved a higher $\dot{V}O_{2peak}$ compared to a sCPET protocol, which is in agreement with previous studies on healthy populations [34,36]~~[31,32]~~. Previously published studies have investigated the reproducibility of physiological variables using sCPET protocols. Froelicher et al. [19]~~[16]~~ found that when using three popular maximal exercise treadmill protocols in a healthy population the CV for $\dot{V}O_{2peak}$ ranged from 4.1-5.8%. In addition, one study completed a succession of CPET tests on cardiac failure patients and reported the average CV for $\dot{V}O_{2peak}$ to be 5.7% [25]~~[23]~~. Other studies have reported "good" test-retest reliability (CV

for $\dot{V}O_{2peak}$ = 3.5-6.9%) during cycling MIE tests in patients with various respiratory conditions [14,31,37]~~[12,28,33]~~. CV's from previous research [12,22,27,32] investigating the use of traditional protocols are lower than those from the post-MI group of the current study. However, it is difficult to make direct comparisons between studies as different patient populations were used.

~~Our~~ The current study results demonstrated a CV for AT of 8.4% (study 2), which is considered as acceptable for test-retest reliability in clinical populations [40]~~[36]~~. Kothmann et al. [28]~~[26]~~ found a CV of 10% for AT in Abdominal Aortic Aneurysm (AAA) patients using a sCPET protocol. Identification of AT from CPET has become an increasingly important tool in clinical exercise testing, primarily due to it giving an objective assessment of cardiopulmonary function which does not require high levels of effort [42]~~[37]~~. Previous literature has demonstrated AT to be a useful predictor of mortality in patients with chronic heart failure. This information can then be used to help prioritise patients for heart transplantation [20]~~[17]~~. The identification of AT prior to major surgery has also been shown on a number of occasions to closely correlate with post-operative outcome [42,49]~~[37,42]~~. It is reassuring to see that in the current study there were no differences in AT when comparing it between the SPV and the sCPET ($p > 0.05$), this combined with the reliability results demonstrate that AT can be reliably determined via the SPV, which is of great importance in clinical exercise testing.

As previously mentioned, two post-MI patients were excluded from the main reliability analysis as they did not successfully complete a second SPV due to misjudging the required work rate during stage RPE 17. However, when looking at their individual test data, both

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patients exercised long enough to demonstrate a valid AT and a $\dot{V}O_{2peak}$. When including their exercise data into the reliability analysis the CV for $\dot{V}O_{2peak}$ increases from 8.2 to 8.4% and CV for AT increases from 8.4 to 8.6%. From a clinical perspective it is encouraging to see that even though these two patients did not complete the full 10-min, important CPET data could still be obtained from the test.

In agreement with data from a healthy population [36]~~[32]~~, post-MI patients achieved a significantly higher $\dot{V}O_{2peak}$ (+8%) during the SPV compared with the sCPET ($P < 0.01$). Peak HR and $\dot{V}E$ were also significantly higher in the SPV than in the sCPET ($p < 0.01$), which is in support of previous work [18,22,34]~~[15,19,31]~~. It is interesting to see that previous studies which failed to find any differences in $\dot{V}O_{2peak}$ between the SPV and a sCPET protocol also found no differences in HR and $\dot{V}E$ [13,47]~~[11,40]~~, potentially leading to the observed differences in $\dot{V}O_{2peak}$. A recently published study [3]~~[2]~~ found significantly higher maximal HR and cardiac output during the SPV compared to a sCPET protocol [3]~~[2]~~. Astorino et al. [3]~~[2]~~ concluded that the greater cardiac output in the SPV suggests a greater oxygen delivery to the exercising muscles, permitting a higher $\dot{V}O_{2peak}$ to be achieved. These findings suggest that the SPV allows individuals to work to a higher physiological work rate when compared to the sCPET. This may be a result of the nature of self-paced exercise providing a more "comfortable" experience for patients. Previous research has in fact suggested that self-paced exercise is less physiologically challenging when compared against enforced paced exercise [30]. Being able to make slight adjustments in effort may minimise fatigue and any peripheral discomfort associated with cycling, particularly in the early stages of the test, which may ultimately lead to a greater work rate being able to be achieved in the final stage [3]~~[2]~~. In traditional CPET no adjustments in effort can be made and the only way to stop any exercise related discomfort would be to stop. In addition, it may be that

knowledge of the test end-point in the SPV also contributes to the higher work rates achieved. Indeed, previous literature has demonstrated that knowledge of exercise duration can improve exercise performance [33]. With all of this in mind, the current findings suggest that in a clinical population, where cardiac function might be limited, the self-paced nature may in fact provide the patient the opportunity to work harder, producing a greater cardiac output and therefore reaching a higher $\dot{V}O_{2peak}$. However, further research is required to support thesesis speculations.

The mean sCPET time-to-exhaustion was 8 minutes 55 seconds (range = 5 min – 12 min 54 sec) compared to the fixed 10 minutes of the SPV. Even though the sCPET mean test time falls within the recommended criteria of 8-12 minutes [11][9], only 15 (of 28) participants successfully completed the test within this recommended time. Therefore, the lower $\dot{V}O_{2peak}$ in the sCPET could be attributable to only 54% achieving the recommended test time. A potential limitation of the current study was the decisionthat we decided to standardize sCPET work rate increments (20W/min) for all patients [10,16,26][8,14,24] instead of doing so oan an individual basis [38,39][34,35]. Individualising work rate increments may have resulted in more patients completing the CPET within the recommended time frame, although the subjectivity of such a choice would not have guaranteed a successful test in all patients. This issue clearly highlights one of the key challenges practitioners face on a day-to-day basis when using CPET with clinical populations. Indeed, if patients are unable to exercise for a sufficient time the utility of test results is severely limited, resulting in a significant waste of finance and time for both patients and health service provider. In particular, an incorrect estimation of the work rate increments may lead to a test which is too short, or too long. A test which is short in duration (< 8 min) is suggested to underestimate $\dot{V}O_{2peak}$ due to increased glycolytic contribution to energy and enhanced fast-twitch muscle fibre recruitment

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[4]. In addition to this, a short test may only acquire limited information making it difficult to confidently assess fitness. Conversely, if a test is long in duration (> 12 min) patients may end up stopping due to such factors as boredom or increased local muscle fatigue [4], rather than a result of their actual cardiopulmonary limit. The SPV eliminates the need for practitioners to estimate the most appropriate starting intensity and work rate increments as it is based on set levels of perceived exertion. Moreover, the closed loop nature of the SPV ensures that each test lasts 10 minutes. The nature of the SPV gives patients the opportunity to complete the test at their own ability whilst exercising for the recommended time to achieve optimal physiological values. This therefore may increase the likelihood of obtaining useable and representative data from patients. Thus, a protocol like the SPV may be a more reliable way of acquiring time efficient and useable data than sCPET methods.

~~The significantly higher PO achieved in the SPV suggests that regardless of the self-paced nature, participants were willing to tolerate significantly higher work rates in the final stage (RPE 20), compared to that demanded by the sCPET. Knowledge of the test end-point in the SPV vs the open-ended sCPET could contribute to the higher tolerance in work rate. Indeed, previous literature has demonstrated that knowledge of exercise duration can improve exercise performance [30]. It could also be suggested that the SPV provides patients with a more "comfortable" experience, as they are able to self-adjust their work rate, potentially making the higher perceived work rates more tolerable, especially when the end is proximate.~~

There were no adverse events reported for the current study, providing support for the current evidence base that maximal exercise testing is a safe procedure to perform on cardiac patients [6,27,46]~~[4,25,39]~~.

A limitation of the current study is that different cycle ergometers were used in study 2. Previous research has suggested that different ergometers might result in differences in the metabolic and cardiovascular response [45]. However, different ergometers were a requirement of the different protocols, as the SPV required patients to freely adjust their PO, and the sCPET required accurate fixing of PO. Indeed, a similar differences in $\dot{V}O_{2peak}$ to that seen in the current study have been found by previous studies who used the same cycle ergometer in both the SPV and sCPET [3,36].

Conclusion

The results of the current study demonstrate that the SPV is a reliable method for determining $\dot{V}O_{2peak}$ in a healthy population, with acceptable reproducibility being seen in the clinical population. The SPV allowed post-MI participants to achieve a significantly higher $\dot{V}O_{2peak}$ than the sCPET. This study provides initial evidence ~~suggests~~ that the SPV may be ~~is~~ a safe, valid and reliable measure of $\dot{V}O_{2peak}$ in both clinical and healthy populations, and should be considered as an accepted means of testing for exercise capacity. However, further robust multicentre data is required to establish the safety of the SPV in such populations. Moreover, the defined test duration and self-administered work rates associated with the SPV addresses common issues that clinicians regularly have to overcome, and go some way to ensuring all patients exercise for the recommended duration in order to obtain a valid and reliable CPET. Future research should seek to assess the SPV in other clinical populations and the utility of the SPV versus sCPET to inform clinical decision making on patient treatment.

Acknowledgements

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We firstly thank Dr Marcus Fletcher for his clinical support for the tests conducting in study 2. We also thank the cardiac rehabilitation nurses at the William Harvey Hospital for their help with recruiting suitable patients and test supervisions. We finally thank Dr. Katharine Richardson for assisting in interpretation of the Anaerobic Threshold data.

Funding: This work was supported by the East Kent Hospitals Charity [1076555/303 to JGH].

Disclosures: None.

References

1. *Albouaini K, Egred M, Alahmar A, Wright DJ.* Cardiopulmonary exercise testing and its application. Heart 2007; 93: 1285-1292.

2. *Astorino TA*. Discussion: The efficacy of the self-paced VO2max test to measure maximal oxygen uptake in treadmill running. Appl Physiol Nutr Metab 2014; 39: 592-593.

3. *Astorino TA, McMillan DW, Edmunds RM, Sanchez E.* Increased cardiac output elicits higher VO2max in response to self-paced exercise. Appl Physiol Nutr Metab 2015; 40: 223-229.

4. *Astorino TA, Rietschel JC, Tam PA, Taylor K, Johnson SM, Freedman TP, Sakarya CE.* Reinvestigation of optimal duration of VO2max testing. J Exerc Physiol 2004; 7: 1-8.

5. *Atkinson G, Nevill AM*. Statistical methods for assessing measurement effort (reliability) in variables relevant to sports medicine. Sports Med 1998; 26: 217-238.

6. *Balady GJ, Arena R, Sietsema K, Myers J, Coke L, Fletcher GF, Forman D, Franklin B, Guazzi M, Gulati M, Keteyian SJ, Lavie CJ, Macko R, Mancini D, Milani RV, on behalf of the American Heart Association Exercise, Cardiac Rehabilitation,and Prevention Committee of the Council on Clinical Cardiology, Council on Epidemiology and Prevention, Council on Peripheral Vascular Disease, Interdisciplinary Council on Quality of Care and Outcomes Research.* Clinician's Guide to Cardiopulmonary Exercise Testing in Adults: A Scientific Statement From the American Heart Association. Circulation 2010; 122: 191-225.

7. *Basset D, Howley ET*. Limiting factors for maximum oxygen uptake and determinants of endurance performance. Med Sci Sports Exerc 2000; 32: 70-84.

8. *Beckles MA, Spiro SG, Colice GL, Rudd RM*. The physiologic evaluation of patients with lung cancer being considered for resectional surgery. Chest 2003; 123: 105-114.

9. *Bland MJ, Altman DG*. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; 327: 307-310.

10. *Brutsche MH, Spiliopoulos A, Bolliger CT, Licker M, Frey JG, Tschopp JM.* Exercise capacity and extent of resection as predictors of surgical risk in lung cancer. Eur Respir J 2000; 15: 828-832.

11. *Buchfuhrer MJ, Hansen JE, Robinson TE, Sue DY, Wasserman K, Whipp DJ*. Optimizing the exercise protocol for cardiopulmonary assessment. J Appl Physiol 1983; 55: 1558-1564.

12. *Buys R, Cornelissen V, Van De Bruaene A, Stevens A, Coeckelberghs E, Onkelinx S, Thomaes T, Delecluse C, Budts W, Venhees L.* Measures of exercise capacity in adults with congenital heart disease. Int J Cardiol 2011; 153: 30.

13. *Chidnok W, DiMenna FJ, Bailey SJ, Burnley M, Wilkerson DP, Vanhatalo A, Jones AM.* VO2max is not altered by self-pacing during incremental exercise. Eur J Appl Physiol 2013; 113: 529-539.

14. *Cox NJM, Hendrink JCM, Binkhorst RA, Folgering HTM, van Herwaarden CLA.* Reproducibility of incremental maximal cycle ergometer tests in patients with mild to moderate obstructive lung disease. Lung 1989; 167: 129-133.

15. *Davidson DM, DeBusk RF.* Prognostic value of a single exercise test 3 weeks after uncomplicated myocardial infarction. Circulation 1980; 61: 236-242.

16. *Eindhoven JA, van den Bosch AE, Oemrawsingh RM, Baggen VJ, Kardys I, Cuypers JA, Witsenburg M, van Schaik RH, Roos-Hesselink JW, Boersma E.* Release of growth-differentiation factor 15 and associations with cardiac function in adult patients with congenital heart disease. Int J Cardiol 2016; 202: 246-251.

17. *Eston RG, Crockett A, Jones AM.* Discussion of: The efficacy of the self-paced V˙ O2max test to measure maximal oxygen uptake in treadmill running. Appl Physiol Nutr Metab 2014; 39: 581-582.

18. *Faulkner J, Mauger AR, Woolley B, Lambrick DM.* The efficacy of a self-paced VO2max test during motorized treadmill exercise. Int J Sports Physiol Perform 2015; 10: 99-105.

19. *Froelicher VF, Brammell H, Davis G, Noguera I, Stewart A, Lancaster MC.* A comparison of the reproducibility and physiologic response to three maximal treadmill exercise protocols. Chest 1974; 65: 512-517.

20. *Gitt AK, Wasserman K, Kilkowski C, Kleemann T, Kilkowski A, Bangert M, Schneider S, Schwarz A, Senges J*. Exercise anaerobic threshold and ventilator efficiency identify heart failure patients for high risk of early death. Circulation 2002; 106: 3079-3084.

21. *Harriss DJ, Atkinson G*. Ethical standards in sport and exercise science research: 2016 update. Int J Sports Med 2015; 36: 1121-1124.

22. *Hogg JS, Hopker JG, Mauger AR.* The self-paced VO2max test to assess maximal oxygen uptake in highly trained runners. Int J Sports Physiol Perform 2014; 10: 172-177.

23. *Hopker JG, Jobson SA, Pandit JJ*. Controversies in the physiological basis of the 'anaerobic threshold' and their implications for clinical cardiopulmonary exercise testing. Anaesthesia 2011; 66: 111-123.

24. *Hopkins WG*. Measures of reliability in sports medicine and science. Sports Med 2000; 30: 1-15.

25. *Janicki JS, Gupta S, Ferris ST, McElroy PA*. Long-term reproducibility of respiratory gas exchange measurements during exercise in patients with stable cardiac failure. Chest 1990; 97: 12-17.

26. *Kahaly GJ, Wagner S, Nieswandt J, Mohr-Kahaly S, Ryan TJ.* Stress Echocardiography in Hyperthyroidism. J Clin Endocrinol Metab 1999; 84: 2308-2313.

27. *Kanthan A, Tan TC, Zecchin RP, Denniss AR.* Early exercise stress testing is safe after primary percutaneious coronary intervention. Eur Heart J Acute Cardiovasc Care 2012; 1: 153-157.

28. *Kothmann E, Danjoux G, Owen SJ, Parry A, Turley AJ, Batterham AM*. Reliability of the anaerobic threshold in cardiopulmonary exercise testing of patients with abdominal aortic aneurysms. Anaesthesia 2009; 64: 9-13.

29. *Kristensen SD, Knuuti J, Saraste A, Anker S, Botker HE, Hert SD, Ford I, Gonzalez-Juanatey JR, Gorenek B, Heyndrickx GR, Hoeft A, Huber K, Lung B, Kjeldsen KP, Longrois D, Luscher TF, Pierard L, Pocock S, Price S, Roffi M, Sirnes PA, Sousa-Uva M, Voudris V, Funck-Bentano C.* 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management. Eur Heart J 2014; 35: 2383-2431.

30. *Lander PJ, Butterly RJ, Edwards AM*. Self-paced exercise is less physically challenging than enforced constant pace exercise of the same intensity: influence of complex central metabolic control. Br J Sports Med 2009; 43: 789-795.

31. *Marciniuk DD, Watts RE, Gallagher CG*. Reproducibility of incremental maximal cycle ergometer testing in patients with restrictive lung disease. Thorax 1993; 48: 894-898.

32. *Markiewicz W, Houston N, DeBusk RF*. Exercise testing soon after myocardial infarction. Circulation 1977; 56: 26-31.

33. *Mauger AR, Jones AM, Williams GA.* Influence of feedback and prior experience on pacing during a 4-km cycle time trial. Med Sci Sports Exerc 2009; 41: 451-458.

34. *Mauger AR, Metcalfe AJ, Taylor L, Castle PC*. The efficacy of the self-paced VO2max test to measure maximal oxygen uptake in treadmill running. Appl Physiol Nutr Metab 2013; 38: 1211-1216.

35. *Mauger AR, Metcalfe AJ, Taylor L, Castle PC*. Reply to "Discussion: Efficacy of the self-paced VO2max test to measure maximal oxygen uptake in treadmill running". Appl Physiol Nutr Metab 2014; 39: 583-585.

36. *Mauger AR, Sculthorpe N*. A new VO2max protocol allowing self-pacing in maximal incremental exercise. Br J Sports Med 2012; 46: 59-63.

37. *McKone EF, Barry SC, FitzGerald MX, Gallagher CG*. Reproducibility of maximal exercise ergometer testing in patients with cystic fibrosis. Chest 1999; 116: 363-368.

38. *Myers J, Buchanan N, Walsh D, Kraemer M, McAuley P, Hamilton-Wessler M, Froelicher VF*. Comparison of the ramp versus standard exercise protocols. JACC 1991; 17: 1334-1342.

39. *Myers J, Prakash M, Froelicher V, Partington S, Atwood E*. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med 2002; 346: 793-801.

40. *Myers J, Goldsmith RL, Keteyian SJ, Brawner CA, Brazil DA, Aldred H, Ehrman JK, Burkhoff D*. The Ventilatory Anaerobic Threshold in Heart Failure: A Multicenter Evaluation of Reliability. J Card Fail 2010; 16: 76-83.

41. *Noakes TD*. Testing for maximum oxygen consumption has produced a brainless model of human exercise performance. Br J Sports Med 2008; 42: 551-555.

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42. *Older P, Hall A, Hader R.* Cardiopulmonary exercise testing as a screening test for perioperative management of major surgery in the elderly. Chest 1999; 116: 355-362.

43. *Poole DC.* Discussion: "The efficacy of the self-paced V˙ O2max test to measure maximal oxygen uptake in treadmill running". Appl Physiol Nutr Metab 2014; 39: 586-588.

44. *Poole DC, Wilkerson DP, Jones AM.* Validity of criteria for establishing maximal O_2 uptake during ramp exercise tests. Eur J Appl Physiol 2008; 102: 403-410.

45. *Reiser M, Meyer T, Kindermann W, Daugs R.* Transferability of workload measurements between three difference types of ergometer. Eur J Appl Physiol 2000; 82: 245-249.

46. *Roffi M, Wenaweser P, Windecker S, Mehta H, Eberli FR, Seiler C, Fleisch M, Garachemani A, Pedrazzini GB, Hess OM, Meier B.* Early exercise after coronary stenting is safe. J Am Coll Cardiol 2003; 42: 1569-1573.

47. *Straub AM, Midgley AW, Zarvorsky GS, Hillman AR.* Ramp-incremented and RPE-clamped test protocols elicit similar $\dot{V}O_{2max}$ values in trained cyclists. Eur J Appl Physiol 2014; 114: 1581-1590.

48. *West M, Jack S, Grocott MPW.* Perioperative cardiopulmonary exercise testing in the elderly. Best Pract Res Clin Anaesthesiol 2011; 25: 427-437.

49. *Wilson RJT, Davies S, Yates D, Redman J, Stone M.* Impaired functional capacity is associated with all-cause mortality after major elective intra-abdominal surgery. Br J Sports Med 2010; 105: 297-303.

Figure legend:

Figure 1. ~~Graphical~~Schematic ~~overview for~~of the experimental ~~procedures~~protocols for~~of~~ study 1 and 2.

Figure 2. Bland-Altman plots of a) differences in $\dot{V}O_{2peak}$ between trials 1 and 2 from study 1; b) trials 2 and 3 from study 1; c) differences in $\dot{V}O_{2peak}$ between SPV1 and SPV2 from study 2; d) differences in AT between SPV1 and SPV2 from study 2. The solid horizontal line represents mean difference, whilst the dashed lines represent the 95% LOA.

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Table 1: Peak values for physiological variables recorded during repeated SPV tests in the healthy population.

	SPV1	SPV2	SPV3
$\dot{V}O_{2peak}$ (L/min^{-1})	3.30 ± 0.86	3.23 ± 0.90	3.25 ± 0.92
$\dot{V}O_{2peak}$ (ml·kg^{-1}·min^{-1})	48.56 ± 8.93	47.87 ± 9.28	47.85 ± 9.40
AT (ml·kg^{-1}·min^{-1})	27.00 ± 6.83	26.67 ± 7.26	26.95 ± 7.34
HR (bpm)	184 ± 10	183 ± 11	182 ± 11
$\dot{V}E$ (L/min^{-1})	137.8 ± 38.9	133.3 ± 41.0	128.4 ± 39.1*
Peak PO (Watts)	312 ± 93	299 ± 109	304 ± 101

*significantly different to SPV1 (< 0.05), data are mean ± SD.

Table 2: Physiological variables recorded over the sCPET, SPV1 and SPV2 in post-MI patients.

	sCPET (n = 28)	SPV1 (n = 28)	SPV2 (n = 25)
$\dot{V}O_{2peak}$ (L/min^{-1})	1.90 ± 0.50	2.05 ± 0.48*	2.00 ± 0.43
$\dot{V}O_{2peak}$ (ml·kg^{-1}·min^{-1})	21.29 ± 4.93	23.07 ± 4.90*	22.68 ± 4.79
AT (ml·kg^{-1}·min^{-1})	12.63 ± 2.41	13.06 ± 2.39	13.21 ± 2.76
HR (bpm)	129 ± 18	138 ± 14*	136 ± 19
$\dot{V}E$ (L/min^{-1})	82.0 ± 27.1	94.5 ± 25.9*	91.1 ± 26.2
Peak PO (Watts)	171 ± 43	209 ± 78*	200 ± 64
TTE (seconds)	535 ± 130	600 ± 0*	600 ± 0

*significantly different from the sCPET (< 0.05), data are mean ± SD.

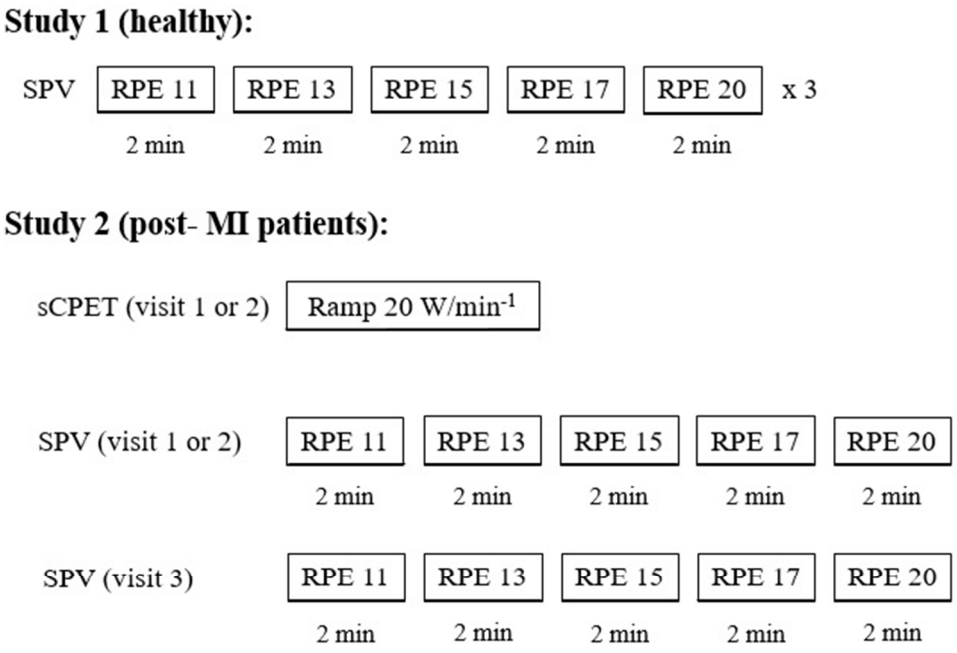

Figure 1. Schematic of the experimental protocols for study 1 and 2.

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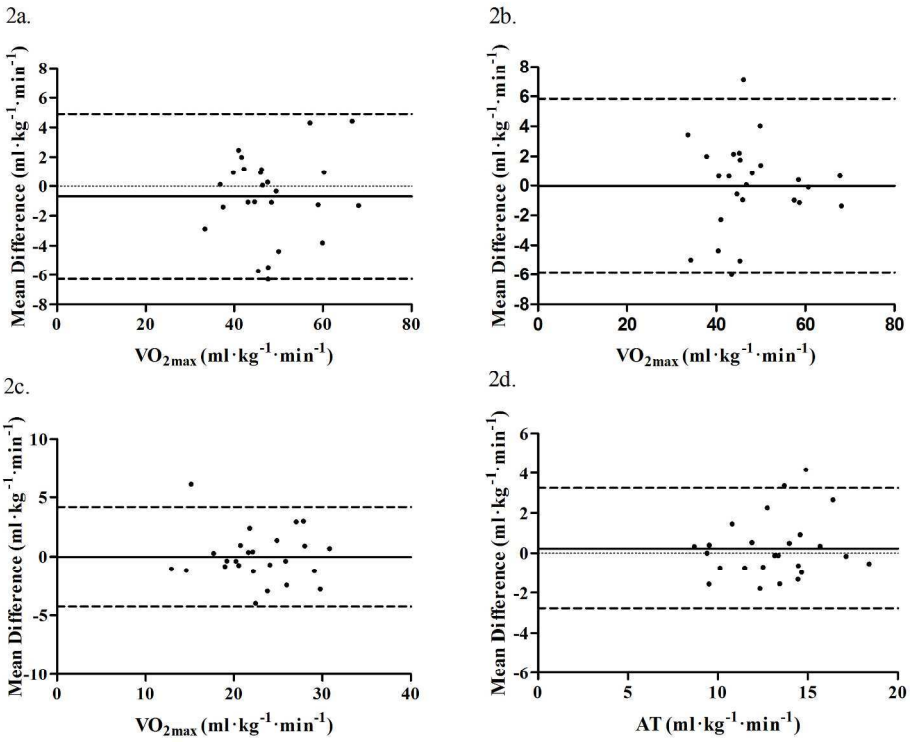

Figure 2. Bland-Altman plots of a) differences in VO2peak between trials 1 and 2 from study 1; b) trials 2 and 3 from study 1; c) differences in VO2peak between SPV1 and SPV2 from study 2; d) differences in AT between SPV1 and SPV2 from study 2. The solid horizontal line represents mean difference, whilst the dashed lines represent the 95% LOA. ├ ┬

224x178mm (300 x 300 DPI)