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ORIGINAL ARTICLE

Relationship between oxygen pulse and arteriovenous oxygen difference in healthy subjects: Effect of exercise intensity

Relation entre le pouls d'oxygène et la différence artérioveneuse chez le sujet sain : effet de l'intensité de l'exercice

N. Gmada[a,b,*], B. Al-Hadabi[a], R. Haj Sassi[a,b], B. Abdel Samia[a], E. Bouhlel[c]

[a] *Physical Education and Sport Sciences Department, College of Education, Sultan Qaboos University, Muscat, Sultanate of Oman*
[b] *Research Unit, ''Sportive Performance and Physical Rehabilitation'', High Institute of Sports and Physical Education, Kef, University of Jendouba, Jendouba, Tunisia*
[c] *Laboratory of Physiology, Faculty of Medicine of Sousse, University of Sousse, Sousse, Tunisia*

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KEYWORDS
Impedance cardiography;
Oxygen uptake;
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Submaximal exercise;
Maximal exercise

Summary
Aims. — Aims were to assess: (1) the relationships between oxygen pulse and areteriovenous oxygen difference; and (2) the reproducibility of cardiac output and stroke volume values during submaximal and maximal exercises.
Methods. — Twelve healthy male participated in the study. They were tested on five occasions, separated by periods of 3 days. After tests familiarization, they performed a duplicate progressive maximal exercise on a cycle ergometer to measure maximal oxygen uptake, maximal aerobic power, maximal cardiac output, maximal Stroke Volume and maximal Heart rate. At the fourth and fifth visits, subjects performed two graded submaximal physical exercises. Values collected during duplicated submaximal and maximal exercises were used for the assessment of the reliability of cardiovascular measurements.
Results. — We found no significant differences between cardiac output and stroke volume values in both first and second trial. All coefficients of variation were under 10% and intra class correlation coefficients values were high than 0.90 during submaximal and maximal exercises. The

* Corresponding author.
E-mail address: ngmada@yahoo.fr (N. Gmada).

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linear regression analyses indicated high r-squared between oxygen pulse and areteriovenous oxygen difference until 50% of maximal aerobic power. However, at 60% and 100% of maximal aerobic power, this relationship was not found. We found significant increases of stroke volume ($P < 0.05$) between each two successive bouts from rest until 40% of maximal aerobic power, after that, stroke volume values were stabilized. In contrast, we found a progressive increase of oxygen pulse ($P < 0.05$) and areteriovenous oxygen difference ($P < 0.05$) from rest until maximal exercise.
Conclusion. — Using the impedance device, cardiac output and stroke volume values were reproducible during submaximal and maximal exercises. Oxygen pulse could be a predictor of arteriovenous oxygen difference during submaximal exercise (until 50% of the maximal aerobic power) in healthy subjects.

MOTS CLÉS
Impédance cardiographie ;
Consommation d'oxygène ;
Fréquence cardiaque ;
Extraction d'oxygène ;
Exercice sous-maximal ;
Exercice maximal

Résumé
Objectifs. — Objectifs étaient (1) d'étudier la relation entre le pouls d'oxygène et la différence artérioveneuse en oxygène ; et (2) de vérifier la reproductibilité du débit cardiaque et du volume d'éjection systolique durant les exercices progressifs sous maximaux et maximaux chez des sujets sains.
Méthodes. — L'étude a porté sur 12 sujets. Ils ont été testés à cinq occasions, séparées par des périodes de trois jours. Après les séances de familiarisation, chaque sujet a effectué un double exercice progressif maximal sur ergocycle afin de mesurer la consommation maximale d'oxygène, la puissance maximale aérobie, le débit cardiaque maximal, le volume d'éjection systolique maximal et la fréquence cardiaque. Lors du quatrième et cinquième visites, les sujets ont effectué deux exercices progressifs sous-maximaux. Les valeurs mesurées lors des exercices progressifs sous-maximaux et maximaux ont été utilisées pour vérifier la reproductibilité des mesures cardiovasculaires.
Résultats. — Aucune différence significative n'a été observée entre les valeurs du débit cardiaque et du volume d'éjection systolique mesurées dans les premiers et deuxièmes essais. Tous les coefficients de variation étaient inférieurs à 10 % et tous les coefficients de corrélation intra-classes étaient supérieurs à 0,90 pour les exercices progressifs sous-maximaux et maximaux. Les régressions linéaires ont révélé un r-carré élevé (supérieur à 50 %) entre le pouls d'oxygène et la différence artérioveneuse en oxygène jusqu'à 50 % de la puissance maximale aérobie. Cependant, à 60 % et 100 % de la puissance maximale aérobie, cette relation n'a pas été trouvée. Du repos jusqu'à 40 % de la puissance maximale aérobie, les valeurs du volume d'éjection systolique ont augmenté significativement ($p < 0,05$) entre chaque deux paliers successifs de l'exercice sous-maximal. De plus, nous avons relevé une augmentation significative du pouls d'oxygène ($p < 0,05$) et de la différence artérioveneuse en oxygène ($p < 0,05$) du repos jusqu'à l'exercice maximal.
Conclusion. — Les mesures du débit cardiaque et du volume d'éjection systolique par méthode non invasive (bioimpédance) durant les exercices progressifs sous maximaux et maximaux sont reproductibles. Le pouls d'oxygène pourrait être un prédicteur de la différence artérioveneuse en oxygène au cours de l'exercice progressif sous-maximal (jusqu'à 50 % de la MAP) chez le sujet sain.

1. Introduction

The assessment of cardiovascular activities during rest and/or physical exercise is provided mainly by the cardiac output (CO), stroke volume (SV) and heart rate (HR). Otherwise, increases in CO during physical exercise are governed by changes in SV and/or HR, reflecting a central cardiorespiratory component of the physical exercise-induced adaptation [1].

During physical activities, the increase of CO is normally associated with respiratory adaptations. On the other hand, several studies showed that during physical exercise and/or after endurance training, an increase of CO is associated with increased of oxygen uptake [2—5]. The increase of CO and oxygen consumption during physical activities is directly related to health status [6,7], age [4,8,9], gender [10,11], intensity and/or duration of exercises [2], and physical fitness level of the subject [5,11,12].

According to the Fick equation, every adaptation influencing oxygen uptake is almost reflected by a change in CO and/or arteriovenous oxygen difference ($\left(a-\overline{v}\right)O_2$). The CO being a central cardiovascular factor related to oxygen transport and depends essentially from stroke volume, which is the amount of blood pumped by the left ventricle of the heart in one contraction.

The $\left(a-\overline{v}\right)O_2$ is a muscular peripheral factor related mainly to oxygen utilisation [13]. It represents the difference in blood oxygen content between the arterial and the venous compartment. The $\left(a-\overline{v}\right)O_2$ is an indicator of how much oxygen is extracted and used by muscles. During physical exercise, the ability of oxygen extraction is directly related to the athlete's physical fitness level [14]. This ability depends essentially on extrinsic factors such as O_2 delivery and on intrinsic ones that regulate both O_2transfer from erythrocytes to the mitochondria and the subsequent utilization in the mitochondria [15].

Oxygen pulse (O_2 pulse) is calculated by the ratio of oxygen uptake and HR, where oxygen uptake is central respiratory parameter and HR being a central cardiovascular parameter. This parameter indicates the volume of oxygen taken up by the pulmonary blood during a heartbeat and depends on the volume of oxygen extracted by the peripheral tissues [16]. Some authors have suggested that this parameter could be used for diagnostic in patients with risk of heart disease patients [16—19], in healthy and in athletes [20,21] to assess and/or to improve physical fitness level.

In addition, several studies have examined the relationship between O_2 pulse and SV during physical exercise in patients [16—19] and in healthy/athletes [20,21]. However, until now, the relationship between O_2 pulse and $\left(a-\overline{v}\right)O_2$ has not been precisely studied. Our study tried to clarify this relationship during physical exercise.

Therefore, the aims of the present study were to examine the relationship between O_2 pulse and $\left(a-\overline{v}\right)O_2$ and to assess the reproducibility of CO and SV values during submaximal and maximal exercises in healthy subjects.

2. Material and methods

2.1. Subjects' characteristics

Twelve healthy male students participated in this study after receiving the description of the protocol and information about risks and benefits of the study. All of them gave their written informed consent to participate in the study as approved by the human research local ethics committee. Participants are not smokers, nor taking drugs nor drinking alcohol. All subjects had been pronounced healthy following a standard clinical examination. The anthropometric and physical characteristics of the subjects are presented in Table 1.

2.2. Experimental design

Subjects visited the laboratory on five occasions, separated by periods of 3 days. Testing was undertaken consistently between 08 h and 10.30 h in the morning after a 12 h fast under the same climatic conditions (temperature ranges: 20—23°C; and relative humidity: 60 ± 2%). Visit 1 included anthropometric measurements and a familiarization with the tests procedure. During the second and third visit, a duplicate progressive maximal exercise tests ($E1_{max}$—$E2_{max}$) were conducted using a cycle ergometer (Monark, 894E, Vansbro, Sweden) to measure Maximal oxygen uptake (VO_{2max}), Maximal Aerobic Power (MAP), maximal Cardiac output (CO_{max}), maximal Stroke Volume (SV_{max}) and maximal Heart rate (HR_{max}). At the fourth and fifth visit, all subjects performed two graded submaximal physical exercises ($E1_{submax}$—$E2_{submax}$) using the same cycle ergometer, and measuring the same cardiovascular and respiratory parameters. Blood lactate has been measured during recovery after graded submaximal and maximal exercises. The data collected during $E1_{max}$—$E2_{max}$ and $E1_{submax}$—$E2_{submax}$were used for the assessment of the reliability of cardiovascular measurements.

2.3. Progressive maximal exercise test

The progressive maximal exercise test was performed according to the protocol proposed by Hansen et al. [22], on a cycle ergometer (Monark 894E, Vansbro, Sweden) to assess VO_2max and maximal aerobic power (MAP). The test began by 3 minutes warm-up at 20% of predicted maximal aerobic power, and the power output increased by 8% every minute until exhaustion. A pedal frequency of 60—70 rpm was paced by metronome, to help participants following the rhythm imposed. The subject stops when he is unable to sustain the exercise intensity even after verbal encouragements. A plateau of oxygen uptake was adopted as a principle criterion to indicate VO_2max. Secondary criteria were also used to verify the maximality of the exercise, such as the maximal values of respiratory exchange ratio, and heart rate [22].

2.4. Submaximal graded exercise tests

The submaximal graded test was performed according to the protocol proposed by Brandou et al. [23], and using the same cycle ergometer. This test has been commonly used to assess metabolic indices, the crossover and the maximal fat oxidation points [24,25]. After 3 min passive rest, each subject underwent five bouts of six min-steady-state workload corresponding to 20, 30, 40, 50, and 60% of Maximal aerobic power. A pedaling frequency of 60—70 rpm was imposed during the test.

2.5. Metabolic measurements

$\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ were measured during progressive maximal test and submaximal graded tests using breath by breath analysis system (Quark b^2, Cosmed, Rome, Italy).

$\dot{V}O_2$, $\dot{V}CO_2$ and $\dot{V}E$ values were averaged over the last two minutes of each bout of submaximal grade exercise. Peak oxygen was recorded as the highest $\dot{V}O_2$ obtained using 30 s data averaging of the last bout of the progressive maximal test [26].

Arterial capillary blood samples were taken from the fingertip. Lactate concentrations were measured after 3 min of passive recovery using a pro lactate analyzer (Akray Inc., Kyoto, Japan) to assess the metabolic stress associated with submaximal graded exercise and maximal exercise.

Table 1 Anthropometric and physical fitness characteristics of the subjects (n = 12).

Age (years)	Height (cm)	Body mass (kg)	BMI	Fat %	MAP (watts)	VO_2max (mL/min/kg)
20.5 ± 1.0	182 ± 10	72.4 ± 12.9	21.7 ± 2.7	12.1 ± 1.2	220 ± 39	45.8 ± 6.2

Data are expressed as means ± SD; BMI: body mass index; Fat %: body fat (%); MAP: maximal aerobic power; VO_2max: maximal oxygen uptake.

2.6. Cardiac parameters measurements

CO, SV and HR were measured during the tests used in this study (submaximal graded exercise and progressive maximal exercise) using impedance cardiography (Physio Flow PF-05 Lab1, Manatec Biomedical, Paris, France).

Before starting each exercise protocol and after cleaning the skin with alcohol, the subject was attached to the impedance cardiograph electrodes of Physio Flow device. A constant sinusoidal alternating current (1.8 mA, 75 kHz) was applied between the couples of electrodes placed on the supra clavicular fossa at the left base of the neck and along of xiphoid. The associated voltage was detected by two pair's electrodes positioned 5 cm apart from the corresponding couples of electrodes that were parallel to the current path. This voltage was transmitted to the amplifier and an impedance signal (z) was produced. Cardiac output measurement by the Physio Flow is based on the following formula:

$$Qc = HR \times SVi \times BSA$$

where Qc is cardiac output (l/min), HR is heart rate, based on R-R interval measurements, determined on the ECG first derivative which provides a more stable signal than the ECG signal itself, BSA is the body surface area, and SVi is the stroke volume index [27].

The SVi was calculated using the formula of Sramek-Bernstein:

SVi = volume of electrically participating intra thoracic tissue × ventricular ejection time index of contractility, which was the ratio of the peak rate of change in the thoracic bio-impedance (dZ/dt_{max}) and the thoracic fluid index or total thoracic impedance. The system was calibrated while the participant was seated on the cycle ergometer.

CO, SV and HR values were averaged over the last two minutes of each bout of submaximal graded exercise. Peak values of these parameters were obtained using 30 s data averaging of the last bout of the progressive maximal test [26].

2.7. $\left(a-\bar{v}\right)O_2$ and O_2 pulse calculation

Gas exchange and cardiac parameters data were averaged every 5 sec. For each parameter, the start of the test was marked while recording. This measured point permitted to obtain a single synchronous database for all parameters. The $\left(a-\bar{v}\right)O_2$ was estimated using the Fick equation: $\dot{V}O_2 = CO\,x\,\left(a-\bar{v}\right)O_2$. Data of $\left(a-\bar{v}\right)O_2$ has been calculated by dividing $\dot{V}O_2$ by CO values averaged over the corresponding time interval and expressed in ml.100 mL^{-1}. This approach was validated during both constant-load and incremental physical exercises [27,28] and used to describe $\left(a-\bar{v}\right)O_2$ evolution during physical exercise [29]. O_2 pulse was calculated by dividing $\dot{V}O_2$ by HR obtained every 5 sec by Quark b^{2}and expressed in ml. beat^{-1}.

2.8. Statistical analyses

The normality of the data was verified using kolmogrov-Smirnov test. All data are presented as mean ± standard deviation (SD). We assessed the relative reliability of CO and SV using the intra class correlation coefficient (ICC) and Student t test for paired samples. We considered an ICC over .90 as high, between .80 and .90 as moderate, and below .80 as low [30]. The precision of our estimates of outcome statistics are shown as 95% confidence intervals (95% CI), which define the likely range of the true value in the population from which the sample was drew.

Absolute reliability is the degree to which repeated measurements vary for individuals and we expressed this form of reliability with the coefficient of variation [31].

To determine the relationship between O_2 pulse $-\left(a-\bar{v}\right)O_2$, linear regression analysis was conducted using raw values of O_2 pulse and $\left(a-\bar{v}\right)O_2$ obtained at each exercise level of the study protocol. The corresponding strength was assessed using Pearson's correlation coefficient (R). All statistical analyses were performed using the SPSS Statistics version 22 (SPSS Inc., Chicago, IL, USA). A value of $P < 0.05$ was accepted as the minimal level of significance.

3. Results

Descriptive data for anthropometric and physiological characteristics are summarized in Tables 1 and 2. Relative and absolute reliability parameters of CO and SV are presented in Table 3.

Results showed no significant differences between cardiac output and stroke volume values in first and second trial. All coefficients of variation were under 10% and ICC values were high for cardiac output and stroke volume during submaximal and maximal exercises (Table 3). In addition, a CI at 95% showed that the proportion is between 0.65 and 0.98 (Table 3).

Linear regression analyses indicated high R-squared between O_2 pulse and $\left(a-\bar{v}\right)O_2$ from the rest until the intensity of 50% of MAP (Fig. 1A—E). At 60% of MAP, R-squared was 0.45 only (Fig. 1F). The decrease was very important at 100% of MAP ($R^2 = 0.06$, Fig. 1G).

Fig. 2 shows the relationships between O_2 pulse, $\left(a-\bar{v}\right)O_2$ and stroke volume related to exercise intensities. We found significant increases of stroke volume ($P < 0.05$)

Table 2 Physical and physiological characteristics of subjects (n = 12).

MAP (watts)	VO_2max (mL/min/kg)	$[La]_{max}$ (mmol.L^{-1})	[La]60%MAP (mmol.L-1)
220 ± 39	45.8 ± 6.2	11.1 ± 1.31	5.03 ± 1.47

Data are expressed as means ± SD; MAP: maximum aerobic power; VO_2max: maximal oxygen uptake; [La]: blood lactate concentration.

between each two successive bouts from rest until 40% MAP, after that, stroke volume values were stabilized in our healthy subjects. In contrast, we found a progressive increase of oxygen pulse and $(a - \bar{v})\, O_2$ from rest until maximal exercise intensities.

4. Discussion

The main findings of the present study are the good reproducibility of cardiac output and stroke volume values when using the impedance technology. Indeed, variation coefficients were under 10% between the first and the second trial for these parameters during submaximal and maximal exercises. Moreover, study results found high significance correlations between O_2 pulse and arteriovenous oxygen difference at rest and during submaximal graded exercise ranging from 20% to 50% of MAP in healthy subjects. However, at 60% and 100% of MAP, this relationship was not found. In addition, despite the stabilization of stroke volume at 40% MAP, oxygen pulse and $(a - \bar{v})\, O_2$ continue to rise progressively until reaching maximal exercise in our healthy subjects.

When assessing the reproducibility of cardiac output and stroke volume values between the first and the second trial, we found that CV values were less than 10% and a high ICC for cardiac output and stroke volume during submaximal and maximal exercises. The physio flow device used in this study was accurate in determining cardiac output and stroke volume of our subjects. Other authors also showed the accuracy of the impedance technology during steady state submaximal exercises ranging between 40.1% and 88.3% of VO_2max [32].

Tordi et al. [33] reported that assessment of cardiac output by electric impedance furnish good data and may substitute the CO_2 rebreathing method during moderate to high steady-state exercise. Welsman et al. [34] also used this non-invasive method in children and found a good reliability of stroke volume, but this reliability was reduced compared with Doppler echocardiography (5%) or CO_2 rebreathing method (12%) at maximal exercise.

In addition, we found significant correlations between O_2 pulse and $(a - \bar{v})\, O_2$ with high r-squared from the rest until the intensity of 50% of MAP. At 60% of the MAP, r-squared was relatively low ($R^2 = 0.45$, Fig. 1F), But the decrease was very important at 100% of MAP ($R^2 = 0.06$, Fig. 1G). Our results support the close relationship between O_2 pulse response and $(a - \bar{v})\, O_2$ during submaximal graded exercise in healthy subject's as shown by the high R^2, thus showing that the O_2 pulse could be a powerful predictor of $(a - \bar{v})\, O_2$ during submaximal graded exercise (until 50% of the MAP). However, the more pronounced increase in O_2 pulse values compared to $(a - \bar{v})\, O_2$ at 60% and 100% of the MAP (Fig. 2) would lead to a reduced R^2 mainly during maximal exercise. This could be explained by the increase of the activation of anaerobic processes during maximal exercise. High blood lactate concentrations obtained at 100% PMA in this study (11.1 ± 1.31 mmol/L, Table 2) may explain the increased solicitation of anaerobic processes and thus support this hypothesis.

Recently, Murata et al. [16] pointed out that O_2 pulse depends on several physiological factors including the volume of oxygen extracted by the peripheral tissues. O_2 extraction could be reduced during maximal intensities and this may induce the solicitation of the anaerobic pathways.

Several studies have shown that O_2 pulse is not a simple variable to consider, because it can be influenced by many factors such as the presence of diastolic dysfunction [35], valvular regurgitation [36], physical fitness level [37], testing protocol [38] and body dimensions [39].

But despite this, it is considered a very important physiological parameter, because it can inform us about some central and/or peripheral physiological indicators related to physical fitness level in healthy and/or sports subjects [20,21] and can be a powerful predictor of mortality in patients with cardiovascular diseases [19]. In addition, it is interesting to notify that O_2 pulse reached steady state values over the last 3-min of each 6-min step, as observed with O_2 and VCO_2 during the graded submaximal test in our participants. This data could provide the basis for a new utilization of the graded 6-min step submaximal test proposed by the Montpellier team [23].

We found significant increases of stroke volume ($P < 0.05$) between each two successive bouts from rest until 40% of MAP, after that stroke volume values were stabilized. In the other hand, we found a progressive increase of oxygen pulse and $(a - \bar{v})\, O_2$ from rest, to submaximal graded exercise, and maximal exercise intensities. Our result is in agreement with Oliveira et al. [20] study who found after excluding the first minute of exercise (rest-exercise transition) that the relative O_2 pulse showed a stable linear increase throughout maximal exercise in non athlete's adults. According to the authors, excluding the first minute of exercise permits the direct use of the O_2 pulse slope, without calculating the VO_2 and HR slopes. A novel finding shown in the present study is the parallel increase in O_2 pulse and $(a - \bar{v})\, O_2$ from rest to maximal exercise in our healthy subjects.

In patients with coronary heart disease, Belardinelli et al. [18] found that O_2 pulse flattening duration and the slope of VO_2/workload were the main predictors of a positive myocardial scintigraphy. Indeed, as work rate increased, an inflection point was evident in most patients with detectable myocardial ischemia. According to the authors, the O_2 pulse

Table 3 Variation coefficients and intra class correlation coefficients with confidence limits of cardiac output and stroke volume calculated over two trials for submaximal graded exercise and progressive maximal exercise tests.

	Mean ± SD	*P* (Paired T test)	ICC	CI 95%	CV (%)
Rest					
CO (L/min)					
1st trial	6.11 ± 0.18	.26	.93	.75—.98	2.68
2nd trial	6.07 ± 0.22				
SV (mL)					
1st trial	75.16 ± 6.40	.68	.91	.70—.97	4.74
2nd trial	74.72 ± 6.26				
20% of MAP					
CO (L/min)					
1st trial	8.72 ± 1.52	.43	.93	.76—.98	8.65
2nd trial	8.54 ± 1.43				
SV (mL)					
1st trial	87.56 ± 11.54	.85	.93	.77—.98	6.30
2nd trial	87.25 ± 10.09				
30% of MAP					
CO (L/min)					
1st trial	11.02 ± 1.86	.39	.91	.68—.97	9.59
2nd trial	11.29 ± 1.84				
SV (mL)					
1st trial	96.11 ± 11.79	.58	.92	.74—.97	6.86
2nd trial	97.20 ± 13.24				
40% of MAP					
CO (L/min)					
1st trial	13.12 ± 2.12	.46	.92	.74—.98	8.28
2nd trial	13.36 ± 2.05				
SV (mL)					
1st trial	100.99 ± 11.14	.16	.95	.83—.98	4.90
2nd trial	103.17 ± 11.93				
50% of MAP					
CO (L/min)					
1st trial	14.87 ± 1.70	.57	.92	.73—.97	7.61
2nd trial	14.68 ± 2.40				
SV (mL)					
1st trial	102.58 ± 8.82	.48	.94	.79—.98	4.88
2nd trial	103.65 ± 11.93				
60% of MAP					
CO (L/min)					
1st trial	16.22 ± 1.07	.75	.90	.65—.97	4.85
2nd trial	16.30 ± 1.48				
SV (mL)					
1st trial	103.78 ± 8.03	.88	.95	.82—.98	3.96
2nd trial	103.96 ± 10.39				
100% of MAP					
CO (L/min)					
1st trial	21.45 ± 2.03	.63	.91	.70—.97	5.14
2nd trial	21.61 ± 1.90				
SV (mL)					
1st trial	107.83 ± 9.68	.49	.92	.70—.98	4.88
2nd trial	108.94 ± 9.29				

CO: cardiac output; SV: stroke volume; ICC: intra class correlation coefficient; CI 95%: confidence interval at 95%; CV: variation coefficient expressed as a percentage. Data are expressed as means ± SD.

reduction observed is likely explained by reduced stroke volume at higher intensity exercise due to myocardial ischemia.

According to the Fick equation, VO_2 equals the product of cardiac output and arteriovenous oxygen difference. In our study, SV increases with the intensity of exercise until 40% MAP, showing a plateau after that. The arteriovenous oxygen difference and O_2 pulse increased progressively until the end of the maximal exercise. The progressive

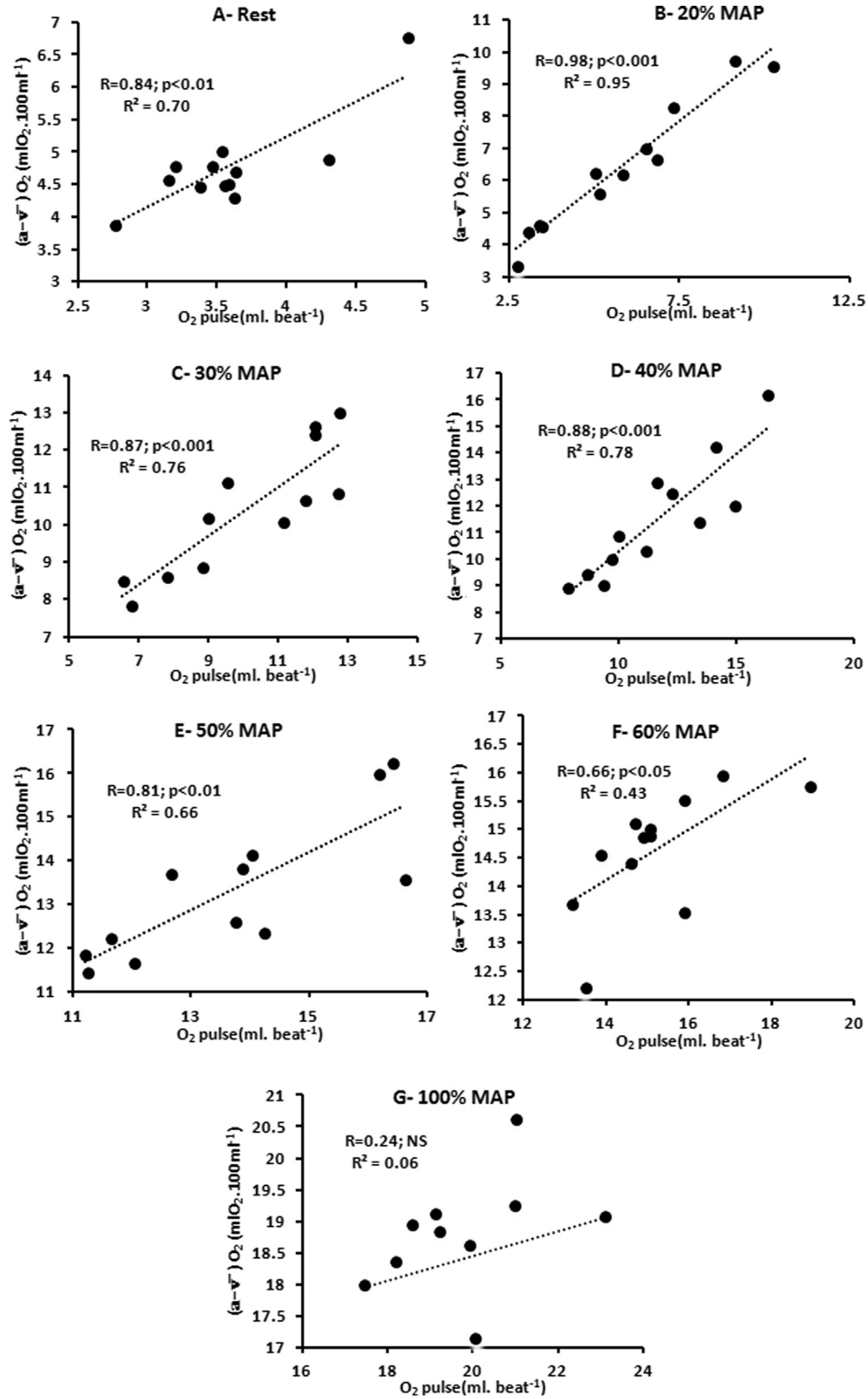

Figure 1 Relationship between O_2 pulse and arteriovenous oxygen difference at rest (A), 20% (B), 30% (C), 40% (D), 50% (E), 60% (F) and 100% (G) of the maximal aerobic power.

increase of these parameters is most likely attributed to the heart rate rise. It is well established that for intensities greater than 40—50% VO_2max, the increase in cardiac output is achieved solely by an increase in heart rate, stroke volume increases rectilinearly initially and then plateaus at approximately 40—50% of VO_2max [40]. Some authors suggested that stroke volume may decrease slightly near the end of maximal exercise in untrained and moderately

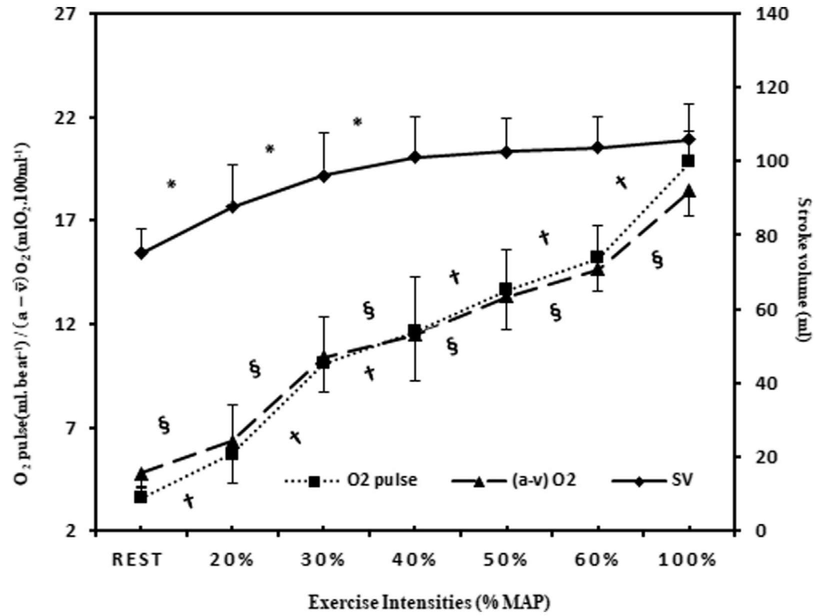

Figure 2 SV, O_2 pulse and $\left(a-\overline{v}\right)O_2$ values during submaximal graded exercises and at the last bout of progressive maximal exercise tests. Significance at $P < 0.05$ between each two successive bouts for: stroke volume (*); O_2 pulse (†); arterio-venous O_2 difference (§). Data are expressed as means ± SD.

trained subjects [41]. Regulator mechanisms related to SV increases are related to the enhancement of left ventricular end—diastolic volume thanks to the return of blood to the heart by the active muscle pump and the increase of sympathetic outflow to the veins causing venoconstriction and augmenting venous return. Left ventricular end—systolic volume decreases because of augmented contractility of the heart, which ejects more blood from the ventricle. The relative contribution of the stroke volume and the arteriovenous oxygen difference depends on many factors, such as the exercise intensity and the physical fitness of the subject. Lepretre et al. [42] pointed out that VO_2max reached during the incremental test resulted in a greater maximal cardiac output compared with the constant p50 workload time to exhaustion exercise. The lower stroke volume seems to be the main factor of the non achievement of maximal cardiac output during time to exhaustion exercise, whereas VO_2 reached its maximal value in the both cases. According to the authors, VO_2max was not reached with the same central and peripheral factors in exhaustive exercises performed at about 88.0 or 100% of MAP in well-trained males.

In soccer players, Perimet al. [21] found that relative O_2 pulse (expressed in terms of the subject body mass) increased linearly up to 90% of the running time. Between 90 and 100% of the running time, values were less stable, with up to 50% of the players showing a tendency to a plateau in the relative O_2 pulse.

5. Conclusion

Cardiac output and stroke volume values using the impedance device were reproducible during submaximal and maximal physical exercises. In addition, our study is the first to demonstrate that Oxygen pulse could be a powerful predictor of arteriovenous oxygen difference during submaximal graded exercise (until 50% of the MAP) in healthy subjects. During incremental exercise, SV increases until 40% of MAP and then stabilizes. In contrast, oxygen pulse and $\left(a-\overline{v}\right)O_2$ increase progressively from rest to maximal exercise. Considering our data and mainly the association between O_2 pulse and $\left(a-\overline{v}\right)O_2$, it would be of importance to add $\left(a-\overline{v}\right)O_2$ evaluation during the graded submaximal test which is mostly designed to assess CHO and lipid utilization, and also to study the association between O_2 pulse and $\left(a-\overline{v}\right)O_2$ in trained or in patients with myocardial ischemia.

Disclosure of interest

The authors declare that they have no competing interest.

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