

HAEMODYNAMIC RESPONSE DURING EXERCISE TESTING IN PATIENTS WITH CORONARY ARTERY DISEASE UNDERGOING A CARDIAC REHABILITATION PROGRAMME

■ Accepted
for publication
12.06.2011

AUTHORS: Siebert J.¹, Zielińska D.², Trzeciak B.¹, Bakula S.²

¹ Department of Family Medicine and University Centre for Cardiology, Dębinki 2, 80-211 Gdańsk, Poland

² Department and Clinic of Rehabilitation, Medical University of Gdańsk, Dębinki 7, 80-211 Gdańsk, Poland

ABSTRACT: Haemodynamic monitoring during exercise testing is seldom used during cardiac rehabilitation. The aim was to evaluate haemodynamic changes using the cardiac impedance method during exercise testing in patients after percutaneous coronary interventions and coronary artery bypass grafting during cardiac rehabilitation. Thirty (25 M; 5 F) patients were included in the programme. The group was divided according to ejection fraction (EF): low – below 50%, normal – equal to or above 50%. The exercise test was performed simultaneously with a four-electrode impedance cardiogram before and after rehabilitation. ECG, blood pressure, thoracic impedance, first derivative dz/dt , stroke volume (SV) and cardiac output were recorded. Contractility index (Heather index – HI) and vascular peripheral resistance were calculated. The pattern of haemodynamic changes was normal in 24 patients. The deflection points for HI and SV trend patterns were observed among patients with low EF. The contractility index decreased 90 s before maximal exercise and after the next 30-60 s a deflection point was observed in SV curve trends. In 24 patients with normal EF the contractility index trends did not decrease and SV trends increased until the end of exercise or a deflection point was not noted. The deflection points of the contractility index and SV curves were observed before the clinical indications for exercise test termination appeared in patients with a low ejection fraction. Impedance cardiography may indicate the threshold of the workload during real-time exercise testing.

KEY WORDS: impedance cardiography, cardiac rehabilitation, coronary artery diseases

INTRODUCTION

Impedance cardiography (ICG) is a non-invasive, rapid and cost-effective technique used to estimate stroke volume (SV), cardiac output (CO) and contractility indices of the heart. Measurement of impedance is becoming increasingly available in the clinical setting as a tool for assessing haemodynamic and volume status, especially in heart failure patients [4,7,9,17,21,24]. It enables one to assess: preload, afterload, contractility (acceleration and Heather index), velocity index, pre-ejection period, left ventricular ejection time, systolic time ratio and heart rate. The accuracy and repeatability of the results have been confirmed in comparative studies with results obtained through invasive methods and echocardiography [14,22].

Comprehensive cardiac rehabilitation (CR) is routine in patients with coronary artery disease after percutaneous coronary interventions (PCI) and coronary artery bypass grafting (CABG). The level of exercise training in patients with coronary artery disease is usually based on the Karvonen formula, which estimates the heart rate at the anaerobic threshold. CR programmes are also based on the clinical status of the patient and oxygen consumption measured by spirometry [1,10]. It seems that assessment of the haemodynamic response

during an exercise test may be useful in limiting exercise intensity in patients undergoing cardiac rehabilitation. The work capacity in patients after myocardial infarction, invasive therapy such as PCI or CABG or valve replacement differ among individuals. The limit of the workload before rehabilitation is described by an empirical formula. The rehabilitation of patients who have had a myocardial infarction requires assessment of their current myocardial competence and the potential for further recovery [1]. Patients should be protected against the risk of cardiovascular complications during physical exertion. Information about the response of the cardiovascular system to exercise in patients with coronary artery disease is necessary. It is proposed that the physical exercise should terminate at the workload limit but with a margin of safety before maximal cardiac capacity is reached. Monitoring of the haemodynamic parameters in real time during an exercise test is essential.

The cardiac impedance method gives an opportunity to assess cardiac function during physical exertion because of its non-invasive nature [16]. The diagnostic value of impedance cardiography (ICG) during exercise in patients with left ventricular dysfunction was tested.

Reprint request to:

Janusz Siebert

Department of Family Medicine and
University Centre for Cardiology,
Dębinki 2, 80-211 Gdańsk, Poland
E-mail: jsiebert@gumed.edu.pl

The authors pointed out that indices obtained from ICG may indicate deterioration of cardiac performance before the last stage of load work during the exercise test [3,11,20]. The benefits of intrathoracic impedance monitoring in patients especially with heart failure has been evaluated in some studies [15,26]. The results of the PARTNERS HF study help identify diagnostic information that may provide early recognition of impending heart failure-related events. It may increase the safety of exercise training in patients with implantable defibrillators (ICD) [25]. The usefulness of impedance cardiography assessed in the DOT-HF trial is designed to investigate whether ambulatory monitoring of intrathoracic impedance together with other device-based diagnostic information can reduce morbidity and mortality in patients with chronic heart failure who are treated with cardiac resynchronization therapy (CRT) and/or an implantable defibrillator (ICD) [8].

The primary objective of our study was to assess the value of ICG during exercise testing as a method of monitoring cardiac function of patients with CAD.

The secondary objective was to assess the influence of CR on haemodynamic parameters during exercise testing before and after cardiac rehabilitation.

MATERIALS AND METHODS

Patients and study protocol. A total of 30 consecutive patients with coronary artery disease (aged 60+/-9 years, 25 males, 5 females), who underwent a PTCA or CABG procedure in a one-month period were included in the cardiac rehabilitation programme. The exclusion criteria were severe ventricular arrhythmias, recent myocardial infarction, acute infections and other co-morbidities that make exercise training difficult or impossible. Six patients had an ejection fraction below 50%. Routine anamnesis, physical examination and echocardiography were performed before rehabilitation. Ergometer exercise test with 25 watt increments every 3 minutes (ITAM cycle

ergometer with computed analysis of ECG – VITACARD) with a simultaneous four-electrode impedance cardiogram was performed before and after 3 weeks of controlled exercise training. Continuous haemodynamic monitoring during the exercise test was performed by the automated ICG system NICCOMO (Cardioscreen Professional, Medis GmbH, Ilmenau, Germany). Four pairs of electrodes were used for recording the thoracic bio-impedance. The modified Bernstein formula was used for the calculation of stroke volume and cardiac output [5]. Monitoring of the ICG and ECG signals and the haemodynamic variables was performed on line. All ICG data were digitally stored and evaluated [5]. Criteria for the termination of the exercise test included the presence of angina pectoris with retrosternal pain, significant ST depression of more than 0.1 mV, dyspnoea, significant arrhythmias, systolic blood pressure ≥ 220 mm Hg, diastolic pressure ≥ 110 mm Hg, decreases in systolic pressure ≥ 20 mm Hg or peripheral exhaustion. For the purposes of this paper, heart rate (HR), stroke volume (SV), cardiac output (CO), contractility Heather index, systolic and diastolic blood pressure, systemic vascular resistance (SVR) and the quality index of the recording were assessed and analysed. The time of exercise was measured. All patients underwent a 3-week supervised exercise training programme. This CR programme included 30 minutes of interval exercise on a cycle ergometer (Elmed EKT) and both aerobic and strength training with exercise intensity calculated with the Karvonen formula according to the guidelines of ESC [2,12]. All patients gave their informed consent for their participation in the study. The study was approved by the local ethics committee.

Statistical analysis

All data are presented as mean values \pm standard deviation (SD), if not indicated otherwise. The Mann-Whitney U-test was used for comparison of haemodynamic variables between the groups of patients. The Wilcoxon test was used for comparisons within the groups. A *p*-value < 0.05 was interpreted as significant.

TABLE 1. COMPARISON OF STROKE VOLUME AND CARDIAC OUTPUT, WORKLOAD, HEART RATE, DOUBLE PRODUCT AND HEATHER INDEX BEFORE AND AFTER CARDIAC REHABILITATION

Parameter	Before rehabilitation	After rehabilitation	<i>p</i>
Number of patients	30	30	
SV at rest [ml]	82.4 \pm 16.0	87.6 \pm 16.8	0.08
SV at end of workload [ml]	114.4 \pm 47.7	110.7 \pm 24.3	0.62
CO at rest [$l \cdot min^{-1}$]	6.1 \pm 1.2	5.9 \pm 1.0	0.42
CO at end of workload [$l \cdot min^{-1}$]	11.3 \pm 4.7	11.0 \pm 3.9	0.64
HR at rest [$f \cdot min^{-1}$]	73.8 \pm 7.4	68.1 \pm 5.9	0.003
HR at end of workload [$f \cdot min^{-1}$]	110.8 \pm 18.1	108.1 \pm 16.0	0.31
Double product (SBPxHR max)	16711 \pm 5834	18044 \pm 4879	0.34
Heather Index at rest [$Ohm \cdot s^{-2}$]	10.4 \pm 3.4	10.4 \pm 2.5	0.98
Heather Index (max) at end of workload [$Ohm \cdot s^{-2}$]	29.7 \pm 10.2	30.6 \pm 9.9	0.68
SBP at rest [mmHg]	126.4 \pm 25.2	122.2 \pm 29.4	0.35
SBP at end of workload [mmHg]	151.2 \pm 22.0	165 \pm 28.8	0.02
LVET/PEP at rest	3.0 \pm 1.5	3.3 \pm 2.0	0.36
LVET/PEP at end of workload	3.5 \pm 1.4	3.8 \pm 2.0	0.52
Workload [W]	81.6 \pm 32.1	98.7 \pm 28.2	0.02
Time of exercise [s]	496 \pm 9.0	590 \pm 8.0	0.05

RESULTS

Observation of trends of HI and SV changes in the studied population during exercise testing revealed two groups. Patients with increasing SV and contractility indices until the end of the exercise test and patients with a definite deflection point on the HI trend before achieving maximal workload followed by a decrease in the SV curve. The deflection points of SV and HI curves were observed before the clinical indications for termination of the exercise test appeared. Three HI and SV trend patterns were observed among patients with low EF. SV decreased 1.5 minutes before maximal exercise in 2 patients with a definite deflection point on the curve, remained at the same level in 2 and increased slowly during the first two stages only in another 2 patients. The contractility indices showed similar trends, with the deflection point detected earlier compared to the SV. In 24 patients with a normal ejection fraction HI and SV trends increased until the end of exercise or there was not a definite deflection point noticeable and the contractility index trends did not decrease. The quality index of the ICG recordings during exercise tests performed by 30 patients ranged from 20 to 99. The impedance curve was of very high quality in 19 patients. Eleven of the records had some artefacts, especially during maximal exercise.

Table 1 shows the mean values of data obtained from the ICG curve during the exercise test for the entire group of patients before and after the cardiac rehabilitation programme. After 3 weeks of supervised exercise training an increase in time of exercise ($496 \pm$

9.0 vs 590 ± 8.0 , $p=0.05$), maximal systolic blood pressure ($151.2 \text{ mmHg} \pm 22.0$ vs $165 \text{ mmHg} \pm 28.8$, $p = 0.02$) and maximal workload ($81.6\text{W} \pm 32.1$ vs $98.7\text{W} \pm 28.2$, $p=0.02$) was observed. The resting heart rate decreased significantly (73.8 ± 7.4 vs 68.1 ± 5.9 , $p=0.003$). LVET/PEP at rest and at the end of workload did not change significantly after rehabilitation.

Figure 1 shows the pattern of blood pressure and systemic vascular resistance SVR trend during the exercise test of the patient with low EF.

In Figure 2 an example of the pattern of the blood pressure (BP) and systemic vascular resistance (SVR) trend during the exercise test in a patient with $EF \geq 50\%$ is presented.

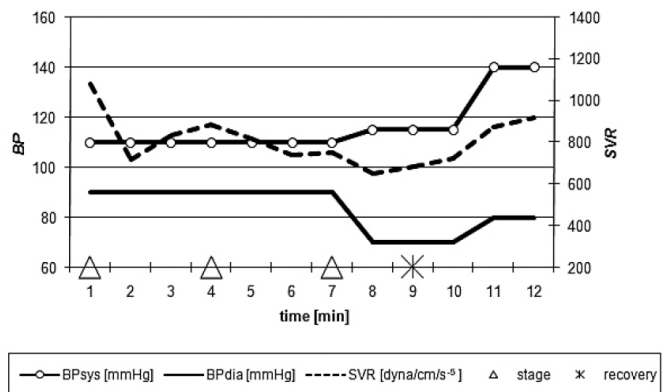


FIG. 1. THE EXAMPLE OF PATTERN OF BLOOD PRESSURE (BP) AND SYSTEMIC VASCULAR RESISTANCE (SVR) TRENDS DURING EXERCISE TEST IN A PATIENT WITH EF 15%

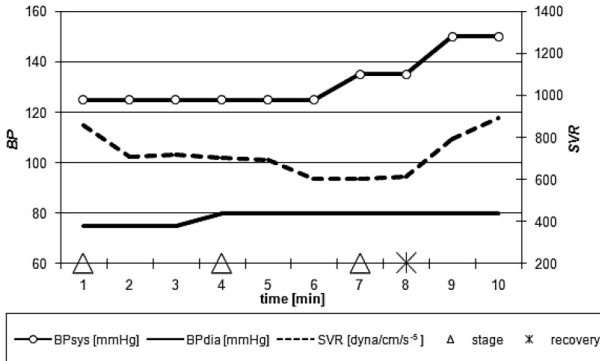


FIG. 2. THE EXAMPLE OF PATTERN OF BLOOD PRESSURE (BP) AND SYSTEMIC VASCULAR RESISTANCE (SVR) TRENDS DURING EXERCISE TEST IN A PATIENT WITH EF 55 %

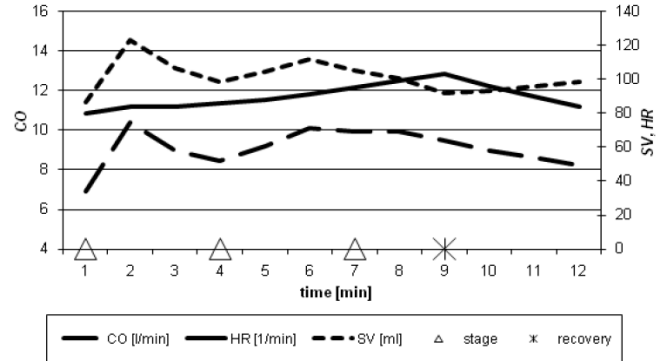


FIG. 3. THE EXAMPLE OF PATTERN OF STROKE VOLUME (SV), CARDIAC OUTPUT (CO) AND HEART RATE (HR) TRENDS DURING EXERCISE TEST IN PATIENT WITH EF 15%

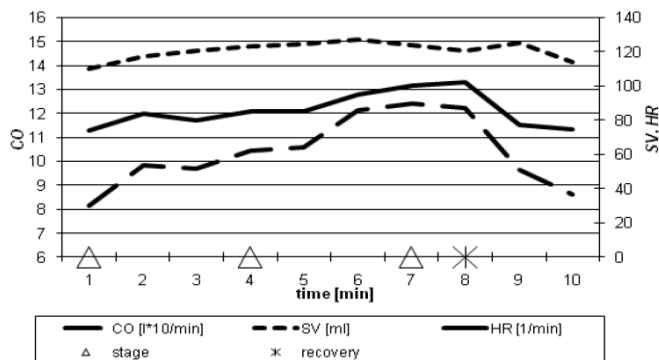


FIG. 4. THE EXAMPLE OF PATTERN OF STROKE VOLUME (SV), CARDIAC OUTPUT (CO) AND HEART RATE (HR) TRENDS DURING EXERCISE TEST IN A PATIENT WITH EF 55%

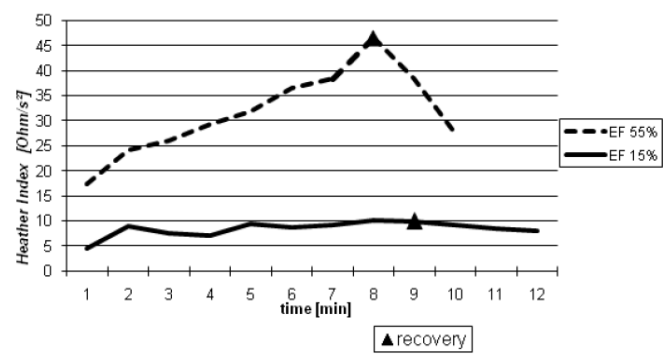


FIG. 5. THE EXAMPLE OF PATTERN OF HEATHER INDEX TEST IN PATIENT WITH EF 15% AND EF 55%

In Figure 3 the pattern of stroke volume (SV), cardiac output (CO) and heart rate (HR) trends during the exercise test in a patient with EF 15% is presented.

Figure 4 shows the trends of haemodynamic response in a patient with ejection fraction $\geq 50\%$. Only a slight decrease in SV beginning 2 min before achieving maximum workload (with increasing value of HI shown in Figure 5 below) is observed.

In Figure 5 an example of the pattern of the Heather index trend in a patient with EF 15% and EF $\geq 50\%$ is presented. The deflection point of the HI curve was observed 1 min before workload termination in patients with low EF (2 min earlier than the deflection point of SV appeared).

DISCUSSION

The data presented in this paper support the validity of the impedance method as a non-invasive, atraumatic way of measuring SV and contractility indices. The method has some limitations, particularly during exercise tests. The quality index of the recording indicated the necessity of eliminating artefacts from the ICG curve. The quality index of an ICG recording during an exercise test performed by 30 patients ranged from 20% to 99%. The impedance curve was very high quality in 19 patients. Eleven of the records had some artefacts, especially during maximal exercise. The analysis was performed after additional filtration. It was possible that movement of the thorax led to disturbances in the contact between the skin, the electrodes and the wires. The results of Scherhag et al. demonstrated that ICG is a feasible method of non-invasive measurement of stroke volume and cardiac output, not only when the patient is at rest but also when cycling, which is closely and significantly correlated with invasive measurements by thermodilution [19]. The authors did not describe any problems with artefacts during the ICG recording. The question of how to measure with precision the effect of rehabilitation posed some problems. Some authors used the impedance cardiography method. Bilińska M. et al. showed significant improvement of haemodynamic responses measured by ICG for handgrip in 60 male patients who underwent 6 weeks of aerobic training on a cycloergometer, 3 times a week, at 70-80% of the maximum tolerated HR, three months after receiving CABG, compared with controls [6]. In our data it appears to be of great importance that the duration of the exercise increased significantly after rehabilitation (7.47 ± 0.12 min vs. 10.19 ± 0.17 min; $p = 0.046$), whereas the double product was at the same level before and after rehabilitation. As well as having the same ejection fraction as before exertion, patients also had the ability to cycle for a longer time. This suggests that physical work capacity increased after the rehabilitation course.

The target intensity level of exercise training close to the upper level of metabolic aerobic exercise in patients with coronary artery disease is usually based on a training heart rate calculated with the Karvonen formula after a conventional exercise test. This formula is not precise enough to prescribe exercise training in some groups of patients with impaired heart function. What is more, it appears to overestimate heart

rate intensity among those of low and average fitness and may be excessive for these groups, and conversely this formula underestimates the heart rate at the anaerobic threshold in patients on beta-blocker therapy, which may lead to under training of these patients [13,23]. Lepretre et al. examined whether the heart rate deflection point in the HR-power relationship coincides with the maximal stroke volume value achieved in an endurance-trained subject. As a result, 72.7% of the subjects presented a break point in their HR-work rate curve at 89.9% of their maximal HR value. The SV value increased up to $78.0 \pm 9.3\%$ of the power associated with maximal O₂ uptake in the first group and up to $94.4 \pm 8.6\%$ of the power associated with VO₂max in the second. SV significantly decreased before exhaustion in the first group. In conclusion they mentioned that in well-trained subjects the heart rate deflection coincided with the optimal cardiac work for which SV_{max} was obtained [18].

Our data indicated that the deterioration of heart-muscle function appeared in some patients before the age-predicted target HR or clinical criteria to terminate the exercise test were achieved. The observation of the HI and SV curves made it possible to indicate these patients in exercise testing before cardiac rehabilitation. During the rehabilitation course the criteria for termination of the exercise test were based on the age-predicted heart rate. Additional criteria for termination of the exercise test are very important for the safety of patients. A decrease in systolic blood pressure in particular may point to deterioration in left ventricular function. The compensatory processes, such as increases in systemic vascular resistance and increase in heart rate, may lead to the cardiac output being maintained at the same level for a short time. Left ventricular dysfunction may be hidden until the decrease in systolic blood pressure is noticed. We discovered that the deflection point in the contractility indices appeared before the decrease in SV and systolic blood pressure. The SV decreased in heart failure patients 30-60 seconds after the Heather index deflection point. Cardiac output was maintained at the same level because the HR increased. The decrease of 20 mmHg SBP appeared only after the haemodynamic changes were observed. It seems that the monitoring of trends of SV, HI, SVR and HR helps to identify the earlier and more precise moment for termination of exercise than using clinical and heart rate criteria. These data suggest that monitoring exercise testing by the impedance cardiography method improves safety for patients during cardiac rehabilitation.

CONCLUSIONS

1. Impedance cardiography is a useful tool in monitoring haemodynamic trends in patients undergoing cardiac rehabilitation programmes. In particular, the trends in the contractility of the heart muscle indices and the different patterns of stroke volume in response to workload may be useful in detecting deterioration of cardiac performance during physical exertion.
2. Exercise capacity increased in patients with coronary artery disease after cardiac rehabilitation.



REFERENCES

1. Arena R., Myers J., Williams M.A., Gulati M., Kligfield P., Balady G.J. et al. Assessment of functional capacity in clinical and research settings: a scientific statement from the American Heart Association Committee on Exercise, Rehabilitation, and Prevention of the Council on Clinical Cardiology and the Council on Cardiovascular Nursing. *Circulation* 2007;116:329-343.
2. Balady G.J., Ades P.A., Comoss P., Limacher M., Pina I.L., Southard D. et al. Core components of cardiac rehabilitation/secondary prevention programs. A statement for healthcare professionals from the American Heart Association and the American Association of Cardiovascular and Pulmonary Rehabilitation. *Circulation* 2000;102:1069-1073.
3. Balasubramanian V., Hoon R.S. Changes in thoracic electrical impedance during submaximal treadmill exercise in patients with ischemic heart disease - A preliminary report. *Am. Heart J.* 1976;91:43-49.
4. Bayram M., Yancy C.W. Transthoracic impedance cardiography: a noninvasive method of hemodynamic assessment. *Heart Fail. Clin.* 2009;5:161-168.
5. Bernstein D.P. A new stroke volume equation for thoracic electrical bioimpedance: theory and rationale. *Crit. Care Med.* 1986;14:904-909.
6. Bilinska M., Kosydar-Piechna M., Gasiorowska A., Mikulski T., Piotrowski W., Nazar K., Piotrowicz R. Influence of dynamic training on hemodynamic, neurohormonal responses to static exercise and on inflammatory markers in patients after coronary artery bypass grafting. *Circ. J.* 2010;74:2598-604.
7. Bour J., Kellett J. Impedance cardiography: a rapid and cost-effective screening tool for cardiac disease. *Eur. J. Intern. Med.* 2008;19:399-405.
8. Braunschweig F., Ford I., Conraads V., Cowie M.R., Jondeau G., Kautzner J. et al. Can monitoring of intrathoracic impedance reduce morbidity and mortality in patients with chronic heart failure? Rationale and design of the Diagnostic Outcome Trial in Heart Failure (DOT-HF). *Eur. J. Heart Fail.* 2008;10:907-916.
9. Castellanos L.R., Bhalla V., Isakson S., Daniels L.B., Bhalla M.A., Lin J.P. et al. B-type natriuretic peptide and impedance cardiography at the time of routine echocardiography predict subsequent heart failure events. *J. Cardiol. Fail.* 2009;15:41-47.
10. Corra U., Gianuzzi P., Adamopoulos S. Executive summary of the position paper of the Working Group on Cardiac Rehabilitation and Exercise Physiology of the European Society of Cardiology (ESC): core components of cardiac rehabilitation in chronic heart failure. *Eur. J. Cardiovasc. Prev. Rehabil.* 2005;12:321-325.
11. Denniston J.C., Maher J.T., Reeves J.C., Cymerman J.C., Grover R.F. Measurement of cardiac output by electrical impedance at rest and during exercise. *J. Appl. Physiol.* 1976;40:91-95.
12. Giannuzzi P., Saner H., Björnstad H., Fioretti P., Mendes M., Cohen-Solal A. et al. Secondary prevention through cardiac rehabilitation. Position paper of the working group on cardiac rehabilitation and exercise physiology of the European Society of Cardiology. *Eur. Heart J.* 2003;24:1273-1278.
13. Goldberg L., Elliot D.L., Kuehl K.S. Assessment of exercise intensity formulas by use of ventilatory threshold. *Chest* 1988;94:95-98.
14. Kleinrok A., Sacharuk A., Rumiński W., Kosicki J., Grzywna R., Markiewicz M., Pałko T. Comparative investigation of cardiac output using impedance rheography and invasive methods. *Kardiol. Pol.* 1989;32:440-445.
15. Knackstedt C., Mischke K., Schimpf T., Waringer J., Fache K., Frechen D. et al. Integration of automatic intrathoracic fluid content measurement into clinical decision making in patients with congestive heart failure. *Pacing Clin. Electrophysiol.* 2008;31:961-967.
16. Kottke F.J., Kubicek W.G., Ollson M.E. Evaluation of cardiac competence during rehabilitation following myocardial infarction. *Israel J. Med. Sci.* 1973;9:568-577.
17. Kułakowski P., Makowska E., Kryński T., Stec S., Czepiel A., Błachnio E., Soszyńska M. Tilt-induced changes in haemodynamic parameters in patients with cardiac resynchronisation therapy - a pilot study. *Kardiol. Pol.* 2009;67:19-26.
18. Lepretre P.M., Foster C., Koralsztein J.P., Billat V.L. Heart rate deflection point as a strategy to defend stroke volume during incremental exercise. *J. Appl. Physiol.* 2004;98:1660-1665.
19. Scherhag A., Kaden J.J., Kentschke E., Sueselbeck T., Borggreffe M. Comparison of impedance cardiography and thermodilution-derived measurements of stroke volume and cardiac output at rest and during exercise testing. *Cardiovasc. Drugs Ther.* 2005;19:141-147.
20. Siebert J. Bioimpedance measurement of hemodynamic response during an exercise test in patients with coronary artery disease. 12th European Conference of the International Society of Noninvasive Cardiology. Varese, Italy, 20-22 October 1994. Congress Book 1994; p.65.
21. Siebert J., Zielińska D., Trzeciak B.G., Bakula S. Impedance cardiography for the assessment of hemodynamic response during cardiopulmonary exercise test in patient with heart failure - a case report. *Kardiol. Pol.* 2010;68:311-313.
22. Sodolski T., Kutarski A. Impedance cardiography: A valuable method of evaluating haemodynamic parameters. *Cardiol. J.* 2007;14:115-126.
23. Tabet J.Y., Meurin P., Teboul F., Tartiere J.M., Weber H., Renaud N. et al. Determination of exercise training heart rate in patients on beta-blockers after myocardial infarction. *Eur. J. Cardiovasc. Prev. Rehabil.* 2006;13:538-543.
24. Tang W.H., Tong W. Measuring impedance in congestive heart failure: current options and clinical applications. *Am. Heart J.* 2009;157:402-411.
25. Whellan D.J., O'Connor C.M., Ousdigian K.T., Lung T.H. Rationale, design, and baseline characteristics of a Program to Assess and Review Trending Information and Evaluate Cor Relation to Symptoms in Patients with Heart Failure (PARTNERS HF). *Am. Heart J.* 2008;156:833-839.
26. Yu C.M., Wang L., Chau E., Chan R.H., Kong S.L., Tang M.O. et al. Intrathoracic impedance monitoring in patients with heart failure: correlation with fluid status and feasibility of early warning preceding hospitalization. *Circulation* 2005;112:841-848.