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ORIGINAL PAPERS, CLINICAL CARDIOLOGY

Relationship between Exercise Hemodynamic and Cardiopulmonary Indices as Measured in Cardiac Patients by Two Separate and Specific Tests

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Background: Direct non-invasive hemodynamic evaluation becomes more and more familiar due to the relatively new impedance cardiography (ICG) test. On the other hand, the cardiopulmonary exercise test (CPET) is well-known as a reliable physiological test for indirect hemodynamic evaluation through CPET indices and the Fick formula. Aim of Study: To correlate and cross-match between direct and indirect hemodynamic indices as measured during exercise by the 2 tests, the ICG and the CPET, separately. Material and Methods: 30 cardiac male patients (pts), aged 41–74 yrs, with documented IHD, who underwent both, ICG and CPET separately and up to 2 weeks apart, were included in the study. Linear correlations were done between all the indices of both tests. Values of $R > 0.6$ and $p < 0.05$ were considered statistically significant. Results: Significant correlations were found between peak-HR of the CPET and the following ICG indices: Peak-CI (Cardiac Index) – $R = 0.74$; $p < 0.0001$; Peak-CO (Cardiac Output) – $R = 0.72$; $p < 0.0001$; Peak-SI (Stroke Index) – $R = 0.72$; $p < 0.0005$. Other specific correlations were shown between: Peak-CI and Peak-VO_2: $R = 0.82$; $p < 0.0001$; Peak-CO and Peak-VO_2: R = O.72; $p < 0.001$; Peak-SI and Peak-O_2P: $R = 0.76$; $p < 0.001$; Peak-SV and Peak-O_2P: $R = 0.76$; $p < 0.001$. Conclusions: Such significant and crossover correlations between the indices of both above tests may validate the ICG indices as reliable for non-invasive hemodynamic evaluation and may further establish the CPET indices for similar, though indirect, physiological assessment. **J Clin Basic Cardiol 2010; 13 (online): 4–7.**

Key words: *cardiopulmonary exercise testing, impedance cardiography, ischemic heart disease*

Accuracy is an important factor to validate a diagnostic test or to monitor technology. It is defined as the degree to which a given test provides measured indices in agreement with a known reference standard.

Impedance cardiography (ICG) is a non-invasive hemodynamic diagnostic test and monitoring technology [1]. In recent years, ICG has established a role in outpatient management of patients (pt) with various hemodynamic disorders or diseases like hypertension, heart failure, and other chronic cardiac diseases [2, 3], while demonstrating improved accuracy by the most recent generation of ICG technology [4–7]. The ICG test enables direct non-invasive measurements of indices like cardiac output (CO), cardiac index (CI), stroke volume (SV) and stroke index (SI), as well as many other hemodynamic indices.

On the other hand, the cardiopulmonary exercise test (CPET) provides for years a reliable non-invasive, though indirect, diagnostic and monitoring tool for functional-physiological evaluation of cardiac diseases as well as others [8–11]. By means of CPET, additional important clinical and functional information may be obtained, compared to regular exercise stress testing [12].

Indices measured by CPET among others are – oxygen consumption (VO_2) and oxygen pulse (O_2P) related to CO and SV respectively, as calculated from the former by the Fick equation, by which VO_2 is directly related to CO, and O_2P to SV, whereas CO or SV are multiplied by the difference between arterial (a) and venous (v) oxygen content – (a–v) O_2 content [13, 14].

The present study tries to correlate the relevant ICG and the CPET indices, while both tests were performed separately during exercise in all pts not more than 2 weeks apart, and under similar conditions. Such significant correlations, if found, might further establish the ICG test as a reliable tool for functional-physiological assessment of cardiac pts, and complete the CPET for this very purpose.

Material and Methods

Patients

We studied 30 pts, all male, aged 41–74 years, with documented ischemic heart disease (IHD) confirmed by coronary angiogram and/or imaging exercise tests (heart mapping or stress echocardiogram). The pts were selected consecutively from a pool of 74 pts according to the preliminary conditions of the study in which all pts underwent CPET followed by an ICG exercise test within 2 weeks, while using the same medications in both tests. Betablockers and calcium channel antagonists were stopped 24 hours before each test.

The study protocol was approved by the local ethics committee.

Cardiopulmonary Exercise Test

An upright symptom-limited test was performed on an electronically braked cycle ergometer (Ergoline 800). Exercise was initiated after a 3-minute rest and 2 minutes of free pedalling at a rate of 60 rpm. The effort was then progressively increased by 10–20 Watt/min until the predefined end-point was reached, namely, symptoms, volitional fatigue, or attainment of the target HR. Cardiopulmonary data were collected by an online metabolic unit (ZAN-GPI-3.00, Cardiopulmonary function, Germany).

Pts breathed through a low-resistance, 2-way valve, connected to the expiratory limb. The breath-by-breath signals were integrated by a computer to yield 30-sec and averages of HR, minute ventilation, VO_2, VCO_2 and O_2-P (VO_2/HR). VAT was defined as the point at which the ventilatory equivalent of O_2 (Ve/VO_2) increased in the absence of a similar increase in the ventilatory equivalent of CO_2 (Ve/VCO_2), as described by Beaver et al [15]. Blood pressure was measured at rest, every 2 minutes, at peak exercise and during recovery.

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Table 1. Summary of patient data (ICG and CPET) (n = 30, all male)

Age	p-HR ICG	SVr	SVe	COr	COe	SIr	SIe	CIr	CIe	P-HR CPET	Peak VO_2	Peak O_2-P	VAT
65	124	66	114	4.4	14.5	34	59	2.3	7.5	115	17.3	13	0.52
73	102	58	61	4	5	32	34	2.2	2.7	113	15.2	11	0.47
56	119	90	96	5.5	11.4	48	51	3	6.1	106	16	13	0.36
74	123	42	60	3.5	7.6	28	40	2.3	5	124	9.7	7.5	0.43
59	117	43	92	3.6	10.5	20	43	1.7	5	116	11.4	10	0.32
41	157	67	130	5	25.2	43	83	3.2	16.2	148	33.7	18	0.65
45	146	56	65	4.3	11.2	37	43	2.8	7.5	147	26.2	13	0.5
73	121	80	87	4.8	10.7	42	46	2.5	5.6	123	19.6	12	0.49
69	104	65	89	4.4	7.5	35	48	2.4	4.1	104	13.1	11	0.35
73	118	76	69	6.6	8.1	37	34	3.2	3.9	119	12.1	10	0.45
54	127	90	112	7	18.8	45	56	3.2	8.7	135	21.8	13	0.54
55	115	99	96	6.7	11.3	51	49	3.2	5.3	125	23.3	16	0.5
45	150	56	125	6	20.3	35	78	3.1	8.3	145	35	17	0.46
51	152	69	130	3.3	23	43	81	2.6	14	147	38	20	0.5
52	136	58	120	4.6	18.9	33	68	2.1	10	141	31	17	0.46
61	132	87	110	7.2	15	43	54	1.8	12	129	34	15	0.43
58	140	99	89	3.6	17.5	52	46	2.2	11	136	20	16	0.42
53	147	73	125	5.8	15.7	37	63	3.4	13.2	143	32	21	0.6
68	127	81	105	6.1	16.7	45	58	1.9	9	132	27	16.5	0.52
59	129	62	112	4.5	16.9	33	60	3.3	11.8	134	30	18.5	0.47
61	125	83	77	4.6	16	46	43	3.4	7.5	121	28	15.5	0.33
58	141	74	89	3.2	22	39	47	2.5	13.7	138	37	16	0.45
56	146	65	121	5.4	23.5	36	67	2.3	15.6	142	30	21	0.53
57	142	80	88	3	20.5	39	43	2.9	14.4	146	24	22	0.36
66	135	79	100	3.3	18	41	52	1.6	13.4	127	31	17.5	0.56
60	138	87	97	6.4	19.8	46	51	3.4	10.3	128	22	14.5	0.54
50	155	59	92	4.7	19	31	48	2.9	11.6	148	30.5	15.7	0.44
59	130	66	115	3.4	13	36	63	3.1	12.5	132	29	20.5	0.49
53	145	85	105	7.1	15	41	51	3.2	9.8	139	33.5	17.5	0.59
54	135	95	125	5.4	10.9	49	65	3.2	8.7	134	32	21	0.62

p-HR: peak heart rate (bpm); ICG: impedance cardiography; SVr/SVe: stroke volume at rest/exercise (cm^3); COr/COe: cardiac output at rest/exercise (l/min); SIr/SIe: stroke index at rest/exercise; CIr/CIe: cardiac index at rest/exercise; CPET: cardio-pulmonary exercise test; VO_2: oxygen consumption; O_2-P: oxygen pulse (cm^3/hb); VAT: ventilatory anaerobic threshold (%-fraction of predicted max. VO_2).

Impedance Cardiography Method

All ICG measurements were collected with the BioZ ICG Monitor (CardioDynamics, San Diego, CA, USA), at rest, at peak exercise, and during recovery. Four dual ICG sensors were placed on the patient, 2 above the base of the neck and just below each ear and one on either side of the thorax in the mid-axillary line at the level of the xiphoid. A cable with 8 ICG lead wires was attached to the individual sensor sites. A constant, low-amplitude, high-frequency alternating electrical current is applied to the thorax and the corresponding voltage changes are measured to calculate changes in thoracic impedance in accordance with Ohm's law. The baseline and changes in the impedance waveform are digitally processed to identify fiducial points that reflect the maximum blood velocity in the aorta (velocity index), the opening and closing of the aortic valve (left ventricular ejection time), and amount of fluid in the chest (thoracic fluid content). These directly measured variables are applied to an algorithm to calculate SV and CO and their indexed values of SI and CI. Other hemodynamic measurements such as systemic vascular resistance (SVR) and its index (SVRI), left cardiac work and its index, are calculated based on accepted equations used in invasive patient monitoring systems [16].

Table 2. Correlations between patient age and relevant indices of both tests

		r	p*
Age	CId	–0.79	0.00
	CIe	–0.83	0.00
	COd	–0.81	0.00
	COe	–0.81	0.00
	p-HR-ICG	–0.89	0.00
	p-HR-CPET	–0.86	0.00
	peak O_2-P	–0.71	0.00
	SId	–0.62	0.00
	SIe	–0.81	0.00
	SVd	–0.56	0.00
	SVe	–0.65	0.00
	peak VO_2	–0.83	0.00

$p = 0.00$ means $p < 0.005$ or less. p-HR: peak heart rate (bpm); ICG: impedance cardiography; SVe: stroke volume at exercise (cm^3); COe: cardiac output at exercise (l/min); SIe: stroke index at exercise; CIe: cardiac index at exercise; CPET: cardio-pulmonary exercise test; VO_2: oxygen consumption; O_2-P: oxygen pulse (cm^3/hb)

Table 3. Correlations between ICG indices and relevant CPET indices

		r	p*
CId	peak HR	0.70	0.00
	peak O_2-P	0.78	0.00
	peak VO_2	0.69	0.00
CIe	peak HR	0.74	0.00
	peak O_2-P	0.80	0.00
	peak VO_2	0.82	0.00
COd	peak HR	0.70	0.00
	peak O_2-P	0.69	0.00
	peak VO_2	0.68	0.00
COe	peak HR	0.72	0.00
	peak O_2-P	0.71	0.00
	peak VO_2	0.72	0.00
SId	peak HR	0.57	0.00
	peak O_2-P	0.75	0.00
	peak VO_2	0.69	0.00
SIe	peak HR	0.72	0.00
	peak O_2-P	0.76	0.00
	peak VO_2	0.78	0.00
SVd	peak HR	0.49	0.01
	peak O_2-P	0.63	0.02
	peak VO_2	0.61	0.00
SVe	peak HR	0.54	0.00
	peak O_2-P	0.76	0.00
	peak VO_2	0.71	0.00

* $p = 0.00$ means $p < 0.005$ or less. HR: heart rate (bpm); ICG: impedance cardiography; SVe: stroke volume at exercise (cm^3); COe: cardiac output at exercise (l/min); SIe: stroke index at exercise; CIe: cardiac index at exercise; VO_2: oxygen consumption; O_2-P: oxygen pulse (cm^3/hb).

Statistical Analysis

The CPET and the ICG indices were correlated by linear correlations. R values of at least 0.6 and P values < 0.05 were considered statistically significant.

Results

Table 1 summarizes patient data through the specific indices of the 2 tests: ICG and CPET.

Table 2 shows the correlations between the age of the pts and the relevant indices of both tests. The significant negative R values indicate, as expected, a decrease of these indices in parallel with age progression.

Table 3 demonstrates the correlations between the ICG indices and the relevant CPET indices.

From Table 3 it is observed that the relevant ICG indices, referred to cardiac output (COd, COe, CId and CIe), and stroke volume (SVd, SVe, SId and SIe), correlate well with the respect cardiopulmonary indices, namely peak-VO_2 and peak-O_2-P, in most cases. They also correlate positively well, with some lower R values, with peak-HR achieved during exercise. This very last finding may indicate that most of the pts who participated in the study did not demonstrate prominent ischemia during exercise since in such an ischemic reaction, a reduction in those indices is expected while HR increases, which might contribute to less correlation between these factors.

As the 2 tests were performed separately, a correlation between peak-HRs of both tests were done and showed a high statistical significance of $R = 0.906$ and $p < 0.0001$ (Fig. 1).

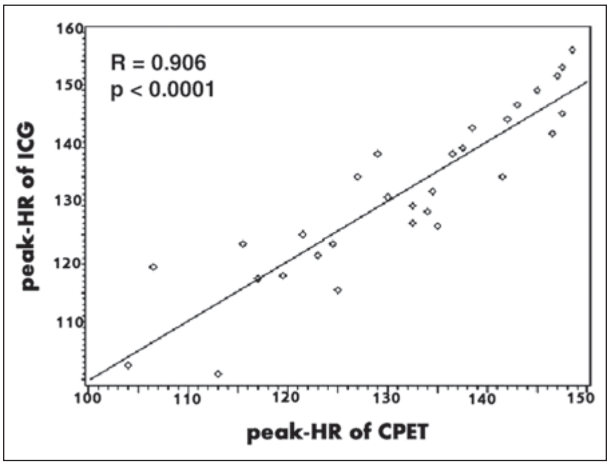

Figure 1. The relationship between HR of the CPET and HR of the ICG at peak exercise of both tests.

Such a correlation might further support the relationship between the indices of both tests.

Discussion

The CPET remains a relevant clinical modality for evaluation and treatment of many commonly encountered clinical problems. It provides objective and reproducible indices for functional capacity assessment, generates invaluable information in determining the origin of exertion dyspnea, and provides unique prognostic capabilities in the evaluation of various cardiac patients [8–11].

Establishing the reproducibility of ICG parameters in stable CAD outpatients is important as well and a relatively high degree of intra- and inter-day reproducibility was demonstrated by Treister et al [17], suggesting that serial ICG measurements provide clinically useful information with which to assess changes in patient status.

Several indices from both above tests are expected to correlate each other like VO_2 (of CPET) and CO or CI (of ICG), as well as O_2-Pulse and SV or SI according to the Fick formula [13, 14]. No relevant studies are found in the medical literature which demonstrate such correlations, especially not when measured during exercise.

The present study did demonstrate such significant correlations between the relevant ICG and CPET indices as expected (Table 3). Such a relationship between those indices during exercise might establish and validate both tests for functional non-invasive evaluation of various outpatients.

These correlations were achieved by 2 separate tests done at time points although under similar conditions. Thus, we may assume that if both tests had been done while using the same exercise test, the correlations might be even more significant. Such findings may support and lead to some conclusions. Firstly, that the ICG test might complete the CPET for further and more accurate functional-physiologic evaluation of IHD pts, non-invasively. Secondly, that the ICG test might supply reliable hemodynamic data for non-invasive assessment of IHD pts by itself, at rest and exercise as well. This ability may provide an additional tool for evaluation of ischemic reaction during exercise since a reduction in SV is expected in pts with significant ischemic response, a finding which may be shown by the exercise ICG test.

As the main limitations of this study were the small sample of pts studied, the separate time of performing both tests and the retrospective characteristics of the study, more investigation is needed and recommended for further establishment the findings of the present study.

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