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Reference values for arm ergometry cardiopulmonary exercise testing (CPET) in healthy volunteers

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ABSTRACT

Introduction The performance of a cardiopulmonary exercise test (CPET) requires an individual to undertake a progressive, maximal exercise test to a symptom-limited end point. CPET is commonly performed using a treadmill or cycle ergometer (CE). Arm ergometry (AE) is an alternative exercise modality to CE; however, AE produces lower peak oxygen uptake (VO_2) values as it involves smaller muscle groups and generates less cardiovascular stress. Current predicted equations for the interpretation of AE CPET are limited by small sample sizes, gender bias and limited age ranges.

Aims To develop predicted equations and reference ranges for AE exercise testing.

Design Incremental ramp protocol CPET, to a symptom-limited end point, via AE was performed in a group of 116 (62 F) healthy volunteers of median age 38 (IQR 29–48) years. Breath-by-breath gas analysis was performed using the Ultima CPX (Medical Graphics, UK) metabolic cart. Quantile regression analysis was used to develop regression equations for AE VO_2, peak work rate (WR), anaerobic threshold, peak ventilation (VE), peak heart rate, oxygen pulse, VE/VCO_2 slope and VO_2/WR slope.

Results Reference equations including upper and/or lower limits, based on quantile regression, were generated and verified using a validation cohort.

Conclusions These findings represent the largest and most diverse set of predicted values and reference ranges for AE CPET parameters in healthy individuals to date. Implementation of these reference equations will allow AE to be more widely adopted, enabling the performance and interpretation of CPET in a wider population.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Findings to date demonstrate that peak oxygen uptake (pVO_2) is significantly lower when obtained using arm ergometry exercise. There are currently no recommended reference equations for use with arm ergometry. In contrast to published equations for cycle ergometry and treadmill, three of the current published regression equations for arm ergometry use achieved work rate to predict pVO_2. In addition, many of the current studies were obtained from single-sex or patient populations.

WHAT THIS STUDY ADDS

⇒ Our study provides predicted values and reference ranges for pVO_2, anaerobic threshold, peak work rate, peak ventilation (VE), peak heart rate, oxygen pulse, VE/VCO_2 slope and the VO_2/work rate slope for cardiopulmonary exercise using arm ergometry. It represents the largest data set for arm ergometry reference values to date.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Reference values developed by this study have the potential to significantly improve the interpretation of arm ergometry exercise tests and standardise interpretation. The data will enable the assessment of clinical populations against a normal range with the view to developing interpretation strategies for a range of clinical applications.

INTRODUCTION

Cardiopulmonary exercise testing (CPET) provides an integrated assessment of the response to exercise of the respiratory, cardiovascular, haematopoietic, neuropsychological and skeletal muscle systems. Standard, static tests of pulmonary and cardiac function, which are performed at rest, do not determine exercise capacity or causes of exercise limitation.[1] However, stressing these systems using CPET can reveal pathologies that are not apparent at rest. Furthermore, exercise capacity is one of the most powerful predictors of cardiovascular and all-cause mortality.[2–4] Consequently, CPET is increasingly used to provide a holistic assessment of exercise limitation and its causes and is widely used to provide clinically meaningful information regarding risks associated with surgical intervention.

CPET requires an individual to undertake a progressive, maximal exercise test to a symptom-limited end point. Tests are commonly performed using a treadmill (T) or cycle ergometer (CE). In normal individuals, the limiting symptoms will usually be physical fatigue or dyspnoea. Measurement of inspired and expired breath (breath-by-breath analysis) while exercising allows the calculation of various parameters which can

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be compared with expected normal values. Concurrent assessment of heart rate (HR) and rhythm, using an ECG, allows an integrative assessment of an array of parameters which evaluate the physiological response to exercise and causes for exercise intolerance. Clinical exercise testing is now routinely used for diagnosis of exercise limitation, surgical risk assessment or for monitoring of progression of disease.

However, there is a cohort of patients in whom the performance of CE or T testing is not possible because of medical conditions leading to impairment of the lower limbs or inability to perform weight-bearing exercise; commonly claudication, previous orthopaedic surgery, lower limb joint dysfunction/pain and certain neurodegenerative diseases. Consequently, the accepted method for determining surgical fitness or estimating prognosis is not available to these individuals, potentially preventing them from accessing essential surgery or therapy.

Arm ergometry (AE) is an alternative exercise modality; however, the data that have been obtained to date in healthy, normal populations for the purpose of generating a normal range of exercise indices are limited by the small size and heterogeneity of the study populations or are based on a fixed percentage of cycle ergometry predicted values.[5–8] The largest study group to date included 60 (30M) healthy volunteers, aged 20–59 years.[8] The output variables of work rate (WR), peak oxygen uptake (pVO_2) and (HR) were derived using a cycle adapted for AE and a 10-watt step ramp protocol. Three further studies reporting reference values were derived using male-only populations, subjects with coronary artery disease and discontinuous step ramp protocols.[5 6] There are currently no recommended reference equations for use with AE, with the wider literature predominately focusing on its relationship to CE instead.

Findings to date demonstrate that pVO_2 is significantly lower when obtained using AE, and this can be explained by the physiology of the muscle groups used for each exercise.[9] In addition, during submaximal phases of exercise, exercise parameters are higher for any given WR when exercising with the arms, suggesting decreased exercise efficiency.[10 11] The fitness measures obtained from AE, therefore, cannot be assumed to correlate with the accepted methods of T and CE. Consequently, the clinical interpretation of maximal exercise parameters obtained from AE may, in the absence of direct comparison of these modalities and a robust normal reference range, be unreliable.

The aim of the present study was to assess the physiological responses of adult males and females (free from underlying cardiac or respiratory disease) to AE exercise testing and to use this data to generate a local set of regression equations for CPET parameters for use in the interpretation of AE exercise.

METHODS

Participant recruitment

Participants were members of staff within our organisation, identified through advertisements including weekly electronic communications, intranet posts and all user emails. Participants were required to be of working age (18–69 years), free from any known cardiac or respiratory impairment and taking any prescribed medication likely to affect exercise performance.

Patient and public involvement

Patients and the public were not involved in the development of the research question, design or recruitment; no patient advisors were required. The results will be disseminated to the scientific community in academic writing.

Preparticipation screening

Prior to CPET, participants were assessed for health risks associated with exercise by completing the Physical Activity Readiness Questionnaire andYou (PAR-Q) questionnaire,[12] consistent with the recommendations of The American College of Sports Medicine(ACSM) guidelines for cardiovascular disease risk stratification.[5] After health screening, anthropometric measurements of height (cm), weight (kg) and calculation of body mass index (kg/m^2) were made according to established procedures.[13]

Baseline physiological measurements of spirometry, ECG and blood pressure (BP) were performed to assess for any evidence of underlying respiratory or cardiac disease. Participants with normal baseline spirometry, ECG and BP were eligible to take part in the study.

Activity questionnaire

Following successful screening, participants were requested to complete the Recent Physical Activity Questionnaire (RPAQ) to quantify their level of physical activity.[14]

Arm ergometer exercise testing

AE exercise was performed using the Ergoselect 400+ (Ergoline, Germany) electronically braked arm ergometer (figure 1). Seat height was not adjustable; however, the height of the ergometric test unit was electrically adjustable and was adjusted to ensure that the participants' arms were slightly bent at the elbow during furthest extension, as per knee flexion for CE.[15]

Incremental exercise

All participants undertook maximal CPET to volitional exhaustion. Incremental AE ramp protocols were calculated for each subject using the equations of Cooper and Storer.[16]

Arm work rate max=[(predicted VO_2 max×0.70)+(BW×3.5)]/18.36

Figure 1 Example of the Ergoline arm ergometer ergoselect 400. https://medicalgraphicsuk.com/wp-content/uploads/ergoselect_400_broschure_2018_11_en.pdf (Accessed 21 January 2025).

Predicted VO_2 max was calculated using the Wasserman regression equations,[7] where predicted VO_2 max using the arms is estimated to be 70% that of the legs, hence the multiplication by 0.70. BW is the subjects' body weight in kilograms.

All participants completed a rest phase of at least 2 min to allow familiarisation of the equipment and ensure accurate equipment function. This was followed by a 3 min unloaded phase.

Previously reported data suggest that arm crank speeds between 50 and 80 rpm have no influence on pVO_2[17] but higher speeds can result in significantly higher values for HR and ventilation (VE),[18 19] our centre employs a cadence of 60 rpm for CE, and so this was standardised across both modalities.

On completion of the unloaded exercise phase, the calculated exercise protocol commenced immediately. All participants were actively encouraged to exercise to a symptom-limited end point, for example, arm fatigue or breathlessness. The test was terminated by the Healthcare Scientist if, following a 60 s period of active encouragement, cadence fell by ≥5%. Measurements of gas exchange were made using the breath-by-breath analysis system Ultima CPX (Medical Graphics, UK) with an averaging method of five of seven breaths. HR was continually monitored using a 12-lead Mortara ECG system (Mortara, model X12+, Milwaukee, Wisconsin, USA). Maximal HR was defined as the highest value recorded during the test.[20] Due to a lack of evidence to demonstrate maximal effort for AE CPET, the accepted CE criteria of a plateau in VO_2, >90% predicted peak HR, peak VE>85% predicted and peak WR>85% were all accepted criteria for the achievement of maximal effort.[21–23]

Statistical analysis

The Kolmogorov-Smirnov test was used to assess data normality. Quantile regression analysis was performed to investigate the relationship between CPET variables and multiple independent variables. A standard bootstrap method with 5000 replications was completed to estimate the standard errors and construct CIs.

The regression equations were validated using a separate data set and differences were assessed by Wilcoxon signed-rank test. Spearman's r was used to analyse the association between all studied parameters. The values $p<0.05$ were considered statistically significant. Statistical analysis was done using Stata V.14.2 (Stata).

RESULTS

A total of 120 participants requested to take part in the study. One participant was excluded due to age (>70

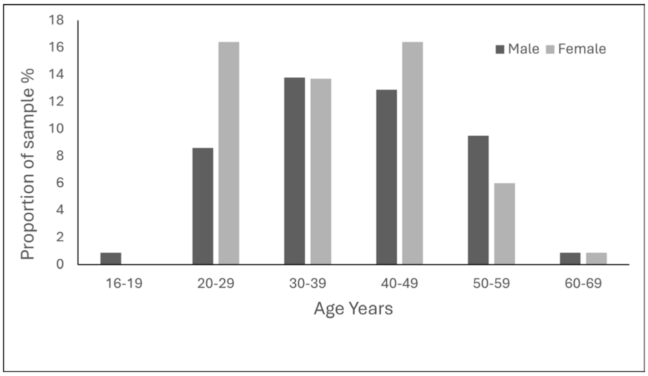

Figure 2 Distribution of the study sample subdivided by decile.

years) and a further participant was excluded following initial screening measurements which demonstrated poorly controlled asthma. In total, 118 subjects were successfully recruited to the study. Of the 118 subjects, a further 2 (1.7%) were excluded after the performance of the first CPET. One due to dysfunctional breathing on exercise which prohibited accurate interpretation of the results, with the second demonstrating significant cardiac arrhythmias requiring a referral for a formal cardiological assessment.

Participants found the RPAQ difficult to accurately answer and demonstrated a tendency to over-report their recreational sporting activities. Consequently, data from the RPAQ questionnaire were excluded from further analysis. Despite participants not undertaking an assessment of their physical activity levels, it was confirmed that none of the participants undertook physical activity at a competitive level, consistent with that reported in previous studies.[24] Many subjects recruited were recreational athletes, with cycling and running the most common pastimes reported.

Of the 116 participants recruited, 62 (53.45%) were female. Subjects met the age range criterion of 18–69 years; however, there were no subjects aged 18 years, only one aged 19 years and only one male and one female subject between the ages of 60 and 69 years. The age distribution of the study sample according to sex is summarised in figure 2. No participants reported a history of respiratory or cardiac disease.

No participants were active smokers; however, 14/116 (12%) had a history of cigarette/tobacco smoking, with 2/14 (14%) reporting exposure of >15 pack years. Both of these participants had normal spirometry (forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) ratio, FEV_1 and FVC all within±1.645 SR), and therefore, no spirometric evidence of smoking-related lung disease.[25 26] Relevant characteristics and distributions of study participants are shown in table 1.

Table 1 Subject characteristics

n=116	Median	IQR
Age, years	38	29–48
Height, m	1.72	1.65–1.72
Weight, kg	74.90	64.60–84.35
BMI, kg/m^2	24.64	22.87–27.27
Smoking history pack years	0	0–0
FEV_1 L	3.69	3.01–4.32
FEV_1 SR	0.07	−0.56 to 0.68
FVC L	4.52	3.64–5.45
FVC SR	0.40	−0.39 to 0.62
FEV_1/FVC %	80.80	76.23–85.11
FEV_1/FVC SR	−0.23	−0.88 to 0.43

BMI, body mass index; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; SR, standardised residual.

AE exercise

Results of AE CPET are summarised in table 2. All values are at peak exercise, except for anaerobic threshold. The median protocol was 7.50 watts/min with a total exercise duration (unloaded and incremental phase) of 14.27 min.

Individual subjects' AE values were compared with their predicted values for cycle ergometry.[7] For the group, median pVO_2 was 80.4% of the predicted VO_2 for cycle ergometry. Anaerobic threshold occurred at 37.3% of the cycle predicted VO_2 and 46.5% of the achieved AE pVO_2. Peak HR was 86.7% of the Tanaka peak predicted HR.[20] Peak WR for AE exercise was 55.1% of that predicted for cycle ergometry,[16] and peak VE reached 54% predicted (measured FEV_1×35).

Table 2 Results of arm ergometry exercise testing

	Median	IQR
HR bpm	157	141–172
WR watts	86	63.5–121.50
VE L/min	69.70	54.70–95.50
AT mL.kg.min	11.30	9.50–13.30
AT mL.min	814.00	662.50–1057.50
VO_2 mL.kg.min	23.30	18.50–29.10
VO_2 mL.min	1750.50	1350.50–2265.00
VCO_2 mL.min	1932.00	1516.50–2654.00
RER	1.14	1.10–1.20
VO_2/HR mL.beat	11.00	9.00–15.00
VE/VCO_2 slope	32.73	29.80–36.11
VO_2/WR mL.min/watt	16.00	14.48–17.67

AT, anaerobic threshold; HR, heart rate; RER, respiratory exchange ratio; VCO_2, maximal carbon dioxide output; VE, ventilation; VO_2, maximal oxygen uptake; WR, work rate.

Table 3 Equations for reference values for arm ergometry cardiopulmonary exercise test parameters, based on the study sample (n=116)

Parameter	Quantile	Equation
pVO_2 mL/min	0.05	2400.736–7.193073*A–637.8861*S–493.1423*H+4.020251*W
	0.10	1653.816–5.280052*A–716.7257*S–23.42231*H+3.783303*W
	0.50	853.0593–12.27326*A–658.9721*S+761.8335*H+6.190653*W
	0.90	−3780.844–11.72478*A–415.1991*S+3773.535*H+4.49441*W
	0.95	−733.6415–16.66981*A–833.566*S+2061.321*H+10.66038*W
VO_2 @AT mL/min	0.05	824.3743–4.888693*A–162.1906*S–106.0921*H+3.634585*W
	0.10	903.4833–4.889745*A–186.4675*S–157.3078*H+4.172682*W
	0.50	455.8201–4.476021*A–241.5648*S+266.3813*H+2.673008*W
	0.90	−1175.497–5.535491*A–261.2774*S+1768.839*H–4.291593*W
	0.95	74.49663–11.89854*A–442.2366*S+1365.285*H–5.288517*W
Work rate watts	0.05	137.5412–0.6847464*A–25.6605*S–35.60681*H+0.356037*W
	0.10	44.02852–0.2521425*A–33.96509*S+22.18859*H+0.2502107*W
	0.50	−49.67362–0.1386996*A–38.16051*S+87.74844*H+0.212474*W
Peak ventilation L/min	0.05	86.69346–0.288336*A–28.18909*S–19.95549*H+0.2610847*W
	0.10	88.6987–0.1124525*A–25.45358*S–12.32568*H+0.0370193*W
	0.50	35.6012–0.4138762*A–25.09783*S+25.34935*H+0.3551099*W
HR bpm	0.05	186.4043–0.1831584*A–9.119053*S–17.53406*H–0.2769712*W
	0.10	172.4908–0.9223429*A–6.013037*S+12.28153*H–0.2286254*W
	0.50	204.0874–0.9913322*A–6.978941*S+8.755818*H–0.2781482*W
	0.90	210.1394–0.7452363*A–2.270317*S+15.52931*H–0.4015619*W
	0.95	228.0533–0.7508408*A–8.981877*S+12.99556*H–0.4802669*W
VE/VCO_2 slope	0.50	33.829+0.0817704*A+0.9082314*S–0.566112*H–0.0505562*W
	0.90	37.95043+0.1108333*A+3.029821*S–5.529981*H+0.0522929*W
	0.95	35.46406+0.1397291*A+4.344474*S–7.071164*H+0.1109959*W
VO_2/WR mL.min/watt	0.05	31.61327–0.1278663*A–2.212916*S–9.873062*H+0.0363297*W
	0.10	31.62712–0.051825*A–2.819948*S–8.682037*H–0.0074095*W
	0.50	6.84879–0.0157613*A+1.199727*S+4.780254*H+0.0120691*W
VO_2/HR mL.beat	0.05	0.8290468–0.0092028*A–2.048818*S+2.773038*H+0.0453437*W
	0.10	−1.829688–0.0259574*A–2.623184*S+5.261638*H+0.0453945*W
	0.50	−6.197716+0.0060765*A–3.545563*S+8.808681*H+0.058024*W

The formula's each contain 50th percentiles as well as upper (95th and 90th) and lower (10th and 5th) reference values where appropriate.
AT, anaerobic threshold; HR, heart rate; VE, ventilation; VO_2, peak oxygen uptake; WR, work rate.

Reference values

Analysis of the AE data and the use of quantile regression analysis allowed the development of regression equations and normal ranges for the prediction of a normal cardiopulmonary exercise response to AE (table 3). A worked example of the regression equation can be found in the online supplemental appendix.

Data are quantile regression analysis for pVO_2, AT, WR, VE, HR, VE/VCO_2 slope, VO_2/WR slope and O_2 pulse. For entering subject's characteristics, sex (S) is coded as 0 for males and 1 for females, A=age in years, H=height in metres and W=weight in kilograms.

Validation

To determine the fit of the model for each exercise parameter, the predictive accuracy was measured in a separate group of healthy volunteers (n=16). The validation group was matched to the study group for age (p=0.299), height (p=0.100), weight (p=0.635) and BMI (p=0.070). Sex distribution was also comparable between the groups (Pearson's χ^2=0.000, p=1.000). The results of the Wilcoxon signed rank test and Spearman's r and the statistical significance are summarised in table 4.

The new reference values were also compared with the predicted equations of Kenney, Balady, Wasserman and Manfre (Healthy and Cardiac). Predicted values for each

Table 4 Results of reference equation validation

	Predicted (IQR)	Actual (IQR)	% Predicted	Difference	r
VO_2 peak mL/min	1746.68 (1320.55–2359.21)	1526.00 (1189.25–2133.50)	87	220.68*	0.885**
VO_2 at AT mL/min	803.87 (635.99–1019.43)	716.50 (596.25–922.50)	89	87.37	0.885**
WR watts	72 (62–120)	69 (54–110)	96	3	0.790**
Peak ventilation L/min	77.09 (58.06–97.79)	55.55 (45.45–72.98)	72	21.54	0.718**
HR bpm	156 (148–168)	163 (133–170)	104	–7	0.085
VE/VCO_2 slope	31.83 (31.11–33.73)	29.33 (25.33–31.74)	92	2.50	0.156
VO_2/WR mL.min/watt	15.93 (15.68–16.10)	15.43 (14.30–16.54)	97	0.50	–0.076
VO_2/HR mL.beat	10.54 (8.81–14.43)	11.00 (8.00–15.00)	93	–0.46	0.525*

Data expressed as median values and IQR.
*p<0.05, **p<0.01.
AT, anaerobic threshold; HR, heart rate; VE, ventilation; $\dot{V}O_2$, peak oxygen uptake; WR, work rate.

equation were calculated for study participants and then plotted against age (figure 3). There was a statistically significant difference between measured pVO_2 and all currently available AE predicted values; p<0.001.

DISCUSSION

We believe this to be the first study providing data for the development of regression equations for pVO_2, anaerobic threshold, WR, peak VE, HR, oxygen pulse, VE/VCO_2 and VO_2/WR slopes obtained by the performance of AE CPET. Data were obtained from 116 normal healthy volunteers, which represents the largest sample size to date for AE reference values. In addition, validation of the regression values has demonstrated an ability to accurately predict CPET parameters in a separate cohort of subjects with a significant correlation between predicted and actual measurements of pVO_2, anaerobic threshold, WR, peak VE and oxygen pulse. Despite a lack of correlation for HR and VE/VCO_2 and VO_2/WR slopes, there was no significant difference between the measured and predicted values.

Compared with other AE reference values, a strength of this study is the inclusion of a greater proportion of female participants at 53.4% and a wider age range of participants. As with the cycle ergometry predicted equations of Gläser *et al* we also included individuals with a BMI>30 kg/m^2.[27] It is recognised that obesity affects gas exchange; however, to exclude these individuals would ultimately limit the use of these equations in the current clinical population.[28] It is felt that the statistical methods employed and the inclusion of weight in the regression equations allow an accurate determination of

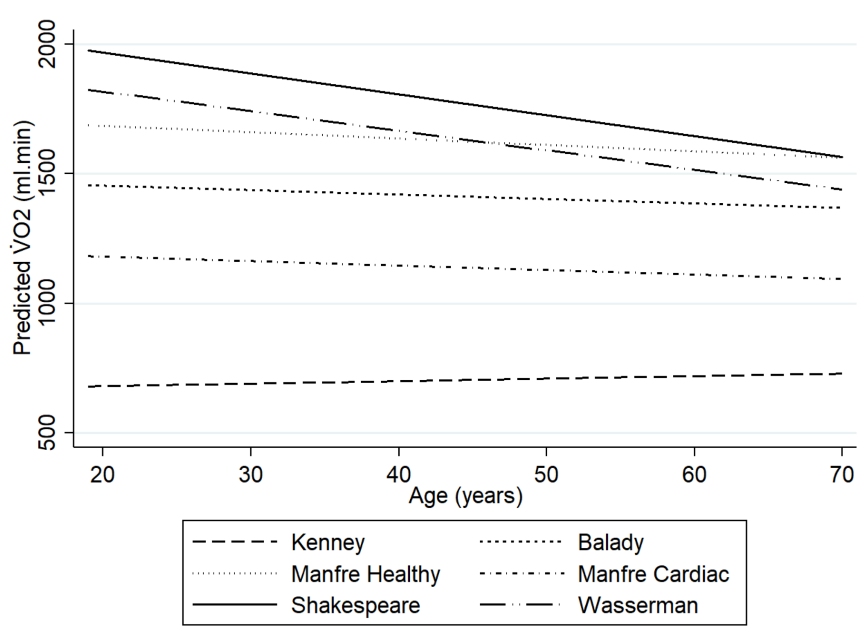

Figure 3 A comparison of the arm ergometry predicted $\dot{V}O_2$ equations according to age. Predicted values were calculated using the demographic data for the 116 study participants. $\dot{V}O_2$, peak oxygen uptake.

AE reference values across a wider range of individuals, including clinical cohorts.

In addition to the methodological and equipment disadvantages of the previous studies reporting reference values for AE, three of the developed regression equations used peak watts to determine predicted VO_2, which is in significant contrast to published equations for cycle ergometry. Systematic reviews of cycle ergometry and treadmill reference values illustrate that maximal oxygen uptake is dependent on age, sex and anthropometric properties and, therefore, it is these parameters that should be used in the development of reference values.[29 30] Comparison of our data to that of previously available reference values demonstrates a significant difference with the current equations significantly underestimating pVO_2. The equations which used wattage demonstrated the largest discrepancy in pVO2 with median differences between predicted equations and measured values varying from 236.75 to 1072.60 mL/min.

Our study methodology was designed to mirror the protocols used in cycle ergometry allowing easier adoption within clinical practice. The currently available reference equations all used step ramp protocols with WR increases of between 10 and 25 watts, with one study using a discontinuous protocol. These protocols were not individualised for each subject, with the same WR protocol used for both males and females and across the age ranges and were significantly greater than our median protocol of 7.5 watts. It is widely recognised that higher intensity exercise leads to increased fatigue and earlier termination of exercise, which may explain the underestimation of pVO2 by these studies. It has also been suggested that this methodology explains how reference values developed in a non-conditioned population[8] significantly underestimated the measured pVO2 in a population with coronary artery disease.[31]

Our incremental ramp protocol was individualised per participant using the AE WR predicted equations of Copper and Storer.[16] Our median total exercise test time of 14.27 min suggests that for some individuals, these equations may underestimate peak WR leading to an extended test duration. Further work needs to be undertaken to determine if the implementation of the predicted peak wattage determined by our cohort leads to a more optimal exercise test time.

The lack of widely available reference equations for AE led to the suggestion that 50%–70% of cycle ergometry VO_2 reference values be used as an estimate of AE predicted values.[21 32] Our data demonstrate that this is an underestimation and that pVO2 determined via AE more accurately aligns to 80% of CE predicted VO_2 values. The arbitrary value of 70% was suggested based on studies of single sex and limited age range populations and, therefore, is unlikely to be representative of the wider population.[33–35] This relatively broad predicted range (50%–70%) does not carry sufficient accuracy when utilising CPET data to make clinical decisions regarding surgical intervention or disease prognostication. Consequently, prior to the current study, interpretation of AE exercise test results carried significant difficulty which may be an important reason as to why this exercise modality has not been more widely adopted into routine clinical practice, despite its advantages in some patient groups.

The absolute physiological values (pVO_2 and anaerobic threshold) measured during AE have been demonstrated to be lower than those obtained when using CE.[9 36] This is likely attributed to the larger muscle mass of the legs[37 38] and the mechanical differences of cycle and arm ergometers.[11] The muscles used during AE CPET are predominantly the biceps, triceps, brachial and deltoid muscles. In contrast, during cycle ergometry, the primary muscles used are the quadriceps, hamstrings, gastrocnemius, soleus plantaris and gluteus maximus. Therefore, the muscles used when arm cycling are smaller and, compared with the legs, which are used for everyday activities such as walking, are generally less well conditioned. A smaller muscle needs to develop a greater percentage of its maximal tension, which leads to an increase in intracellular metabolites such as H^+, lactate and inorganic phosphate (P_i) resulting in skeletal muscle fatigue earlier than would occur in a larger muscle group.[37 38]

In addition to muscle size, the muscles of the arms have a larger percentage of Type II fibres (fast twitch) which have a higher oxygen cost than slow twitch,[39] resulting in acute fatigue during high-intensity dynamic exercise when there is an over-reliance on anaerobic metabolism resulting in earlier termination of exercise. A larger static exercise component during AE testing due to the requirement to grip the arm crank may also be a contributing factor.[11] This is important as it has been shown that even light static exercise can induce a greater increase in HR and BP than dynamic exercise at the same VO_2 level.[40]

Mean oxygen extraction in the muscle of the arms is closely related to the mean in vivo P50 value (oxygen tension when haemoglobin is 50% saturated with oxygen).[41] For a given P50, the upper extremities extract less oxygen than the lower extremities, which is associated with lower oxygen conductance.[41] Therefore, for a given oxygen demand, a greater oxygen delivery is needed for exercising arms than leg muscles, resulting in greater cardiovascular strain.[42] This lower oxygen extraction in the arms is associated with several factors including a higher heterogeneity in blood flow distribution, shorter mean transit times, a smaller diffusing area and a larger diffusing distance in arm muscle when compared with leg muscles.[41]

This all leads to an earlier AT when exercising with the arms, and this needs to be considered when using AE CPET in a clinical population such as those requiring preoperative assessment. In our study cohort, 62 (53%) participants demonstrated an AT of <11 mL.kg.min with a normal range of between 9.50 and 13.30 mL.kg.min. This highlights the importance of using modality-specific recommendations when using CPET for preoperative risk stratification and prognosis. Further work is required to identify AE CPET risk thresholds prior to its wider adoption for preoperative assessments. The clinical application of other parameters such as the VE/VCO_2 and VO_2/WR slopes also needs to be further evaluated as they have been demonstrated in this cohort to be significantly greater than the values achieved when exercising with the legs. A higher VO_2/WR slope can be explained by the lower mechanical efficiency when exercising with the arms, a greater contribution of accessory muscles and a higher cardiovascular strain. The higher VE/VCO_2 slope could be influenced by the lower peak VCO_2 generated when exercising with the arms. There is also the potential for compromised respiratory muscles when exercising with the arms due to the mechanical restraints of stabilising the torso and positioning the arms, which can influence tidal and end-expiratory lung volumes.[43 44]

The implementation of the predicted values and reference ranges developed in the current study for routine CPET parameters does have the potential, however, to improve the interpretation of AE exercise tests and standardise interpretation across sites in the UK. The data will enable the assessment of clinical populations against a normal range with the view to developing interpretation strategies for a range of clinical interventions.

Study limitations

Participants were deemed suitable for this study subject to successful completion of health screening and normal baseline measurements of spirometry, BP and ECG. It is, however, recognised that normal spirometry does not preclude a normal gas transfer (TLCO) in a symptomatic population.[45] pVO_2, VE/VCO_2 slope and oxygen pulse all rely on effective oxygen diffusion and therefore the lack of TLCO data in our subject cohort may lead to bias by assuming homogeneity of lung function that does not exist. Excluding TLCO data from CPET regression equations may compromise their reliability; however, this has been demonstrated to be more of a risk in populations where potential pulmonary limitations are more likely than in our cohort.[45 46]

The performance of CPET relies on the concomitant measurements of ECG and BP. Both provide important clinical information on the cardiovascular response to exercise, but they also allow the identification of test termination criteria relating to patient safety. The most common site for BP measurement is the upper arm; however, AE exercise limits accurate measurement due to continual movement of the arm during testing. The lower leg is the most commonly chosen site for BP measurements when the arm is not possible; however, the large muscle bulk of the gastrocnemius, soleus and plantaris muscles leads to significantly increased participant discomfort during measurements.[47] Previous studies have suggested BP measurements can be taken from the participants' ankle using the posterior tibial artery due to ease of access, similar circumference to the arm muscles and lack of muscle bulk providing a more comfortable and tolerable mode of measurement.[48]

Unfortunately, the BP device used in our study repeatedly failed to obtain measurements when positioned on the ankle. Oscillometric BP measurements have previously been demonstrated to be a reliable alternative to conventional BP measurements made at the ankle.[49 50] The poor reliability of the readings in the current study may, therefore, relate to the BP device itself which is not listed on the British and Irish Hypertension Societies list of recommended oscillometric devices for specialist use.[51] As a result, accurate measurement of BP was not possible during AE testing. Due to the low risk of exercise-induced hypertension in the study population, this was not considered to pose a safety risk. However, prior to any further work in patient populations, it will be essential to identify equipment that will accurately measure ankle BP so that test termination criteria can be identified and acted on accordingly.

The reference values developed are from a study population aged 19–69 years of age; however, it should be recognised that only two subjects over 60 years were recruited. The applicability of the reference values to an older population is, therefore, not known. We recommend the results from individuals aged above 75 years should be interpreted with a degree of caution. The use of these predicted values and reference ranges is, however, still recommended as the alternative equations have additional significant limitations.

Our study methodology included the completion of the RPAQ to quantify the level of activity regularly undertaken by participants in an attempt to limit participation bias. Unfortunately, participants found the questionnaire difficult to accurately answer and demonstrated a tendency to over-report their sporting activities. Other studies have also suggested that these questionnaires have limited reliability and validity due to over-reporting of exercise rates and frequency, with the highest levels of physical activity having the greatest discrepancy with actual activity levels.[52–54]

In conclusion, the current study of 116 healthy male and female volunteers aged 19–69 years has provided data for the development of predicted values and reference ranges for VO_2, anaerobic threshold, WR, peak VE, peak HR, oxygen pulse and the VE/VCO_2 and VO_2/WR slopes obtained using AE exercise. This is the largest data set for AE reference values to date and represents the widest age range for healthy individuals.

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