Original article

Tilt-induced changes in haemodynamic parameters in patients with cardiac resynchronisation therapy – a pilot study

Piotr Kułakowski, Ewa Makowska, Tomasz Kryński, Sebastian Stec, Aleksandra Czepiel, Elżbieta Błachnio, Małgorzata Soszyńska

Department of Cardiology, The Medical Centre of Postgraduate Education, Grochowski Hospital, Warsaw, Poland

Abstract

Background: Cardiac resynchronisation therapy (CRT) has become a standard care in selected patients with advanced chronic heart failure (CHF). In order to achieve an adequate clinical response, CRT parameters have to be optimised following implantation. This procedure is usually performed on a patient in a supine position; however, measurement of haemodynamic parameters in an upright position may be clinically important.

Aim: To compare haemodynamic parameters obtained in supine and erect positions in CRT patients undergoing optimisation procedures.

Methods: The study group consisted of 10 consecutive patients (mean age 69.6±9 years, all males) who were scheduled for control outpatient CRT follow-up visits. Apart from routine device check-up, haemodynamic parameters [impedance cardiography (ICG) Task Force Monitor Systems, CNSystems, Austria] were measured. The ICG parameters were recorded during 20-min periods while supine and while tilted to 80 degrees. The last 30 cardiac cycles from each period were taken for further analysis. Parameters measured included heart rate (HR), systolic and diastolic blood pressure, stroke volume, cardiac output (CO) and total peripheral resistance (TPR).

Results: Out of 60 measurements performed (6 parameters in 10 patients) all but nine differed significantly when comparing supine and erect positions. There was no uniform pattern regarding these changes. For example, HR increased after tilting in five patients, did not change in four, and slowed down in one patient. The changes in CO were significant in all but two patients, reaching a 50% increase in one patient. An abnormal response of TPR (significant decrease) was observed in 5 patients. There was no apparent association between tilt-induced changes in haemodynamic parameters and clinical response to CRT, whereas a significant negative correlation between tilt-induced changes in CO and left ventricular ejection fraction was found ($r=-0.7$, $p<0.025$).

Conclusions: Tilting causes significant and often abnormal changes in haemodynamic parameters in CRT patients. The clinical significance of these findings needs further evaluation.

Key words: impedance cardiography, cardiac resynchronisation therapy, tilt testing

Kardiol Pol 2009; 67: 19–24

Introduction

Cardiac resynchronisation therapy (CRT) has become a standard care in selected patients with advanced chronic heart failure (CHF) [1]. In order to achieve an adequate clinical response, CRT parameters have to be optimised following implantation, usually using echocardiography [2]. Impedance cardiography (ICG) is another non-invasive tool which can be used for the assessment of haemodynamic parameters in various settings [3-5]. Recently, ICG has been proposed for non-invasive optimisation of CRT parameters [6-10] and for acute assessment of haemodynamic effects of CRT [11].

Regardless of the method used (echocardiography or ICG), optimisation of CRT is routinely performed on a patient in a horizontal position. One of the main goals of the CRT is to improve the patient's physical capacity during everyday activities, usually performed in an upright position. However, the effects of postural changes on haemodynamic parameters in patients with CRT have not yet been studied. Accordingly, the aim of our study was to compare the ICG parameters obtained in supine and erect positions in our CRT patients undergoing optimisation procedures.

Methods

Study group

The study group consisted of 10 consecutive patients (mean age 69±69 years, all males) who were scheduled

Address for correspondence:
Piotr Kułakowski MD PhD, Klinika Kardiologii, Centrum Medyczne Kształcenia Podyplomowego, Szpital Grochowski, ul. Grenadierów 51/59, 04-073 Warszawa, tel.: +48 22 871 12 57, e-mail: kulak@kkcmkp.pl
Received: 11 September 2008. **Accepted:** 12 October 2008.
The study was supported in part by the research grant 501-1-1-09-42/07 from the Medical Centre of Postgraduate Education, Warsaw, Poland

Table I. Demographic and clinical characteristics of the studied patients (n=10)

Parameter	
Age [years]	69.9±9
Aetiology of heart failure	
Ischaemic (post-infarction) (%)	7 (70)
Non-ischaemic dilated cardiomyopathy (%)	3 (30)
NYHA class before CRT implantation	
Class III (%)	7 (70)
Class IV (%)	3 (30)
NYHA class at the time of the study	
Class II (%)	5 (50)
Class III (%)	3 (30)
Class IV (%)	2 (20)
Time from CRT implantation to the present study [months]	11.8±7.5
Baseline left ventricular ejection fraction [%]	24.8±5.5 (range 15-30)
Medication at the time of the study	
Beta blockers (%)	10 (100)
ACE-I / ARBs (%)	10 (100)
Diuretics (%)	10 (100)
Digitalis (%)	1 (10)
Amiodarone (%)	3 (30)

Abbreviations: NYHA – New York Heart Association, CRT – cardiac resynchronisation therapy, ACE-I – angiotensin-converting enzyme inhibitor, ARBs – angiotensin receptor blockers

for control outpatient CRT follow-up visits and gave informed consent to undergo ICG recording and tilting. Apart from routine device check-up, ICG measurements were performed. The clinical and demographic characteristics of the studied patients are presented in Table I. In all patients the CRT pacing settings were programmed in order to obtain 100% ventricular pacing. Responders were defined as those in whom NYHA class improved by at least one class following CRT implantation. None of the patients had a history of reflex syncope.

Impedance cardiography

The measurements were performed using commercially available equipment (Task Force Monitor Systems, CNSystems, Austria) which allows a non-invasive assessment of various haemodynamic parameters by measuring changes in the transthoracic electrical impedance. The detailed methodology was described elsewhere [12]. In brief, the patients were studied during morning hours after at least 15 minutes of rest. All the recordings were performed in a room used for tilt table testing, which guaranteed stable and comparable conditions for all patients. We used a routine ICG electrode configuration, placed at both sides of the abdomen and at the neck base [12]. The CRT parameters were optimised before the test and were identical during the ICG recording while supine or standing.

First, the ICG measurements in supine position were performed. The recordings consisted of a 10 min baseline period from which the last 30 cardiac cycles were taken for further analysis. All 30 consecutive measurements, automatically computed by the system, were taken into account and the average of these measurements was used in the final analysis. Care was taken to include only good-quality signals and all the artefacts were excluded after a visual assessment of the recordings.

Next, the patients were tilted to 80 degrees. Again, a period of 10 min of ICG was recorded and the last 30 cardiac cycles of this period were used for further computations performed identically to those obtained while in the supine position. Ten-minute periods were chosen to allow the autonomic nervous system and haemodynamic parameters to stabilise following orthostatic stress.

The following ICG parameters were measured [12]:

1. Stroke volume (SV) in ml, calculated using the formula: $V_{EPT} \times (dZ_{max}/Z0) \times LVET$, where V_{EPT} is the part of the electrically participating thoracic volume, calculated from weight, height, age and gender, dZ_{max} is systolic amplitude (Ohm/s), Z0 stands for total thoracic impedance (Ohm) and LVET is the left ventricular ejection time (ms).
2. Cardiac output (CO) in L/min, calculated using the formula: CO=SV × heart rate.
3. Total peripheral resistance (TPR) (in dyn s/cm^2) calculated from the formula: (MABD – CVP)/CO × 80, where MABD is the mean arterial blood pressure (mmHg), CVP is central venous pressure and CO is cardiac output.

In addition, finger plethysmography was used to obtain beat-to-beat systolic and diastolic blood pressure values.

Statistical analysis

The results are presented as means ± one standard deviation or numbers and percentages. Differences between the studied parameters obtained in supine and erect positions were compared using paired Student t-test. A Pearson correlation coefficient was calculated to assess the correlation between tilt-induced changes in haemodynamic parameters and left ventricular ejection fraction (LVEF). A $p < 0.05$ was considered significant.

Results

All ten patients underwent tilting without any complications – none of them developed syncope or a presyncopal episode. The analysis of haemodynamic parameters measured during tilting revealed that these parameters stabilised after the first 1-3 minutes, thus enabling reliable analysis of the last 30 cardiac cycles at the end of a 10-min period. A representative example of the pattern of haemodynamic changes following tilting is

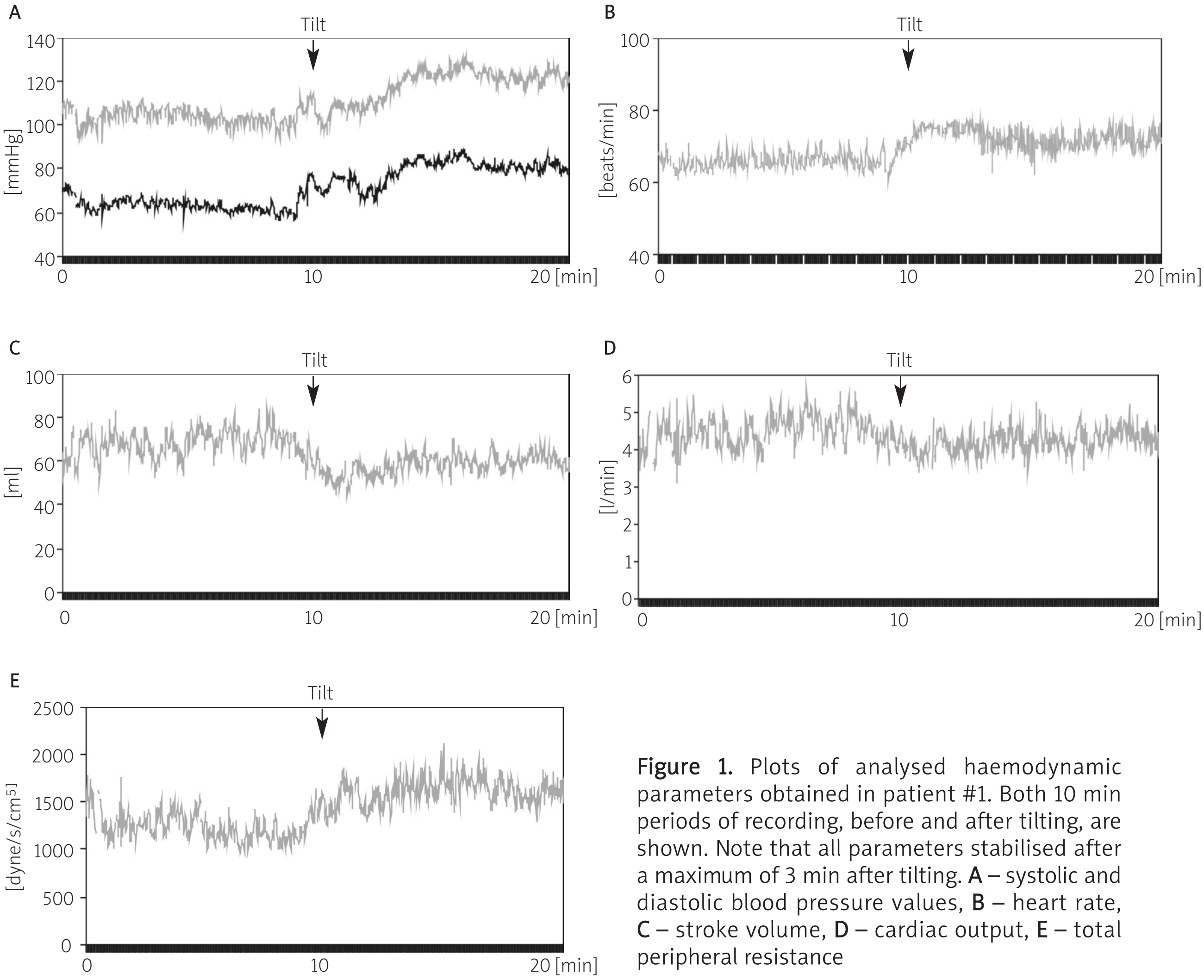

Figure 1. Plots of analysed haemodynamic parameters obtained in patient #1. Both 10 min periods of recording, before and after tilting, are shown. Note that all parameters stabilised after a maximum of 3 min after tilting. **A** – systolic and diastolic blood pressure values, **B** – heart rate, **C** – stroke volume, **D** – cardiac output, **E** – total peripheral resistance

shown in Figure 1.

Comparison of individual ICG parameters obtained in supine and erect positions are presented in Table II. Out of 60 measurements performed (6 parameters in 10 patients) all but nine differed significantly when comparing supine and erect positions. Only heart rate values in four patients, CO and SV in two as well as TPR in one patient did not change significantly after tilting.

Qualitative changes (Δ) in the analysed parameters in individual patients are presented in Table III. There was no uniform pattern regarding these changes. For example, heart rate increased while tilting in five patients did not change in four, and slowed down in one patient. The changes in CO were significant in all but two patients, reaching a 50% increase in patient #5.

There was no apparent association between tilt-induced changes in haemodynamic parameters and long-term response to CRT (Table III). For example, CO increased while standing in 2 responders and 3 non-responders, decreased in 3 responders, and did not change in 2 non-responders.

There was a significant negative correlation between LVEF and changes in CO ($r=-0.7$, $p<0.025$); patients with more reduced LVEF (15-20%) had greater increase in CO following tilting than patients with less reduced LVEF (25-30%). No significant correlation between LVEF and other haemodynamic parameters was found.

Discussion

The main finding of the study is that body position significantly influences the results of ICG in patients with CRT and that these changes are not uniform, varying from patient to patient.

The optimisation of CRT is usually performed on a patient in a horizontal position. However, almost all daily activities and physical exercises are performed in an upright position and these are circumstances when CRT is needed the most. The present study showed that indeed almost all haemodynamic parameters measured during

Table II. Comparison of individual results of the analysed parameters

Pt	HR [beats/min]		SBP [mmHg]		DBP [mmHg]		SV [ml]		CO [l/min]		TPR [dyne*/s/cm^5]	
#	Sup	Tilt	Sup	Tilt	Sup	Tilt	Sup	Tilt	Sup	Tilt	Sup	Tilt
1	66±2	73±2*	100.8±2.6	122.2±2.7*	60.7±1.1	80.5±2.1*	69.6±3.1	58.6±2.5*	4.6±0.2	4.3±0.2**	1162±68	1631±86*
2	70±0	70±0	89.8±3	96.1±3.5*	61.8±2.7	65.8±2.6*	59.3±4	68.2±2.3*	4.1±0.3	4.8±0.2*	1305±124	1181±80**
3	69.8±0.1	69.8±0.1	81.5±1	70.1±1.9*	45.8±0.2	36.3±1.03*	55.2±2.1	54.6±2.9	3.85±0.2	3.8±0.2	1059±41	932±47*
4	80±2.2	118±5.6*	99.1±5	106±6*	67.2±1.9	91±3.2*	60.6±3.6	51.2±1.9*	4.84±0.3	6.0±0.4*	1191±91	1205±79
5	70±4.2	70±2.8	123.4±2.3	131±1.4*	89.9±1.3	92.4±1.2*	53.7±7.6	80±6.2*	3.74±0.6	5.6±0.46*	2084±264	1426±103*
6	69.8±0.5	76.7±1.2*	100.3±1.5	90±1.2*	68.5±1	63.8±0.9*	59±2.7	48±0.6*	4.1±0.2	3.68±0.06*	1434±67	1451±35**
7	81±2	81±2.9	122±2	108.8±7.7*	78.7±1.7	70.8±9*	52±2.6	64.6±2.7*	4.19±0.2	5.2±0.3*	1643±92	1214±113*
8	85.5±0.9	71.6±1.8*	129.4±4.3	132.9±2.1*	92.2±4.5	100.4±1.2***	50.9±1.2	50.6±1.4	4.35±0.1	3.62±0.14*	1822±103	2178±80*
9	57.4±0.4	56.1±0.5*	116.1±3	82±2*	72.3±1.6	58.8±1.3*	45.8±3.9	49.8±1.2**	2.6±0.22	2.79±0.07***	2605±261	1844±70*
10	57.9±6.3	67±15.7	97.6±3.9	109.6±8.3*	69.1±2.2	73.7±3.9*	58.6±2.9	55.4±1.4*	3.41±0.41	3.49±0.41	1723±178	1951±197*

Abbreviations: pt – patient, sup – supine, HR – heart rate, SBP – systolic blood pressure, DBP – diastolic blood pressure, SV – stroke volume, CO – cardiac output, TPR – total peripheral resistance
$^*p$ <0.0001, $^{**}p$ <0.001, $^{***}p$ <0.05, otherwise NS
#9 – permanent bigeminy during supine and tilt – only sinus CRT-paced beats were taken into analysis
#10 – frequent ectopy both during supine and tilt – only sinus CRT-paced beats were taken into analysis

tilting were significantly different from those obtained in a supine position. Whether this phenomenon has any clinical relevance needs to be examined prospectively.

Data on the use of ICG for optimisation of CRT are very scarce. There are only a few studies which deal with this problem. They showed that ICG can be successfully used for the optimisation of the atrioventricular delay in CRT patients and that ICG-derived parameters correlate with those obtained by echocardiography [4-11]. However, in those studies the ICG parameters were measured only in patients in a supine position.

A normal haemodynamic response to tilting in healthy persons includes a fall in SV and CO which is rapidly (within seconds) compensated by an increase in heart rate and peripheral vasoconstriction, preventing a fall in arterial pressure. This rapid short-term compensation for haemodynamic instability caused by orthostatic stress is mediated by the autonomic nervous system – mainly by the baroreceptor reflex. During prolonged tilt, further compensation is achieved by neuroendocrine system activation – mainly the renin-angiotensin-aldosterone system and vasopressin [13]. All these mechanisms protect against hypotension and tissue hypoperfusion.

Table III. Qualitative changes in the analysed parameters in individual patients

Pt#	ΔHR	ΔSBP	ΔDBP	ΔSV	ΔCO	ΔTPR	Responder
1	□	□	□	↓	↓	□	Yes
2	→	□	□	□	□	↓	No
3	→	↓	↓	→	→	↓	No
4	□	□	□	↓	□	→	No
5	→	□	□	□	□	↓	No
6	□	↓	↓	↓	↓	□	Yes
7	→	↓	↓	□	□	↓	Yes
8	↓	□	□	→	↓	□	Yes
9	↓	↓	↓	□	□	↓	Yes
10	→	□	□	↓	→	□	No

Abbreviations: see Table II
□ – increase while standing, ↓ – decrease while standing, → – no change while standing, Δ – qualitative difference between analysed parameter recorded while supine and after tilting

In our CRT patients a variable response to the orthostatic stress was observed. In 7 patients heart rate did not increase and in 5 TPR decreased. Also changes in SV and CO were divergent. The finding that tilt-induced enhancement in CO was significantly greater in patients with more severe LVEF reduction is difficult to explain. It may suggest that patients with severely reduced LVEF have a greater reserve in CO, brought up by tilting, than those with less reduced LVEF. However, due to a small number of patients this relationship might occur just by chance. It is possible that differences in underlying aetiology, degree of cardiac impairment, concomitant diseases or medication used might play a role in the variable response to orthostatic stress. Definitely, the response in some CRT patients was different from healthy subjects [13, 14], which implies that patients treated with CRT have altered mechanisms protecting against the consequences of orthostatic stress.

Patients undergoing CRT usually have significant cardiac disease and it has been shown that such haemodynamic parameters as SV or CO are diminished in these patients [15]. However, there are no data in the literature on the effects of tilting on haemodynamic parameters in CRT patients. ICG has been shown to be a reliable method for haemodynamic measurements in both supine and tilted positions [14]. In a different group of patients – subjects with a history of syncope undergoing tilt testing – ICG was found to be a valuable tool for the measurement of haemodynamic changes prior to and during syncope, enabling classification of a positive response to tilting [16] or to evaluate cardiac contractility and filling before and during syncope [17].

Limitations of the study

The number of patients was very small; therefore, the results should be considered as preliminary and need to be validated in larger studies. However, the differences between ICG parameters measured in supine and standing positions were evident. Also, the clinical meaning of the obtained results has to be further studied. Whether these differences are patient- or disease-specific and whether there is any impact of these findings on CRT optimisation in everyday practice deserve further investigation. The 30 cardiac cycle-period at the end of 10 min of tilting was chosen arbitrarily for analysis, and it might be possible that the analysis of other periods or assessment of dynamics of changes in haemodynamic parameters may add important clinical information.

References

1. Vardas PE, Auricchio A, Blanc JJ, et al. Guidelines for cardiac pacing and cardiac resynchronization therapy. *Europace* 2007; 9: 959-98.
2. Vanderheyden M, Backer TD, Rivero-Ayerza M, et al. Tailored echocardiographic interventricular delay programming further optimizes left ventricular performance after cardiac resynchronization therapy. *Heart Rhythm* 2005; 2: 1066-72.
3. Strobeck J, Silver M. Beyond the four quadrants: the critical and emerging role of impedance cardiography in heart failure. *Congest Heart Fail* 2004; 10 (supl. 2): 1-6.
4. Kindermann M, Frohlig G, Doerr T, et al. Optimizing the AV delay in DDD pacemaker patients with high degree AV block: mitral valve Doppler versus impedance cardiography. *Pacing Clin Electrophysiol* 1997; 20: 2453-62.
5. Cybulski G, Kozluk E, Michalak E, et al. Holter-type impedance cardiography device. A system for continuous and non-invasive monitoring of cardiac haemodynamics. *Kardiol Pol* 2004; 61: 138-46.

Zmiany parametrów hemodynamicznych pod wpływem pionizacji u chorych ze stymulacją resynchronizującą serca – doniesienie wstępne

Piotr Kułakowski, Ewa Makowska, Tomasz Kryński, Sebastian Stec, Aleksandra Czepiel, Elżbieta Błachnio, Małgorzata Soszyńska

Klinika Kardiologii, Centrum Medyczne Kształcenia Podyplomowego, Szpital Grochowski, Warszawa

Streszczenie

Wstęp: Terapia resynchronizująca (CRT) stała się rutynowym postępowaniem u chorych z zaawansowaną niewydolnością serca (CHF). W celu uzyskania jak najlepszych efektów CRT, po implantacji wykonuje się optymalizację ustawień CRT. Zmian tych dokonuje się zwykle u chorego leżącego, jednak pomiar parametrów hemodynamicznych i optymalizacja CRT w pozycji stojącej może mieć również istotne znaczenie kliniczne.

Cel: Porównanie parametrów hemodynamicznych u chorych z CRT w pozycji leżącej i stojącej.

Metody: Grupa badana składała się z 10 kolejnych chorych (średni wiek 69,6±9 lat, sami mężczyźni), którzy mieli zaplanowaną optymalizację CRT. Poza rutynową kontrolą urządzenia, dokonano pomiarów hemodynamicznych przy użyciu kardiografii impedancyjnej (ICG) (Task Force Monitor Systems, CNSystems, Austria). Parametry ICG oceniano podczas 20-minutowych rejestracji w pozycji leżącej oraz po pionizacji pod kątem 80° na stole używanym do testów pochyleniowych. Analizie poddawano ostatnie 30 cykli sercowych z każdego 20-minutowego pomiaru. Oceniane parametry hemodynamiczne obejmowały częstotliwość pracy serca, ciśnienie skurczowe i rozkurczowe, objętość wyrzutową, rzut serca oraz całkowity opór obwodowy.

Wyniki: Pionizacja miała istotny wpływ na parametry hemodynamiczne – spośród 60 pomiarów (6 parametrów u każdego chorego) tylko dla 9 nie było istotnych różnic pomiędzy wynikami otrzymanymi w pozycji leżącej i stojącej. Nie zaobserwowano jednolitego u wszystkich chorych kierunku zmian. Na przykład, częstotliwość pracy serca zwiększyła się po pionizacji u 5 chorych, pozostała bez zmian u 4 chorych, a zmniejszyła się u jednego chorego. Zmiany w wartościach rzutu serca pod wpływem pionizacji były istotne u 8 chorych, u jednego z nich wzrost sięgał 50%. Nieprawidłowa odpowiedź ze strony oporu naczyniowego (istotny spadek po pionizacji) wystąpiła u 5 chorych. Nie wykazano istotnego związku pomiędzy zmianami w parametrach hemodynamicznych wywołanymi pionizacją a kliniczną odpowiedzią na CRT (chorzy z poprawą *vs* chorzy bez poprawy po wszczepieniu urządzenia). Wykazano obecność istotnej ujemnej korelacji pomiędzy zmianami w wartościach rzutu serca pod wpływem pionizacji a frakcją wyrzutową lewej komory ($r=-0,7$, $p<0,025$).

Wnioski: Pionizacja powoduje istotne zmiany w parametrach hemodynamicznych u chorych z CRT. Znaczenie kliniczne tych zmian i ewentualnego wykonywania optymalizacji CRT u chorego w pozycji pionowej wymagają dalszych badań.

Słowa kluczowe: terapia resynchronizująca, optymalizacja, parametry hemodynamiczne, pionizacja, kardiografia impedancyjna

Kardiol Pol 2009; 67: 19–24

Adres do korespondencji:
prof. dr hab. n. med. Piotr Kułakowski, Klinika Kardiologii, Centrum Medyczne Kształcenia Podyplomowego, Szpital Grochowski, ul. Grenadierów 51/59, 04-073 Warszawa, tel.: +48 22 871 12 57, e-mail: kulak@kkcmkp.pl
Praca wpłynęła: 11.09.2008. **Zaakceptowana do druku:** 12.10.2008.