

Received: 2015.07.28
Accepted: 2015.11.13
Published: 2016.06.15

Relationship Between Changes in Pulse Pressure and Frequency Domain Components of Heart Rate Variability During Short-Term Left Ventricular Pacing in Patients with Cardiac Resynchronization Therapy

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABCDEF 1 **Bożena Urbanek**
ACDEF 1 **Jan Ruta**
C 2 **Krzysztof Kudryński**
FG 1 **Paweł Ptaszyński**
EFG 1 **Artur Klimczak**
ACDG 1 **Jerzy Krzysztof Wranicz**

1 Department of Electrophysiology, Medical University of Łódź, Łódź, Poland
2 Institute of Electronics, Technical University of Łódź, Łódź, Poland

Corresponding Author: Bożena Urbanek, e-mail: bozena_urbanek@op.pl
Source of support: Departmental sources

Background: The aim of the study was to explore the relationship between changes in pulse pressure (PP) and frequency domain heart rate variability (HRV) components caused by left ventricular pacing in patients with implanted cardiac resynchronization therapy (CRT).





Material/Methods: Forty patients (mean age 63 ± 8.5 years) with chronic heart failure (CHF) and implanted CRT were enrolled in the study. The simultaneous 5-minute recording of beat-to-beat arterial systolic and diastolic blood pressure (SBP and DBP) by Finometer and standard electrocardiogram with CRT switched off (CRT/O) and left ventricular pacing (CRT/LV) was performed. PP (PP=SBP-DBP) and low- and high-frequency (LF and HF) HRV components were calculated, and the relationship between these parameters was analyzed.

Results: Short-term CRT/LV in comparison to CRT/O caused a statistically significant increase in the values of PP ($P < 0.05$), LF ($P < 0.05$), and HF ($P < 0.05$). A statistically significant correlation between Δ PP and Δ HF ($R = 0.7384$, $P < 0.05$) was observed. The Δ HF of 6 ms^2 during short-term CRT/LV predicted a PP increase of $\geq 10\%$ with 84.21% sensitivity and 85.71% specificity.

Conclusions: During short-term left ventricular pacing in patients with CRT, a significant correlation between Δ PP and Δ HF was observed. Δ HF $\geq 6 \text{ ms}^2$ may serve as a tool in the selection of a suitable site for placement of a left ventricular lead.

MeSH Keywords: **Blood Pressure • Cardiac Resynchronization Therapy • Heart Failure**

Full-text PDF: <http://www.medscimonit.com/abstract/index/idArt/895489>

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Background

Chronic heart failure (CHF) remains a disease associated with an unfavorable prognosis despite developments in pharmacological treatment, particularly in patients with dis-coordinate contraction due to left bundle branch block (LBBB) [1]. Cardiac resynchronization therapy (CRT) applied to enhance synchrony has been beneficial in approximately 60% of patients, who have demonstrated improvement in clinical and hemodynamic parameters and reduced mortality [2–5]. One of the causes of failure of CRT therapy in 40% of cases is suboptimal left ventricular lead placement [6,7]. Its recommended position is lateral or postero-lateral veins, but in individual cases a positive hemodynamic response was observed when stimulation of other sites was performed [8–10]. So far, attempts at intraoperatively reaching the suitable site for epicardiac pacing with an invasive hemodynamic technique or noninvasive echocardiographic methods have not been implemented on a regular basis because they are time-consuming [8,11,12]. Thus, it seems necessary to find new methods in order to assess the hemodynamic immediate response to left ventricular pacing.

The aim of the study was to find the relationship between changes in pulse pressure (PP) and heart rate variability (HRV) components in frequency domain analysis caused by left ventricular pacing in patients with implanted CRT.

Material and Methods

Study population

The study population consisted of patients with non-ischemic and ischemic cardiomyopathy, symptomatic and stable CHF (NYHA III/IV) on optimal medical therapy, with sinus rhythm and QRS duration >120 ms with LBBB in electrocardiogram (ECG) and left ventricular systolic dysfunction (left ventricular ejection fraction, LVEF) $\leq 35\%$ who were enrolled into a study with implanted CRT. Exclusion criteria were: atrioventricular II/III° block, sick sinus syndrome, atrial fibrillation, premature ventricular and supraventricular extrasystoles (>1/min), diabetes mellitus, arterial hypertension, and current use of Class III antiarrhythmic drugs. The study was approved by the local Ethics Committee, and all patients gave their written informed consent.

Study protocol

In all the patients, the device was switched off (CRT/O) in the early hours of the morning of the second day following the CRT implantation and programmed in DDD mode with a lower rate limit of 40 ppm with maximal atrioventricular (AV) delay. Patients remained in a silent environment in a supine

position for a period of 15 minutes. Their breathing was stable (12 to 16 breaths/min) and individually controlled. Next, finger beat-to-beat arterial systolic blood pressure (SBP) and diastolic blood pressure (DBP) for 5 minutes with a Finometer (Finapres Medical Systems, Amsterdam, The Netherlands) were measured. The technique developed by Peñáz [13] is well validated for measuring instantaneous changes in blood pressure [14,15]. Simultaneously, a standard 12-lead ECG (500 Hz) (MEDEAKardio PC, Gliwice, Poland) was performed to measure frequency domain HRV components using in-house software based on the Matlab Mathematical Language [16]. Then, SBP, DBP, and ECG recordings were repeated with AV delay programmed 100 ms resulting in 100% left ventricular pacing (CRT/LV). The results were used to calculate the mean values of hemodynamic parameters. The mean value of PP during CRT/O ($PP_{CRT/O} = SBP_{CRT/O} - DBP_{CRT/O}$) and CRT/LV ($PP_{CRT/LV} = SBP_{CRT/LV} - DBP_{CRT/LV}$) was calculated. Next, the change of PP value was calculated ($\Delta PP = PP_{CRT/O} - PP_{CRT/LV}$) as well as the percentage change of PP ($\% \Delta PP = \Delta PP / PP_{CRT/O} \times 100\%$). The components of HRV – low-frequency power (LF), high-frequency power (HF), and low-to-high frequency ratio (LF/HF) during CRT/O ($LF_{CRT/O}$, $HF_{CRT/O}$, $LF/HF_{CRT/O}$), and next during CRT/LV ($LF_{CRT/LV}$, $HF_{CRT/LV}$, $LF/HF_{CRT/LV}$) – were computed. Then, the change of HRV values – ΔLF , ΔHF , and $\Delta LF/HF$ – were analyzed. The parameters of blood pressure were expressed in mmHg and the components of HRV in absolute units (ms^2).

Statistical analyses

Statistical analyses were performed with STATISTICA PL 9.0 software. The Shapiro-Wilk test was used for measurable variables to verify whether the variable had a normal distribution. For the normal distribution, the results were given as mean and standard deviation (SD) and for the lack of normal distribution measures of position, median (Me), and interquartile range (IQR) (Q25 – quartile I and Q75 – quartile III). The chi square test was used for categorical variables. To compare variable values in the studied groups, we used the Student's t-test for linked samples if the variable distribution in both cases was normal. For non-normality analysis, we used the Wilcoxon test. Spearman's rank correlation coefficient was applied to evaluate correlations between the variables. ROC curves (AUC) were used to present measurable variables. The results were considered statistically significant for $p < 0.05$.

Results

Baseline characteristics

The 40 analyzed patients were 63 ± 8.5 years old, 65% were male and 65% had non-ischemic etiology of heart failure,

Table 1. Baseline clinical characteristic in heart failure patients.

Parameters	Value	
Sex: men (n, %)	26	(65%)
Age (y)	63±8.5	
NYHA III class (n, %)*	37	(92.5%)
LVEF (%)**	25.7±6.6	
QRS (ms)	175±27	
Etiology and other disease		
Non-ischemic cardiomyopathy (n,%)	26	(65%)
Ischemic cardiomyopathy (n,%)	14	(35%)
Hyperlipidemia (n,%)	4	(10%)
Hypertension (n,%)	25	(62.5%)
Pharmacotherapy		
β-Adrenolytic (n,%)	40	(100%)
Angiotensin converting enzyme inhibitor (n,%)	37	(92%)
Aldosterone angiotensin (n,%)	37	(92.5%)
Diuretics (n,%)	36	(90%)
Acetylsalicylic acid (n,%)	16	(40%)
Statins (n,%)	27	(67.5%)

*NYHA – New York Heart Association; ** LVEF– left ventricular ejection fraction.

92.5% were in III class of NYHA, the QRS width was 175±27 ms, and mean LVEF was 25.7±6.6%. All patients had an LBBB configuration on surface ECG. The left ventricular lead was positioned anterior (5%), antero-lateral (15%), lateral (55%), posterior (10%), and poster-lateral (10%). Patient baseline characteristics are summarized in Table 1.

Influence of short-term left ventricular pacing on pulse pressure and heart rate variability

Value of blood pressure and pulse pressure

Short-term CRT/LV caused a statistically significant increase in the values of SBP (P<0.05) and PP (P<0.05). No statistical significance in the DBP value was observed (Table 2).

Value of heart rate variability

Short-term CRT/LV caused a statistically significant increase in the LF power (P<0.05) and HF power (P<0.05), but the LF/HF ratio did not change significantly (NS) (Table 3).

Figure 1 presents the example of the measurement of HRV components.

Relationship between changes of PP and HRV components during short-term CRT/LV

During short-term CRT/LV, a statistically significant correlation between ΔPP and ΔHF (R=0.7384, P<0.05) was observed (Figure 2).

Table 2. Value of blood pressure and pulse pressure (PP) in patients with CRT/0 and CRT/LV.

Parameters	CRT/0	CRT/LV	P value
SBP (mm Hg)*	113.9±17	118.5±17.4	<0.05
DBP (mm Hg)**	68.5±7.1	69.6±8.1	NS
PP (mm Hg)***	45.5±13.6	49±14	<0.05

* SBP – systolic blood pressure; ** DBP – diastolic blood pressure; *** PP – pulse pressure.

Table 3. Value of components of heart rate variability (HRV) in patients with CRT/0 and CRT/LV.

Components of HRV	CRT/0		CRT/LV		P value
LF (ms ²)*	16.5	(5.5–34.5)	20.5	(7–45)	<0.05
HF (ms ²)**	13	(4–20)	22	(7.5–38)	<0.05
LF/HF***	1.5	(0.6–2)	1.31	(0.6–2)	NS

* LF – low frequency power; ** HF – high frequency power; *** LF/HF – low-to-high frequency ratio.

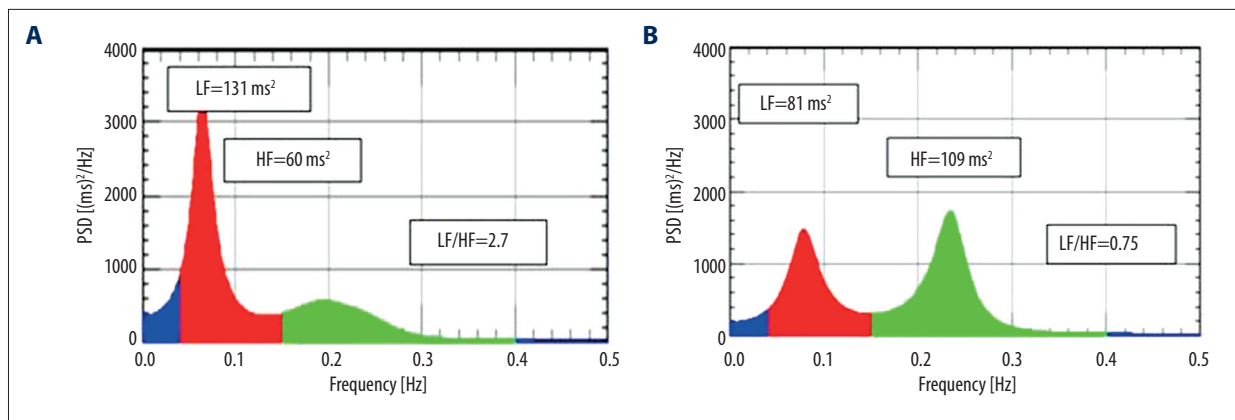


Figure 1. Power spectral density in HRV: low- (LF) and high- (HF) frequency and low-to-high frequency ratio (LF/HF) with: (A) CRT/O and (B) CRT/LV.

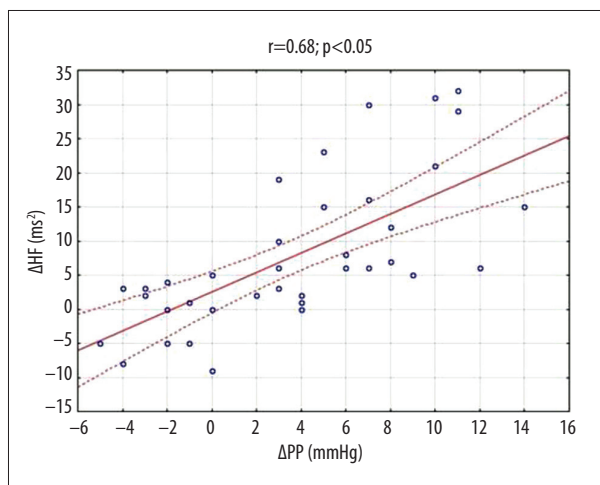


Figure 2. Correlation between change of pulse pressure (ΔPP) and high frequency power (ΔHF).

There were no statistically significant correlations between ΔPP and ΔLF ($R=0.2821$, NS) or ΔPP and $\Delta LF/HF$ ($R=0.0711$, NS).

Percent of change value of pulse pressure (% ΔPP)

Positive immediate individual hemodynamic response ($\Delta PP \geq 10\%$) was observed in 19 (47.5%) patients, whereas 21 (52.5%) patients did not show such a response. We observed that ΔHF ($AUC=0.882$, $P<0.05$) is a component which best differentiates changes during short-term CRT/LV in patients who demonstrated $\Delta PP \geq 10\%$ (Figure 3). Thus, the increase in the HF component correlates with increased PP. Table 4 presents the basic values of ROC curves.

Moreover, we determined the referential value for ΔHF , which will allow predicting an increase for $PP \geq 10\%$. $\Delta HF \geq 6 ms^2$ with a sensitivity of 84.21% and specificity of 85.71% implies a possibility of immediate positive hemodynamic response ($\Delta PP \geq 10\%$) during short-term left ventricular pacing (Figure 4).

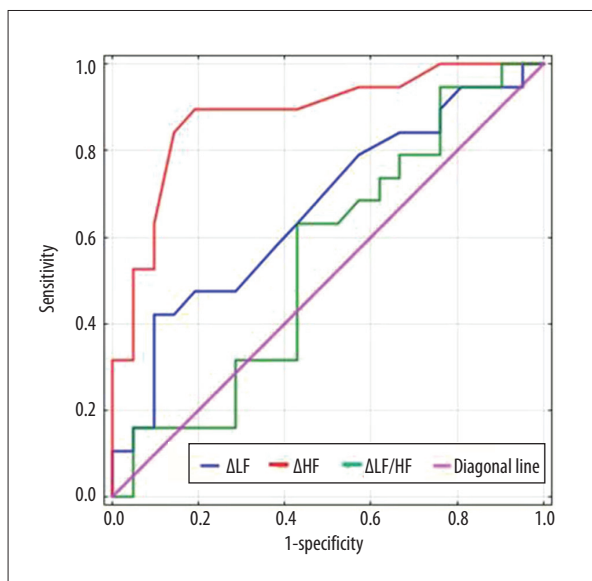


Figure 3. ROC curves showing prognostic ability of ΔLF , ΔHF , and $\Delta LF/HF$ in the prediction of significant change $\Delta PP \geq 10\%$ during short-term left ventricular pacing.

Of the 19 patients with $\Delta PP \geq 10\%$, 16 (84.21%) demonstrated a change in $HF \geq 6 ms^2$ ($P<0.05$) (Table 5).

Discussion

We observed that in patients with implanted CRT, short-term left ventricular pacing can immediately improve left ventricular systolic performance. Based on invasive studies, Dekker et al. observed that biventricular pacing with an optimal left ventricular lead position significantly increased stroke volume (+39%, $P=.01$) and ejection fraction (+30%, $P=.007$) [8]. Nelson et al. confirmed that left ventricular or biventricular pacing strongly enhances systolic function (18±4% rise in arterial pressure and 43±6% increase in dp/dt_{max}) [17]. Auricchio et al. observed

Table 4. Basic values of ROC curves.

Components of HRV	AUC****	*****SE	P value	95% confidence interval	
				-95%CI	+95%CI
DLF*	0.673	0.086	NS	0.505	0.841
DHF**	0.882	0.056	P <0.05	0.773	0.991
DLF/HF***	0.548	0.093	NS	0.366	0.730

* Δ LF – change of low frequency power; ** Δ HF – change of high frequency power; *** Δ LF/HF – change of low-to high frequency ratio; **** AUC – area under curve ROC; ***** SE – standard error.

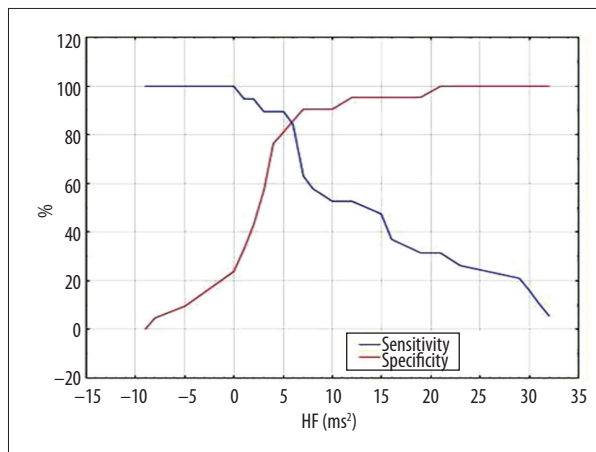


Figure 4. Relationship between sensitivity and specificity of the method of forecasting an immediate positive response to short-term left ventricular pacing and Δ HF value.

that effective left ventricular pacing results in an immediate increase in PP, as evaluated with an invasive method [1]. Other authors confirmed that the increased value of PP positively correlates with improved left ventricular systolic performance, increased stroke volume, and cardiac output [8,17,18]. The method of non-invasive evaluation of changes in PP was used in a study conducted by Butter et al. The authors confirmed that the values of the PP parameter, evaluated with the application of non-invasive photoplethysmography, were correlated with the values of the PP parameter, evaluated with the application of an invasive aortic PP [19].

The results we obtained in our study – increased systolic pressure by 4.6 mmHg and increased PP value by 3.5 mmHg – confirmed the above observations. In the clinical observation, cardiac insufficiency is accompanied by symptoms of a dysfunction of the autonomic nervous system. It is manifested by decreased activity of the parasympathetic system [20,21] and increased sympathetic activity [22,23]. One of the non-invasive markers of the autonomic system is HRV [24]. Patients with cardiac insufficiency demonstrate decreased values of HRV parameters evaluated in both the time domain and frequency analyses, and results of these measurements have high repeatability [24]. In our study, we observed that patients with CRT/O demonstrated low values of HRV components, which were evaluated with short-term frequency domain analysis, both in the LF and HF spectral components. Casolo et al. observed 10-fold lower values of frequency parameters (LF and HF) in patients with CRT in comparison with healthy subjects. Moreover, the parameters remained stable throughout the day [25].

Values of parameters of the frequency domain analysis are closely related to the progression of the disease. Some authors have noted that in an early stage of a disease, patients demonstrate higher spectral values of the LF component and lower spectral values of the HF component, which confirms a shift in the balance of the autonomic system towards the sympathetic component [26–28]. Other authors have made similar observations while conducting studies on patients with advanced heart failure. It was confirmed that there is a relationship in the long-term improvement in hemodynamic parameters and improvement in decreased HRV parameters.

Table 5. The number of patients with Δ PP \geq 10% and Δ HF \geq 6 ms².

GROUP		DHF <6 ms ² **	DHF \geq 6 ms ²	P value
DPP <10%*	N	18	3	
	%	85.71%	14.29%	
DPP \geq 10%	N	3	16	
	%	15.79%	84.21%	

* Δ PP – change of pulse pressure; ** Δ HF – change of high frequency power.

Piccirillo et al. observed patients with implanted CRT within a period of 1 year. They evaluated the impact of the therapy on the tone of the autonomic system by analyzing 5-minute ECG records with the use of the frequency domain method. These authors noted the CRT therapy positively contributed to HRV component values [29]. It positively influenced the ventricular systolic performance, which immediately resulted in a change of PP values [17]. In our study, short-term left ventricular pacing caused a statistically significant increase in the HRV value of LF and HF components.

Percentage change of PP ($\Delta PP\%$) was used to evaluate the immediate hemodynamic response to left ventricular pacing. Auricchio et al. noted that a change in PP higher than 5% evaluated by an invasive method proves an immediate positive response to resynchronization therapy [30]. Butter et al. observed that an 8% change in the PP value proves an immediate positive hemodynamic response to effective left ventricular pacing [18]. In the group of patients we studied, an immediate individual positive hemodynamic response to short-term left ventricular pacing was observed in 47.5% of the patients. Vogt et al. noted that a 10% increase in the PP value might facilitate the identification of the suitable site for epicardial pacing, and patients who have had electrodes implanted in this site demonstrate clinical and echocardiographic improvement in long-term observation [31]. Our study confirmed a highly positive, statistically significant correlation between ΔPP and ΔHF . Thus, an increased value of HF might imply the possibility of an immediate individual positive hemodynamic response ($\Delta PP \geq 10\%$) during short-term left ventricular pacing.

In the literature, there is no thorough analysis of any relationships between ΔPP and ΔHF measured during short-term left ventricular pacing. The results of our study require confirmation in a larger number of patients.

References:

- Auricchio A, Stellbrink C, Block M et al: Effect of pacing chamber and atrioventricular delay on acute systolic function of paced patients with congestive heart failure. The Pacing Therapies for Congestive Heart Failure Study Group. The Guidant Congestive Heart Failure Research Group. *Circulation*, 1999; 99: 2993-3001
- Bleeker GB, Kaandorp TA, Lamb HJ et al: Effect of posterolateral scar tissue on clinical and echocardiographic improvement after cardiac resynchronization therapy. *Circulation*, 2006; 113: 969-76
- Bilchick KC, Lardo AC: Cardiac resynchronization therapy: application of imaging to optimize patient selection and assess response. *Curr Heart Fail Rep*, 2008; 5: 119-27
- Bristow MR, Saxon LA, Boehmer J et al: Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure. *N Engl J Med*, 2004; 350: 2140-50
- Bleeker GB, Bax JJ, Fung JW et al: Clinical versus echocardiographic parameters to assess response to cardiac resynchronization therapy. *Am J Cardiol*, 2006; 97: 260-63
- Ypenburg C, Van D, Westenberg JJ et al: Noninvasive imaging in cardiac resynchronization therapy. Part 2: Follow-up and optimization of settings. *Pacing Clin Electrophysiol*, 2008; 31: 1628-39
- Ypenburg C, van Bommel RJ, Delgado V et al: Optimal left ventricular lead position predicts reverse remodeling and survival after cardiac resynchronization therapy. *J Am Coll Cardiol*, 2008; 52: 1402-9
- Dekker AL, Phelps B, Dijkman B et al: Epicardial left ventricular lead placement for cardiac resynchronization therapy: optimal pace site selection with pressure-volume loops. *J Thorac Cardiovasc Surg*, 2004; 127: 1641-47
- Gold MR, Auricchio A, Hummel JD et al: Comparison of stimulation sites within left ventricular veins on the acute hemodynamic effects of cardiac resynchronization therapy. *Heart Rhythm*, 2005; 2: 376-81
- Gasparini M, Mantica M, Galimberti P et al: Is the left ventricular lateral wall the best lead implantation site for cardiac resynchronization therapy? *Pacing Clin Electrophysiol*, 2003; 26: 162-68
- Derval N, Steendijk P, Gula LJ et al: Optimizing hemodynamics in heart failure patients by systematic screening of left ventricular pacing sites the lateral left ventricular wall and the coronary sinus are rarely the best sites. *J Am Coll Cardiol*, 2010; 9: 55: 566-75
- van Gelder BM, Meijer A, Bracke FA: Timing of the left ventricular electrogram and acute hemodynamic changes during implant of cardiac resynchronization therapy devices. *Pacing Clin Electrophysiol*, 2009; 32(Suppl.1): S94-97

Conclusions

A significant correlation between ΔPP and ΔHF was observed during short-term left ventricular pacing in patients with CRT. $\Delta HF \geq 6 \text{ ms}^2$ may serve as a tool in the selection of a suitable site for placement of a left ventricular lead.

What is innovative in the study?

The present study provides important new data that might be useful in a potential application of changes in HF spectral components of HRV. HF power might facilitate the selection of a left ventricular lead placement site when we assume that a positive hemodynamic response (i.e., a change in the PP value) is the evaluation criterion.

Study Limitations

The limitations of the study include the small number of patients because of the exclusion of patients with diabetes, hypertension, a great number of premature ventricular and supraventricular extrasystoles, and disorders of AV conduction of the 2nd and 3rd degree. The obtained HRV results were not verified with any available commercial software. Pressure parameters were evaluated with the use of only one 5-minute non-invasive measurement. With regards to HRV parameters, we used only 1 ECG record. Factors affecting arterial tension and HRV might have affected the obtained results to some extent.

Conflicts of interest

The authors report no conflicts of interest.

13. Peñaz J: Photoelectric measurement of blood pressure, volume and flow in the finger. *Digest of the 10th International Conference on Medical and Biological Engineering*. Dresden, 1973
14. Smith NT, Wesseling KH, de Wit B: Evaluation of two prototype devices producing noninvasive, pulsatile, calibrated blood pressure measurement from a finger. *J Clin Monit*, 1985; 1: 17–29
15. Petersen ME, Williams TR, Sutton R: A comparison of non-invasive continuous finger blood pressure measurement (Finapres) with intra-arterial pressure during prolonged head-up tilt. *Eur Heart J*, 1995; 16: 1641–54
16. Kudryński K, Strumiłło P, Ruta J: Computer software tool for heart rate variability (HRV), T-wave alternans (TWA) and heart rate turbulence (HRT) analysis from ECGs. *Med Sci Monit*, 2011; 17(9): MT63–71
17. Nelson GS, Berger RD, Fetis BJ et al: Left ventricular or biventricular pacing improves cardiac function at diminished energy cost in patients with dilated cardiomyopathy and left bundle-branch block. *Circulation*, 2000; 102: 3053–59
18. Butter C, Auricchio A, Stellbrink C et al: Effect of resynchronization therapy stimulation site on the systolic function of heart failure patients. *Circulation*, 2001; 104: 3026–29
19. Butter C, Stellbrink C, Belalcazar A et al: Cardiac resynchronization therapy optimization by finger plethysmography. *Heart Rhythm*, 2004; 1: 568–75
20. Nolan J, Flapan AD, Capewell S et al: Decreased cardiac parasympathetic activity in chronic heart failure and its relation to left ventricular function. *Br Heart J*, 1992; 67: 482–85
21. Fei L, Keeling PJ, Gill JS et al: Heart rate variability and its relation to ventricular arrhythmias in congestive heart failure. *Br Heart J*, 1994; 71: 322–28
22. Kienzle MG, Ferguson DW, Birkett CL et al: Clinical, hemodynamic and sympathetic neural correlates of heart rate variability in congestive heart failure. *Am J Cardiol*, 1992; 69: 761–67
23. Malliani A, Lombardi F, Pagani M: Power spectrum analysis of heart rate variability: a tool to explore neural regulatory mechanisms. *Br Heart J*, 1994; 71: 1–2
24. Van Hoogenhuyze D, Weinstein N, Martin GJ et al: Reproducibility and relation to mean heart rate of heart rate variability in normal subjects and in patients with congestive heart failure secondary to coronary artery disease. *Am J Cardiol*, 1991; 68: 1668–76
25. Casolo G, Balli E, Fazi A et al: Twenty-four-hour spectral analysis of heart rate variability in congestive heart failure secondary to coronary artery disease. *Am J Cardiol*, 1991; 67: 1154–58
26. Saul JP, Arai Y, Berger RD et al: Assessment of autonomic regulation in chronic congestive heart failure by heart rate spectral analysis. *Am J Cardiol*, 1988; 61: 1292–99
27. Floras JS: Clinical aspects of sympathetic activation and parasympathetic withdrawal in heart failure. *J Am Coll Cardiol*, 1993; 22(4 Suppl.A): 72A–84A
28. Casolo GC, Stroder P, Sulla A et al: Heart rate variability and functional severity of congestive heart failure secondary to coronary artery disease. *Eur Heart J*, 1995; 16: 360–67
29. Piccirillo G, Magri D, di Carlo S et al: Influence of cardiac-resynchronization therapy on heart rate and blood pressure variability: 1-year follow-up. *Eur J Heart Fail*, 2006; 8: 716–22
30. Auricchio A, Ding J, Spinelli JC et al: Cardiac resynchronization therapy restores optimal atrioventricular mechanical timing in heart failure patients with ventricular conduction delay. *J Am Coll Cardiol*, 2002; 39: 1163–69
31. Vogt J, Heintze J, Lamp B et al: Standard haemodynamic measurements. *Eur Heart J*, 2004; Supplements 6(Supplement D), D29–34