

Assessment of left ventricular diastolic function by radionuclide ventriculography in patients with chronic heart failure and reduced ejection fraction

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Summary

Study objective: To compare parameters of diastolic function as assessed by radionuclide ventriculography (RNVG) and Doppler echocardiography (ECHO) in the patients with chronic heart failure and reduced ejection fraction (HF REF). **Patients and methods:** RNVG and ECHO were performed on the same day in 40 patients with systolic chronic HF, NYHA II and III, with LV EF < 50 % and sinus rhythm, followed at tertiary HF clinic. Diastolic function was assessed by RNVG using parameters: PFR (peak filling rate [% SV/sec]), TFR – time to peak filling rate (ms), and by ECHO using pulse Doppler parameters: the peak Doppler velocities of early (E) and late diastolic flow (A), the E/A ratio, the calculated mean of the early (E') diastolic velocity of septal and lateral mitral annulus measured by tissue Doppler imaging, and the E/E' ratio. **Results:** The mean PFR was 421.7 (median 371.0) % SV/sec and TPF was 198.7 ms (median 169.5), the mean E/A ratio was 1.21 (median 0.85) and the E/E' ratio was 9.0 (median 8.40). TPF correlated significantly (inverse correlation) with the E/A ratio ($r = -0.34$, $p = 0.030$), and not significantly with E' ($r = -0.27$, $p = 0.082$), the PFR/age ratio correlated with the E/E' ratio ($r = -0.31$, $p = 0.05$). **Conclusion:** Significant correlations of parameters of diastolic function as assessed by radionuclide and Doppler studies were identified in the HF REF patients.

Key words: diastolic function – Doppler echocardiography – heart failure with reduced ejection fraction – radionuclide ventriculography

Hodnocení diastolické funkce levé komory pomocí radionuklidové ventrikulografie u pacientů s chronickým srdečním selháním a sníženou ejekční frakcí

Souhrn

Cíl práce: Zjistit, zda u pacientů s chronickým srdečním selháním a sníženou ejekční frakcí korelují parametry diastolické funkce levé komory hodnocené radionuklidovou ventrikulografií (RNVG) s parametry získanými dopplerovskou echokardiografií (ECHO). **Soubor a metodika:** RNVG a ECHO byly provedeny u 40 pacientů (36 mužů a 4 žen) s CHSS (EF LK < 50 %). K posouzení diastolické funkce levé komory byly použity pro RNVG: PFR (peak filling rate [% SV/sec]), TFR – time to peak filling rate (ms), pro ECHO: vrcholová rychlost časného transmitrálního diastolického toku (E), rychlost pozdního diastolického toku (A) měřených pulzní dopplerovskou echokardiografií a vypočtený poměr E/A a vypočtený průměr rychlostí diastolického pohybu septálního a laterálního mitrálního anulu (E') měřených tkáňovou dopplerovskou echokardiografií a vypočtený poměr E/E'. RNVG a ECHO byly provedeny týž den. **Výsledky:** Průměrný poměr E/A byl dle ECHO 1,21 (medián 0,85) a E/E' 9,0 (medián 8,40). Průměrný PFR byl 421,7 (medián 371,0) % SV/sec a průměrný TPF byl 198,7 ms (medián 169,5). TPF koreloval významně s E/A ($r = -0,34$, $p = 0,030$), korelace TPF k E' ($r = -0,27$, $p = 0,082$) nedosáhla statistické významnosti, poměr PFR/věk koreloval s E/E' ($r = -0,31$, $p = 0,05$). **Závěr:** U pacientů s chronickým srdečním selháním a sníženou ejekční frakcí byly nalezeny významné korelace mezi některými parametry diastolické funkce levé komory hodnocené pomocí radionuklidové ventrikulografie a dopplerovské echokardiografie.

Klíčová slova: diastolická funkce – dopplerovská echokardiografie – radionuklidová ventrikulografie – srdeční selhání se sníženou ejekční frakcí

Introduction

Radionuclide studies showed significant correlation of the parameters of diastolic function as assessed by radionuclide ventriculography (RNVG) with parameters obtained by Doppler echocardiography (ECHO) in the patients with heart failure with preserved ejection fraction (HF REF) [1,2]. An assessment of diastolic function in subjects with systolic heart failure brings important prognostic information: subjects with reduced ejection fraction and advanced diastolic dysfunction have worse outcome and higher natriuretic peptides levels [3]. Doppler echocardiography and tissue Doppler imaging are standard methods for the non-invasive assessment of left ventricular diastolic function [4]. The assessment of left ventricular diastolic function using another method might be of advantage in the subjects with poor echocardiographic images.

The aim of the present study was to compare the parameters of diastolic function as assessed by RNVG and ECHO in the patients with chronic heart failure and reduced ejection fraction (HF REF).

Patients and methods

RNVG and ECHO were performed on the same day in 40 patients (36 men and 4 women) with systolic chronic heart failure (CHF), functional class according to New York Heart Association (NYHA) II and III, left ventricular ejection fraction (LV EF) < 50 % and sinus rhythm. All subjects were followed at tertiary HF clinic at Na Homolce Hospital, Cardiovascular Center. The mean age of the patient cohort was 64 years.

All patients signed inform consent and approval for the study was granted by Local Board Ethics Committee Na Homolce Hospital in 2010.

Patients were treated with optimal medical therapy including betablockers, angiotensin-converting enzyme inhibitors or angiotensin receptor blockers and mineralocorticoid receptor antagonists for at least six months before study entry. Ischemic etiology of CHF was present in 22 patients, 18 subjects had dilated

cardiomyopathy. Patients with valvular heart disease as a primary cause of CHF were not included in the study. Patients with moderate to severe functional mitral regurgitation were not included in the study too. Cardioverter defibrillator was implanted in 36 patients (90 %) in the past. The mean LV EF as assessed by dual-mode echocardiography (Simpson's method) was 30 %.

Gated equilibrium radionuclide ventriculography (RNVG) was realized using standard protocol in the Department of Nuclear Medicine and the acquired data were interpreted by a specialist in Nuclear Cardiology. Patient's red blood cells (RBCs) were radiolabeled and electrocardiograph gated cardiac scintigraphy was obtained. Data were collected from several hundred cardiac cycles to generate an image set of the beating heart that was presented as a single, composite cardiac cycle [5,6]. The administered activity was 570 MBq and autologous RBCs were labeled with ^{99m}Tc using the in vivo techniques. Acquisition was performed by a gamma camera interfaced to a dedicated computer. SPECT E. CAM, Siemens, system and Biomedical 101NR, Biomedical Systems, Inc. were used.

Diastolic function was assessed by RNVG using parameters: PFR (peak filling rate [% EDV/sec]), TPF – time to peak filling (ms). The normal values for PFR and TPF vary according to different published reports, normal values are usually: PFR > 250 % EDV/sec and TPF < 150 ms [1].

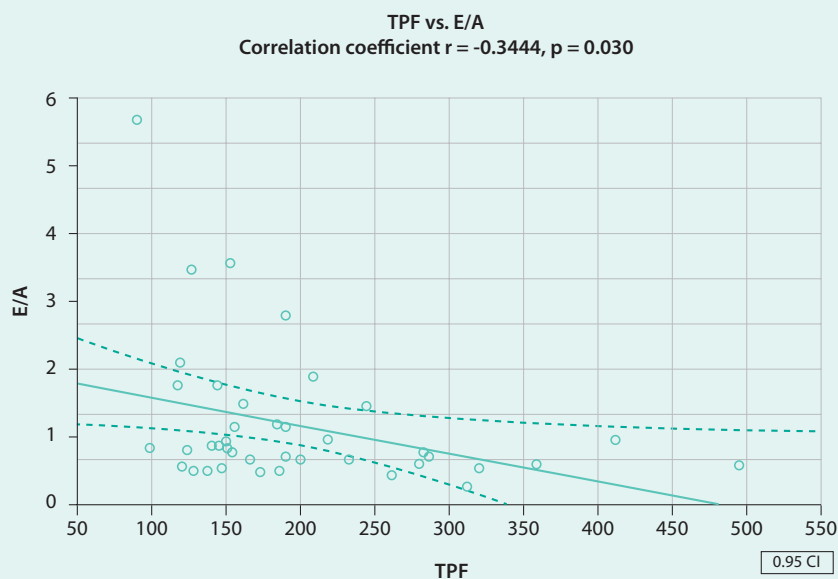
Echocardiography studies were realized on the same day as RNVG and the results were interpreted by two specialists. An echocardiographic examination of the each patient was performed using a broadband transducer with a transmitting frequency from 1.7 to 4.0 MHz on commercially available equipment (GE Vivid 7, USA).

Doppler echocardiography is widely used for the noninvasive assessment of diastolic filling of the left ventricle [7]. Mitral flow is dependent on multiple factors, tissue Doppler imaging (TDI) of mitral annular motion corrects the influence of myocardial relaxation on transmitral flows [8]. Diastolic function was assessed by ECHO using pulse Doppler parameters: the peak

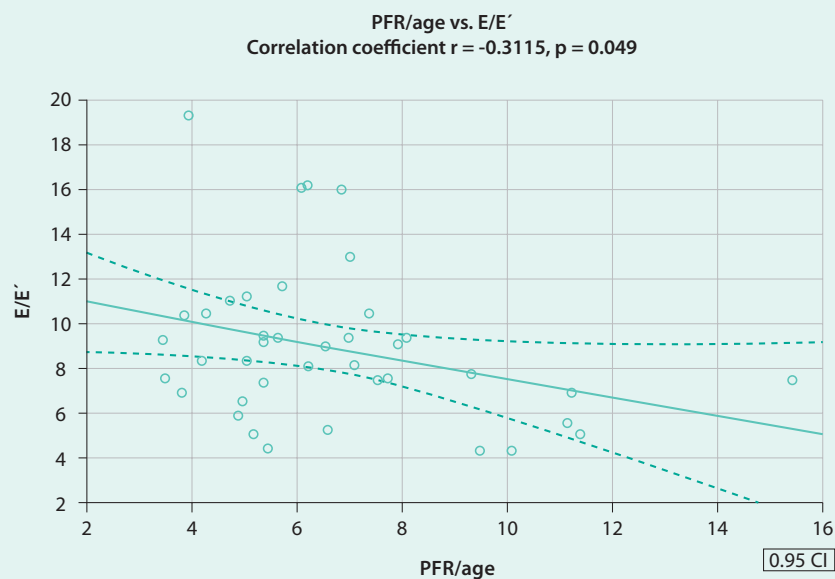
Table. Parameters of diastolic function as assessed with Doppler echocardiography and radionuclide ventriculography

	mean	CI -95 %	CI +95 %	median	minimum	maximum	SD
E cm/sec	65.6	18.9	29.8	62	27	116	23.2
A cm/sec	69.0	18.2	28.5	67.5	18	113	22.2
E/A	1.21	0.87	1.36	0.85	0.29	5.70	1.1
mean E' cm/sec	7.7	1.9	3.1	7.0	4.0	13.0	2.4
E/E'	9.0	2.8	4.4	8.4	4.4	19.3	3.4
PFR % EDV/sec	421.7	139.6	218.8	371.0	214.0	1186.0	170.4
TPF sec	198.7	170.6	226.8	169.5	90.0	494.0	87.8
PFR/age	6.6	5.8	7.4	6.1	3.4	15.4	2.5

A – late diastolic flow velocity CI – confidence interval E – early diastolic flow velocity mean E' – calculated mean of E' wave velocities of septal and lateral mitral annulus assessed by tissue Doppler imaging PFR/age – the peak filling rate/age ratio PFR – peak filling rate RNVG – radionuclide ventriculography SD – standard deviation TPF – time to peak filling

Fig. 1. Correlation of time to peak filling with the E/A ratio

r – Spearman's correlation coefficient p – level of significance E – early diastolic flow velocity A – late diastolic flow velocity TPF – time to peak filling

Fig. 2. Correlation of time to peak filling rate/age ratio with E/E' ratio

r – Spearman's correlation coefficient p – level of significance E – early diastolic flow velocity **Mean E'** – calculated mean of E' wave velocities of septal and lateral mitral annulus assessed by tissue Doppler imaging **PFR** – peak filling rate

velocities of early (E) and late (A) diastolic flow, the E/A ratio, the calculated mean of the early (E') diastolic velocity of the septal and lateral mitral annulus measured by tissue Doppler imaging, and the E/E' ratio.

Spearman's correlation coefficient was used for the statistical analysis.

Results

The parameters of diastolic function obtained by ECHO and RNVG are shown in the [table](#) (p. 111). As shown in the table, mean PFR was 421.7 (median 371.0) % SV/sec and TPF was 198.7 ms (median 169.5), mean E/A ratio was 1.21 (median 0.85) and E/E' ratio was 9.0 (median

8.40). Peak filling rate is influenced by age and TPF is influenced by heart rate. PFR/age ratio and TPF/HR ratio were used for further evaluation.

Correlation of parameters of diastolic function as assessed by RNVG and ECHO are shown in the figures. TPF correlated significantly (inverse correlation) with the E/A ratio (fig. 1) and not significantly with E' (inverse correlation). PFR/age ratio correlated with the E/E' ratio significantly (fig. 2).

Discussion

In the present study, significant correlations of parameters of diastolic function as assessed by radionuclide and Doppler studies were identified in the HF REF patients.

Our study has several limitations. From the logistic issues, it was not possible to record echo Doppler studies and radionuclide studies simultaneously. Both methods were used on the same day. Patients were instructed not to change their regular medication and stayed fasting before ECHO and RNVG studies. Other limitations get along with each method.

Doppler echocardiography is widely used for the noninvasive assessment of diastolic filling of the left ventricle. Mitral flow is dependent on multiple inter-related factors including heart rate, atrial and ventricular compliance and left atrial pressure [9]. Tissue Doppler imaging of the mitral annulus during diastole has been proposed for assessment of cardiac function. The velocity of the earliest diastolic motion measured by pulse-wave TDI is not dependent on pressure gradient as is blood flow [8].

Radionuclide ventriculography has several limitations too. Many studies have demonstrated a negative correlation between age and PFR and a positive correlation between heart rate and PFR in normal subjects [10]. Thus the age and heart rate of the patient must be considered when diastolic measurements are assessed. In patients with impairment of LV systolic function, PFR is reduced in proportion to the fall in ejection fraction [11].

On the other hand, radionuclide studies have some advantages. The major advantages of the radionuclide ventriculography is its ability to measure relative volume changes with time without the geometric assumptions necessary with contrast angiographic and echocardiographic techniques. Other advantages include: lack of dependence on patient anatomy, production of data in a digitized format ready for computer processing and high reproducibility [5,6]. This was a reason, why studies in different clinical settings put back the interest in the assessment of diastolic function by radionuclide ventriculography.

In one study, the assessment of LV diastolic function in the patients with subclinical hypothyroidism was useful in prediction of response to levothyroxine replacement [12]. However, not parameters of diastolic dysfunction including PFR and TPF but ejection

fraction were predictive for new heart failure onset and mortality in asymptomatic patients referred for RNVG for cardiac function evaluation [13].

Our result showed that radionuclide studies may be used for cardiac function assessment in the patients with systolic heart failure. The RNVG might be indicated with HF REF subjects with poor echocardiographic images.

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