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Factors Influencing the Tissue Doppler Echocardiography Indices of Systolic and Diastolic Function of Left Myocardial Ventricle in Patients Treated with Intermittent Hemodialysis

Czynniki wpływające na wskaźniki tkankowej echokardiografii dopplerowskiej funkcji skurczowej i rozkurczowej mięśnia sercowego lewej komory u chorych leczonych powtarzaną hemodializą

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Abstract

Background. Uremic toxicity and overhydration are cardiovascular risk factors, which are significantly, although transiently, decreased by each hemodialysis (HD) session.
Objectives. Evaluation of tissue Doppler echocardiography (echo) indices estimating function of left myocardial ventricle before and after HD session with relation to demographic, clinical and laboratory parameters of examined patients.
Material and Methods. The 56 patients underwent tissue Doppler echo before and after 4-hour HD with ultrafiltration volume (UFV) depended on difference between actual and dry body mass. Pre- and post-HD echo indices and their differences were related to demographic, clinical and laboratory data.
Results. Pre-HD echo indices revealed systolic dysfunction (LVEF < 50%) in 12.5% patients, diastolic dysfunction – in 92.9% patients (mild in 39.3%, moderate in 46.4%, severe in 7.1%). After HD session (UFV 2.1 ± 1.0 L, Kt/V 1.33 ± 0.14) systolic dysfunction was shown in 10.7% patients, diastolic dysfunction – in 92.9% (mild in 60.7%, moderate in 26.8%, severe in 5.4%). Pre- and post-HD echo indices correlated with age, HD vintage, Hb/Hct/RBC, CRP and PTH. Differences in pre- and post-HD echo parameters correlated with UFV, Hb/Hct/RBC, WBC, Ca, P, Ca x P, uric acid, and daily urine volume. Independent predictors of echo parameters were age, ischemic heart disease, valvular disease, treatment with ACEI/ARB and/or β-blockers, UFV and CRP.
Conclusions. In HD patients echo indices and beneficial effects of HD-induced decrease in preload on echo indices are negatively related to anemia, inflammation, decreased renal function, ischemic heart disease and valvular disease (**Adv Clin Exp Med 2010, 19, 4, 469–480**).

Key words: tissue Doppler echocardiography, left ventricular function, hemodialysis, uremic toxicity.

Streszczenie

Wprowadzenie. Toksemia mocznicowa i przewodnienie są czynnikami ryzyka chorób sercowo-naczyniowych, które znacząco, chociaż przejściowo, zmniejszają się podczas każdego zabiegu hemodializy (HD).
Cel pracy. Ocena wskaźników tkankowej echokardiografii (echo) dopplerowskiej szacujących czynność mięśnia sercowego lewej komory przed i po zabiegu HD w odniesieniu do parametrów demograficznych, klinicznych i laboratoryjnych badanych chorych.
Materiał i metody. U 56 chorych wykonano echo z Dopplerem tkankowym przed i po 4-godzinnej HD z objętością ultrafiltracji (UFV) zależną od różnicy między bieżącą a suchą masą ciała. Wskaźniki echo, uzyskane przed i po HD, oraz różnice między nimi odniesiono do danych demograficznych, klinicznych i laboratoryjnych.
Wyniki. Przeddializacyjne parametry echo wskazywały na dysfunkcję skurczową (LVEF < 50%) u 12,5% chorych,

a dysfunkcję rozkurczową – u 92,9% chorych (łagodną u 39,3%, umiarkowaną u 46,4%, ciężką u 7,1%). Po zabiegu HD (UFV 2,1 ± 1,0 l, Kt/V 1,33 ± 0,14) dysfunkcja skurczowa występowała u 10,7% chorych, a dysfunkcja rozkurczowa – u 92,9% (łagodna u 60,7%, umiarkowana u 26,8%, ciężka u 5,4%). Przed- i podializacyjne wskaźniki echo korelowały z wiekiem, długością leczenia HD, Hb/Hct/RBC, CRP i PTH. Różnice między wskaźnikami przed i po HD korelowały z UFV, Hb/Hct/RBC, WBC, Ca, P, Ca x P, kwasem moczowym i dobową objętością moczu. Niezależnymi predyktorami wskaźników echo były wiek, choroba niedokrwienna serca, choroba zastawek, leczenie ACEI/ARB i/lub lekami blokującymi kanał β, UFV i CRP.

Wnioski. U chorych leczonych HD zarówno wskaźniki echo, jak i dobroczynny wpływ obniżonego w wyniku zabiegu HD obciążenia wstępnego na te wskaźniki, podlegają niekorzystnym oddziaływaniom niedokrwistości, zapalenia, upośledzonej czynności nerek, niedokrwiennej choroby serca i choroby zastawek serca (**Adv Clin Exp Med 2010, 19, 4, 469–480**).

Słowa kluczowe: tkankowa echokardiografia dopplerowska, czynność mięśnia sercowego lewej komory, hemodializa, toksemia mocznicowa.

Cardiovascular disease is the leading cause of premature mortality and disability of dialyzed patients. Many of the well documented ("traditional") cardiovascular risk factors in the general population (older age, obesity, elevated blood pressure, physical inactivity, cigarette smoking, dyslipidemia, glucose intolerance, hyperuricemia, hyperfibrinogenemia) are also present in end-stage renal disease. The presence of chronic kidney disease independently predicts risk for the onset or progression of cardiovascular disease and mortality, even after adjustment for traditional cardiovascular risk factors [1]. "Uremic" risk factors are related to salt or volume overload with consequent hypertension, anemia, increased oxidative stress, chronic inflammatory process, deranged calcium-phosphate metabolism, loss of residual renal function, accumulation of specific uremic toxins, malnutrition, metabolic acidosis, and hemodialysis arterio-venous fistula. All these risk factors, uremic cardiomyopathy, coronary artery disease and valvular disease lead to myocardial damage that may eventually result in congestive heart failure (CHF) [2].

Uremic toxicity and overhydration are cardiovascular risk factors, which are significantly, although transiently, decreased by each HD session. Changes in echo parameters due to HD-induced volume contraction were already examined showing not uniform results [3–10], but influence of parameters related to uremic state on echo indices and their changes in response to HD ultrafiltration are totally unknown. The aim of this study was to assess the prevalence of left ventricular dysfunction in HD patients and to examine an influence of single HD session on the echo indices evaluating systolic and diastolic function of the left myocardial ventricle. Cardiac parameters obtained in standard two dimensional (2D) projection, transmitral pulsed Doppler and tissue Doppler echo were related to patients` clinical data and laboratory parameters usually influenced by occurrence of uremic state.

Material and Methods

Having obtained written informed consent, 56 stable patients in stage 5 of chronic kidney disease treated with intermittent HD in one dialysis center (Rawicz) volunteered for participation in the study. Causes of end-stage renal disease (ESRD) included chronic tubulointerstitial nephritis (n = 16), diabetic nephropathy (n = 14), hypertensive nephropathy (n = 7), obstructive nephropathy (n = 6) and chronic glomerulonephritis (n = 5). In 8 cases the cause of ESRD remained unknown. Patients with cancers or those who finished treatment of neoplasm no longer than 5 years from this study entry were excluded. The cardiac exclusion criterion was a condition making measurement of cardiac flows related to atrial function impossible (example persistent atrial fibrillation, heart rhythm from cardiac stimulator).

In the examined group there were 33 men and 23 women in the age of 64.4 ± 14.8 years. HD vintage was 117; 1–219 months, body mass index 26.6 ± 5.2 kg/m^2, residual urine volume – 225, 0–2300 mL/day.

Medical histories of all patients were carefully evaluated in respect to evidence for diagnosis of cardiac disease and CHF. Additionally, attention was paid for arterial hypertension and treatment with angiotensin converting enzyme inhibitors (ACEI), angiotensin receptor blockers (ARB), and ß-adrenergic receptor blockers. Patients with CHF (n = 43) were evaluated using the New York Heart Association (NYHA) functional classification of CHF patients [11]. Valvular disease was classified using guidelines of the European Society of Cardiology [12].

Ischemic heart disease was diagnosed in 23 cases (myocardial infarction – in 9 patients: inferior infarction – 4 cases, inferior-anterior infarction – 2 cases, anterior infarction – 2 cases and infarction without established localization – 1 case). Revascularization was done in 3 patients. The number of more than mild aortic/mitral/tricuspid/

pulmonary stenosis or more than a mild degree of aortic/mitral/tricuspid/pulmonary regurgitation was 1/0/0/0 and 4/14/14/1, respectively, in 25 patients (moderate – in 18, severe – in 7 cases). The examined group included 14 patients with NYHA class I, 20 patients with NYHA class II, 8 patients with NYHA class III and one patient with NYHA class IV. Arterial hypertension was shown in 46 patients. Nineteen patients were treated with ACEI/ARB, 33 patients with ß-adrenergic receptor blockers.

All patients were conducted with three HD sessions per week lasting 4 hours each. HD machines used were Fresenius type 4008 S equipped polysulfone-based membranes regulated to a blood flow rate of 200–300 mL/min and a dialysate flow rate between 500 and 800 mL/min. Dialyzers were not reused. On-line Kt/V was measured by the conductivity method. Arterio-venous fistula in 49 cases and permanent catheter in 7 cases were used as vascular access. Ultrafiltration volume (UFV) depended on difference between pre-HD body weight and dry body mass, which was estimated based on clinical signs of hydration and blood pressure behavior during previous HD sessions. Effective dehydration was considered when post-HD body weight equaled dry body mass ± 1%.

Results of laboratory data, routinely performed in all HD patients, were as follows: hemoglobin 10.8 ± 1.4 g/dL, hematocrit 33.7 ± 4.3%, red blood cells 3.62 ± 0.52 T/L, white blood cells 6.23 ± 1.90 K/mL, platelets 232.1 ± 106.8 K/mL, C-reactive protein 7.86 (2.42; 20.9) mg/dL, total Ca 8.68 ± 0.88 mg/dL, phosphates 4.95 ± 1.49 mg/dL, intact parathyroid hormone (PTH) 149.2 (71.4; 385.3) pg/mL, Ca x P 42.8 ± 13.6 mg^2/dl^2, uric acid 5.31 ± 0.94 mg/dL.

All patients underwent echo examination two times: images were recorded 20–30 minutes prior to commencing HD and 20–30 minutes after the end of 4 hour HD session.

All echo measurements were made with the Pro-Sound 4000 device (Aloka, Japan) by a single echocardiographer (A.R.). The pulsed Doppler was used to measure the velocity of transmitral blood flow (protodiastolic E wave and end-diastolic A wave, and E/A ratio), the deceleration time (DT), the isovolumetric relaxation time (IVRT), the atrial reversal (Ar), diastolic superior pulmonary vein velocity (D), systolic superior pulmonary vein velocity (S), and S/D ratio. The tissue Doppler with four chambers of the medial mitral annulus was used for measuring the velocity of the cardiac muscle with the E´ protodiastolic wave and the A´ end-diastolic wave, the E´/A´ ratio, and the ratio of the pulsed Doppler E wave and the tissue Doppler E´ wave (E/E`). Measurements in 2D projection included inferior vena cava (IVC) diameter, left atrium (LA) diameter, LA surface, left ventricular end – diastolic diameter (LVEDd), left ventricular end – systolic diameter (LVESd), left ventricular ejection fraction (LVEF), and right atrium (RA) surface. During each examination echo parameters were taken at least two times, dependently on quality of Doppler recordings, and measurements were averaged. Pre- and post-HD echo parameters (registered and calculated) were compared and differences between them were statistically evaluated.

LVEF was evaluated using Simpson`s method. Systolic dysfunction was diagnosed when LVEF was < 50% [13]. The echo criteria for the diagnosis of diastolic dysfunction are shown in Table 1. They were elaborated basing on recommendations of the European Society of Cardiology [13, 14] and on the Canadian consensus guidelines [15]. Three groups of diastolic dysfunction were distinguished using complex analysis of transmitral pulsed and tissue Doppler echo parameters: mild (abnormal relaxation pattern), moderate (pseudonormal pattern) and severe (restrictive pattern).

For comparisons of own results with selected previously published data [16, 17], the authors grouped E/A ratio using the algorithm cited by Khouri et al. [18] and Gagliardi et al. [17]. The algorithm cited by Khouri et al. [18] was applied in HD patients with LVEF > 50%: E/A ratio < 0.75 indicated ventricular relaxation impairment; normal or pseudonormal pattern was diagnosed when E/A ratio was 0.75–1.50 and restrictive pattern – when E/A was > 1.50. Gagliardi et al. [17] grouped patients (26 on HD, 5 on peritoneal dialysis) by E/A ≤ 0.50, > 0.50 – < 1.0, ≥ 1.0 – ≤ 2.0 and > 2.0, but abnormal relaxation pattern was characterized by E/A < 1.0 and restrictive filling pattern by E/A > 2.0. Additionally, E/E' ratio > 10 was used to define increased left ventricular filling pressure in patients with LVEF > 50% [18, 19].

The normality of distribution of variables was checked by the Shapiro-Wilk test. Descriptive statistics are presented as percentages for categorical (nominal) variables, as means with one standard deviation for normally distributed continuous variables, or as medians and lower and upper quartiles for not-normally distributed continuous variables. Comparisons of results before and after HD session were performed using the t-Student test for paired data if distribution of variables was normal or by the Wilcoxon test if this condition was not present. Results of non-paired data were compared using the t-Student test for non-paired data if distribution of variables was normal or the Mann-Whitney test for other than normal distributions. The prevalence of variables was assessed by the chi-square test. The Spearman correlation was

Table 1. The echocardiographic criteria for diagnosis of diastolic dysfunction of the left ventricle (based on ref. 13, 14, 15)

Tabela 1. Kryteria echokardiograficzne rozpoznania dysfunkcji rozkurczowej lewej komory (na podstawie pozycji piśmiennictwa 13, 14, 15)

	Pattern of filling (Profil napływu)	E/A	DT (ms)	E'/A'	IVRT (ms)	S/D	Ar m/s)
Normal (Czynność prawidłowa)	true normal	1–2	150–220	> 1	76 ± 13	≥ 1	< 0.35
Mild dysfunction (Łagodna dysfunkcja)	abnormal (slowed) relaxation	< 1	> 220 (< 50 yrs) > 280 (> 50 yrs)	< 1	> 92 (< 30 yrs) >100 (30–50 yrs) > 105 (> 50 yrs)	≥ 1	< 0.35
Moderate dysfunction (Umiarkowana dysfunkcja)	pseudonormal filling	1–2	150–220	< 1	76 ± 13	< 1	> 0.35
Severe dysfunction (Ciężka dysfunkcja)	restrictive filling	> 2	< 150	< 1	< 60	< 1	> 0.35

Abbreviations:
A – mitral late diastolic velocity.
A` – mitral annular late diastolic velocity.
Ar – atrial reversal.
D – diastolic pulmonary vein velocity.
DT – deceleration time.
E – mitral early diastolic velocity.
E` – mitral annular early diastolic velocity.
IVRT – isovolumetric relaxation time.
S – systolic pulmonary vein velocity.

Skróty:
A – prędkość maksymalna w czasie skurczu przedsionka.
A` – prędkość pierścienia zastawki mitralnej po skurczu przedsionka.
Ar – faza przedsionkowa – faza przepływu wstecznego krwi do żyły płucnej podczas skurczu przedsionka.
D – faza rozkurczowa przepływu w żyle płucnej.
DT – czas deceleracji/spadku prędkości przepływu.
E – prędkość maksymalna wczesnego napływu mitralnego.
E` – wczesnorozkurczowa prędkość pierścienia zastawki mitralnej.
IVRT – czas rozkurczu izowolumetrycznego.
S – faza skurczowa przepływu w żyle płucnej.
yrs – lata.

performed between selected parameters. Stepwise backward multiple linear regression model was used for determination of independent variables influencing selected parameters. The significance of the regression model was checked by Fisher-Snedecor test. The accuracy of the model was determined by coefficient of determination – R^2. The significance of dependent variables was checked by t-Student test. Logistic regression analysis was used to show predictors for development of systolic and diastolic dysfunction of the left ventricle. Odd ratio (OR) and confidence interval (CI) at the levels ± 95% were shown for significant predictors. All tests were analyzed at the significance level $\alpha = 0.05$. Statistical analysis was performed using *STATISTICA PL 8.0* (StatSoft).

This study was reviewed and approved by the Institutional Review Board of Poznań University of Medical Sciences.

Results

At the day of the echo examination online Kt/V at the end of HD session was 1.33 ± 0.14, UFV 2.1 ± 1.0 L. Arterial blood pressure before HD session was 127 ± 17 mm Hg, after HD session 120 ± 21 mm Hg. Respective values of mean arterial pressure were 92 ± 10 mm Hg and 88 ± 11 mm Hg and of pulse pressure 53 ± 13 mm Hg and 48 ± 17 mm Hg. Loss of total body weight,

Abbreviations (Tables 2 and 3):
A – mitral late diastolic velocity, A` – mitral annular late diastolic velocity, Ar – atrial reversal, D – diastolic pulmonary vein velocity, DT – deceleration time, E – mitral early diastolic velocity, E` – mitral annular early diastolic velocity, HD – hemodialysis, IVC – inferior vena cava, IVRT – isovolumetric relaxation time, LA – left atrium, LVEDd – left ventricular end – diastolic diameter, LVESd – left ventricular end – systolic diameter, LVEF – left ventricular ejection fraction, RA – right atrium, S – systolic pulmonary vein velocity.

Skróty (tabela 2 i 3):
A – prędkość maksymalna w czasie skurczu przedsionka, A` – prędkość pierścienia zastawki mitralnej po skurczu przedsionka, Ar – faza przedsionkowa – faza przepływu wstecznego krwi do żyły płucnej podczas skurczu przedsionka, D – faza rozkurczowa przepływu w żyle płucnej, DT – czas deceleracji/spadku prędkości przepływu, E – prędkość maksymalna wczesnego napływu mitralnego, E` - wczesnorozkurczowa prędkość pierścienia zastawki mitralnej, HD – hemodializa, IVC – żyła główna dolna, IVRT – czas rozkurczu izowolumetrycznego, LA – lewy przedsionek, LVEDd – wymiar końcoworozkurczowy lewej komory, LVESd – wymiar końcowoskurczowy lewej komory, LVEF – frakcja wyrzutowa lewej komory, RA – prawy przedsionek, S – faza skurczowa przepływu w żyle płucnej.

Table 2. Changes in echocardiography parameters in patients treated with intermittent hemodialysis (medians, lower and upper quartiles are presented)

Table 2. Zmiany parametrów echokardiograficznych chorych leczonych powtarzaną hemodializą (zaprezentowano mediany, dolne i górne kwartyle)

Parameter (Wskaźnik)	Pre-HD value (Wartość przed dializą)	Post-HD value (Wartość po dializie)	Pre- and post-HD difference (Różnica przed i po dializie)	p value
Two dimensional (2D) projection				
LVEDd (mm)	49.5 46.0–53.0	47.0 44.0–51.5	1.0 0.0–3.0	0.000084
LVESd (mm)	34.0 30.0–38.0	33.0 29.0–35.0	1.0 0.0–3.0	0.000000
LVEF (%)	65.5 56.0–72.0	68.25 63.0–75.0	–2.0 –6.0–0.0	0.000052
LA diameter (mm)	42.0 37.5–45.0	40.0 35.0–44.0	1.0 0.0–3.0	0.000272
RA surface (cm^2)	15.6 13.2–18.5	14.675 12.5–17.36	1.22 0.04–2.54	0.000087
LA surface (cm^2)	20.1 16.9–22.2	17.4 14.1–20.4	1.72 0.60–3.47	0.000001
IVC diameter (mm)	23.0 20.5–24.5	21.5 20.0–23.0	1.0 1.0–2.0	0.000000
Pulsed Doppler				
E (m/s)	0.885 0.705–1.06	0.77 0.58–0.94	0.12 0.0–0.22	0.000045
A (m/s)	0.83 0.68–1.06	0.82 0.67–1.0	0.035 –0.075–0.12	0.139770
E/A	0.98 0.78–1.37	0.83 0.73–1.12	0.10 –0.02–0.25	0.000900
DT (ms)	224.0 179.0–288.5	246.0 208–326.0	–16.0 –61.5–32.0	0.043031
IVRT (ms)	85.0 75.0–96.0	91.0 80.0–101.0	–5.0 –16.0–3.5	0.001161
Ar (m/s)	0.42 0.36–0.53	0.41 0.34–0.49	0.02 –0.03–0.07	0.131199
S (m/s)	0.65 0.54–0.80	0.55 0.47–0.66	0.09 –0.02–0.19	0.000055
D (m/s)	0.64 0.49–0.82	0.60 0.49–0.74	0.04 –0.08–0.14	0.221118
S/D	1.06 0.77–1.38	0.85 0.75–1.24	0.07 –0.10–0.28	0.034629
Tissue Doppler				
E` (m/s)	0.06 0.05–0.07	0.06 0.05–0.07	0.00 –0.01–0.01	0.817468
A` (m/s)	0.09 0.06–0.11	0.09 0.07–0.12	–0.01 –0.02–0.00	0.015208
E`/A`	0.65 0.58–0.80	0.62 0.55–0.71	0.05 –0.04–0.13	0.019496
Pulsed/tissue Doppler				
E/E`	13.8 10.38–21.6	12.29 9.56–16.83	1.71 –0.36–4.43	0.000279

Table 3. Selected correlations between echocardiography parameters and demographic, clinical and laboratory data of patients treated with intermittent hemodialysis

Tabela 3. Wybrane korelacje między parametrami echokardiograficznymi a danymi demograficznymi, klinicznymi i laboratoryjnymi chorych leczonych powtarzaną hemodializą

Parameters being correlated (Korelowane parametry)	Pre-HD results (Wyniki przed dializacyjne)		Post-HD results (Wyniki podializacyjne)		Difference in pre-HD and post-HD results (Różnica)	
	r	P	r	p	r	p
Age (Wiek)						
LA diameter	0.290	0.030	0.216	0.111	0.164	0.226
RA surface	0.273	0.041	0.400	0.002	–0.150	0.269
Dialysis vintage (Długość leczenia dializą)						
S/D	–0.117	0.391	–0.349	0.008	0.205	0.130
LA surface	0.293	0.028	0.358	0.007	–0.226	0.094
Residual urine volume (Resztkowa objętość moczu)						
LVEDd	–0.059	0.664	0.115	0.400	–0.340	0.006
E	–0.116	0.394	0.112	0.412	–0.349	0.008
S	0.173	0.199	0.397	0.002	–0.259	0.054
S/D	–0.028	0.840	0.323	0.015	–0.340	0.006
IVC diameter	–0.261	0.052	–0.047	0.730	–0.349	0.008
Difference between pre- and post-HD body mass (Różnica między masą ciała przed i po HD)						
LVEDd	not examined		0.096	0.483	0.281	0.036
A	not examined		–0.233	0.084	0.297	0.026
S	not examined		–0.395	0.003	0.173	0.202
Ultrafiltration volume (Objętość ultrafiltracji)						
LVEDd	not examined		0.120	0.377	0.307	0.022
E	not examined		–0.137	0.312	0.290	0.030
IVRT	not examined		0.141	0.299	–0.272	0.043
S	not examined		–0.390	0.003	0.223	0.099
S/D	not examined		–0.326	0.014	0.292	0.029
Hemoglobin (Hemoglobina)						
LA diameter	0.285	0.033	0.166	0.222	0.305	0.022
LVEF	–0.264	0.049	–0.342	0.010	0.047	0.731
E	0.206	0.127	–0.100	0.465	0.325	0.015
S	0.016	0.904	–0.298	0.026	0.251	0.062
Ar	0.182	0.180	–0.084	0.537	0.287	0.032
E’	–0.375	0.004	–0.411	0.002	–0.079	0.563
A’	–0.302	0.024	–0.211	0.119	–0.211	0.119
E/E’	0.383	0.004	0.227	0.092	0.302	0.023
IVC diameter	0.331	0.013	0.174	0.200	0.254	0.059
White blood cells (Białe komórki krwi)						
DT	0.126	0.354	–0.126	0.355	0.297	0.026
E’	–0.249	0.065	–0.288	0.032	–0.010	0.939
E/E’	0.179	0.187	0.289	0.031	0.018	0.983
C-reactive protein (Białko C-reaktywne)						
LA diameter	0.373	0.005	0.414	0.002	–0.033	0.810
LA surface	0.320	0.016	0.288	0.031	–0.001	0.994
LVEF	–0.273	0.042	–0.169	0.214	–0.201	0.138
Parathyroid hormone (Parathormon)						
LVEF	0.352	0.008	0.284	0.034	0.065	0.632
E’	0.295	0.027	0.214	0.114	0.165	0.225
Total calcium and E/A (Wapń całkowity i E/A)	–0.118	0.385	0.051	0.709	–0.358	0.007
Phosphates and LA surface (Fosforany i powierzchnia LA)	0.263	0.050	0.017	0.900	0.311	0.020
Ca x P and LA surface (Ca x P i powierzchnia LA)	0.249	0.064	–0.020	0.881	0.317	0.017
Uric acid (Kwas moczowy)						
LVESd	0.259	0.054	0.122	0.370	0.381	0.004
LA surface	0.100	0.461	–0.178	0.189	0.479	0.000

Table 4. Independent predictors of echocardiographic parameters in hemodialysis patients

Tabela 4. Niezależne wyznaczniki wskaźników echokardiograficznych hemodializowanych chorych

Independent predictor (Niezależny wyznacznik)	Dependent variable (Zmienne zależne)	Corrected R^2	β	p
Age (Wiek)	pre-HD E	0.236[1]	–0.293	0.030
	pre-HD E`	0.203[1]	–0.455	0.001
	pre-HD E/A	0.392[2]	–0.355	0.004
	post-HD E/A	0.298[2]	–0.357	0.007
	pre-HD DT	0.278[2]	0.359	0.007
	post-HD DT	0.315[2]	0.282	0.030
Ischemic cardiac disease (Choroba niedokrwienna serca)	pre-HD E	0.236[1]	0.297	0.030
	pre-HD E/A	0.392[2]	0.414	0.001
	post-HD E/A	0.298[2]	0.266	0.045
	pre-HD E/E`	0.233[3]	0.323	0.015
	post-HD DT	0.260[3]	0.254	0.048
	pre-HD LA diameter	0.213[3]	0.281	0.035
Valvular disease (Wada zastawkowa)	pre-HD LA diameter	0.225[2]	0.293	0.023
	post-HD LA diameter	0.226[3]	0.494	0.000
	post-HD RA surface	0.244[2]	0.434	0.001
	pre-HD E/A	0.392[2]	0.451	0.000
	post-HD E/A	0.298[2]	0.475	0.000
	pre-HD DT	0.278[2]	–0.478	0.000
	post-HD DT	0.315[2]	–0.573	0.000
	pre-HD E/E`	0.233[3]	0.332	0.010
	post-HD E/E`	0.216[2]	0.464	0.001
Administration of ACEI/ARB (Leczenie ACEI/ARB)	pre-HD E	0.236[1]	0.401	0.002
	pre-HD E/A	0.265[1]	0.275	0.026
Administration of β-blocker (Leczenie β-blokerami)	pre-HD E`	0.203[1]	–0.282	0.026
C-reactive protein (Białko C-reaktywne)	pre-HD LA diameter	0.210[4]	0.260	0.038
Ultrafiltration volume (Objętość ultrafiltracji)	post-HD S	0.218[4]	–0.448	0.001

Variables being used in the model as independent predictors:
1) age, ischemic cardiac disease, arterial hypertension, administration of ACEI/ARB, administration of β-blocker,
2) age, ischemic cardiac disease, arterial hypertension, valvular disease,
3) ischemic cardiac disease, arterial hypertension, valvular disease, residual diuresis,
4) age, ischemic cardiac disease, arterial hypertension, ultrafiltration volume, C-reactive protein.

Zmienne użyte w modelu jako niezależne predyktory:
1) wiek, choroba niedokrwienna serca, nadciśnienie tętnicze, przyjmowanie ACEI/ARB, przyjmowanie leków blokujących kanał β,
2) wiek, choroba niedokrwienna serca, nadciśnienie tętnicze, wada zastawkowa serca,
3) choroba niedokrwienna serca, nadciśnienie tętnicze, wada zastawkowa serca, diureza resztkowa,
4) wiek, choroba niedokrwienna serca, nadciśnienie tętnicze, objętość ultrafiltracji, białko C-reaktywne.

evaluated as a difference between pre- and post-HD body weight, was 1.8 ± 1.0 kg. All patients but one (98.2%) reached dry body mass and were in stable clinical condition at the time of the echo examination.

Table 2 shows the medians, lower and upper quartiles of several Doppler echo indices before and after HD session, as well as their differences from baseline pre-HD conditions. After HD session, mitral flow E-wave (E) decreased, but mitral flow A-wave (A) remained unchanged, resulting in a significant decrease in the E/A ratio. The IVRT prolonged and LVEF increased significantly. The tissue Doppler-derived diastolic parameters showed significant change after HD for A`, E'/A` and E/E`, but not for E`.

In patients with LVEF > 50%, E/A ratio grouped according to the algorithm cited by Khouri et al. [19] was < 0.75 in 10/48 (20.9%), 0.75–1.5 in 34/48 (70.8%) and > 1.5 in 4/48 (8.3%) persons before HD session. The respective frequency after HD session was 16/49 (32.7%), 28/49 (57.1%) and 5/49 (10.2%).

Using the algorithm cited by Gagliardi et al. [17] in all examined patients, pre-HD values of E/A ≤ 0.50 not shown, E/A > 0.50 – < 1.0 were shown in 29/56 (51.8%) patients, ≥ 1.0 – ≤ 2.0 – in 24/56 (42.9%) patients, and > 2.0 – in 3/56 (5.3%) patients. The respective post-HD values were 1/56 (1.8%), 37/56 (66.1%), 15/56 (26.8%) and 3/56 (5.3%).

Patients with LVEF > 50% showed before HD session E/E` ratio ≤ 10 in 12/56 (21.4%) cases, whereas 44/56 (78.6%) patients had E/E` greater than 10, what indicated in the latter group the increased left ventricular filling pressure [18, 19]. Respective values after HD were 28.8% and 73.2%.

Pre-HD systolic dysfunction was shown in 7/56 (12.5%) patients, diastolic dysfunction – in 52/56 (92.9%). Mild diastolic dysfunction (slowed relaxation pattern) was present in 22/56 (39.3%) patients, moderate (pseudonormal pattern) – in 26/56 (46.4%), severe (restrictive filling pattern) – in 4/56 (7.1%). Post-HD systolic dysfunction was shown in 6/56 (10.7%) patients, diastolic dysfunction – in 52/56 (92.9%). Mild diastolic dysfunction was present in 34/56 (60.7%) patients, moderate – in 15/56 (26.8%), severe – in 3/56 (5.4%). After HD session prevalence of mild dysfunction significantly increased (p = 0.0015), while moderate dysfunction decreased (p = 0.0056) as compared to respective prevalence before HD session. A change from moderate to mild dysfunction was shown in 46.2% of patients with pseudonormal filling. The patients who converted from moderate to mild pattern (n = 12) as compared to patients without conversion (n = 14) showed insignificantly higher LVEF (69.3 ± 8.2% vs 59.5 ± 17.0%, p = 0.081).

Correlations between selected demographic, clinical and laboratory data of examined patients and their echo parameters are shown in Table 3. Hemoglobin, hematocrit and red blood cells showed similar pattern of correlations. There were no significant correlations between echo parameters and platelet count as well as online Kt/V. Among correlations, not shown in Table 3, S values correlated with LVEF shown before (r = 0.288, p = 0.032) and after (r = 0.342, p = 0.010) HD session.

Six sets of predictors were applied for each echo parameter in a stepwise multiple linear regression analysis. In Table 4 only significant predictors derived from 4 sets with corrected R^2 > 0.200 are shown.

Age, ischemic heart disease, arterial hypertension and valvular disease were chosen as possible predictors for development of left ventricular dysfunction. Significant predictor for development of systolic dysfunction was valvular disease (OR 4.754, CI 1.270–17.791, p = 0.022), for mild diastolic dysfunction – age (OR 1.066, CI 1.007–1.128, p = 0.029). Predictors for moderate and severe diastolic dysfunction could not be established.

Discussion

Left ventricular hypertrophy (LVH) occurs in over 70% of dialysis patients [17]. Reduced relaxation velocities are characteristic for early functional disturbances in LVH and proceed to contraction impairment. Diastolic dysfunction of the left ventricle was evaluated to be present in 40–100% of dialyzed patients [6, 16, 17]. Systolic dysfunction, following diastolic impairment, was shown in 10–20% of dialyzed persons [6, 17]. Differences in prevalence of diastolic/systolic dysfunction in dialysis patients, reported in the literature, may depend on patients` characteristics. Advanced age, arterial hypertension, ischemic cardiac disease and valvular disease influence heart dimensions and functional parameters. In own study they all but hypertension were independent predictors of atrial dimensions and/or Doppler echo velocities. Moreover, age was a significant predictor for development of diastolic dysfunction, and valvular disease – of systolic dysfunction. If examined populations differ significantly in respect to prevalence of these comorbidities, results of frequency of left ventricle malfunction can be different as well. On the other hand, various methods applied for diagnosis and not uniform classification of data may also participate in reported differences in prevalence of left ventricular dysfunction in HD patients.

Acute changes, occurring during HD session being a clinical model of preload reduction,

influence both cardiac dimensions and cardiac functional parameters [3, 6–8, 20]. In own study, decreases in LVEDd, LVESd, RA surface, LA dimensions and IVC diameter were shown with reduced preload and afterload during HD session. A decrease in preload diminished pulsed Doppler velocities: mitral early diastolic velocity (E), systolic pulmonary vein velocity (S), mitral peak E-wave velocity to peak A-wave velocity (E/A ratio) and S/D ratio. These changes occurred with simultaneous prolongation of DT and IVRT. HD-induced volume contraction, leading to decreased preload, may be roughly estimated by HD UFV and a difference between pre-HD and post-HD body mass. Volume contraction approximated by UFV or body mass difference was 2.2 ± 1.0 L or 1.8 ± 1.0 kg, respectively. Both these estimates correlated positively with changes in LVEDd, A, E or S/D, and inversely with IVRT. In the study of Drighil et al. [3] peak mitral inflow E wave velocity of young patients (31 ± 10 years) without remarkable cardiac comorbidities correlated with UFV adjusted for pre-HD weight. This indicates that despite differences in age and comorbidities between studied groups, pulsed echo Doppler indices are similarly influenced by preload reduction. Post-HD S or S/D were also associated with volume contraction. Moreover, UFV was independent predictor of post-HD S. All these data not only indicate association between preload and pulsed Doppler velocities, but also show numerical coupling between indices of preload decrease and some echo parameters.

Own relatively older HD patients (64.4 ± 14.8 years) had greater atrial diameters with increasing age and HD vintage. Although no significant correlation was shown between age and E/A ratio, age appeared to be independent predictor of pulsed Doppler parameters: pre-HD E, pre- and post-HD E/A and pre- and post-HD DT. Additionally, dialysis vintage and S/D correlated negatively, what may be related to progression of diastolic dysfunction in the course of prolonged HD treatment.

Early mitral annulus velocity (E`) [6, 8, 9] and E`/A` ratio [9, 10] were reported as preload independent markers of left ventricular diastolic function, however, not in all studies [5, 7]. In own study, age and administration of β-blockers were significant predictors of pre-HD E`, and the tissue Doppler parameters showed significant changes after HD session: mitral annular late diastolic velocity (A`) increased and consequently E`/A` decreased as compared to the pre-HD values. However, correlations did not occur between A` or E`/A` and UFV or pre- and post-HD difference in body mass. Peak mitral annulus early diastolic velocity (E`) did not change significantly after HD session as compared to pre-HD value, confirming that E` is preload independent marker of left ventricular diastolic function in HD patients, at least with UFV of 2.2 ± 1.0 L suitable for obtaining the normovolemic state in the examined patients. Barberato et al. [6] concluded that the HD effect on E` may be ignored as long as no excess fluid is removed. Hsiao et al. [5] showed that with volume removal over than 2 L, there is the trend of preload dependency also of peak early diastolic velocity of mitral annulus (E`).

E/A ratio of pulsed Doppler echo, indicating diastolic dysfunction (abnormal relaxation pattern and restrictive filling pattern), was shown in 80.6% of HD/peritoneal dialysis patients studied by Gagliardi et al. [17]. When the same criteria for E/A were applied in own HD patients for post-HD results, diastolic dysfunction was diagnosed in 73.2% of cases. True normal pattern and pseudonormal pattern could not be distinguished in the study of Gagliardi et al. [17], because tissue Doppler imaging was not used. In own study, complex analysis of transmitral pulsed and tissue Doppler parameters resulted in overall diagnosis of diastolic dysfunction in near 93% of HD patients, independently whether echo examination was done before or after HD session.

When the authors applied the algorithm for E/A cited by Khouri et al. [18] in the examined patients and compared their results to those of Roselló et al. [16], who also used this algorithm, it was shown that majority (> 50%) of their peritoneal dialysis patients and their HD patients with LVEF > 50% presented normal or pseudonormal pattern. Interestingly, results of E/A ratio of peritoneal dialysis patients, showing 47.6% of cases with ventricular relaxation impairment and 52.4% – with normal or pseudonormal pattern, were more comparable to those shown in HD patients after HD session when dry body mass was obtained (32.7% of cases with ventricular relaxation impairment and 57.1% – with normal or pseudonormal pattern, both non significant as compared to respective results of Roselló et al. [16]). However, using E/E` ratio > 10 in peritoneal dialysis patients with LVEF > 50%, a clear diastolic malfunction was shown in 40.5% of cases [16]. It was less than in own HD patients with LVEF > 50%, who showed diastolic dysfunction, diagnosed by post-HD E/E` ratio > 10, in 69.4% of cases. The examined HD patients seemed to be in a worse clinical condition than that of Roselló et al. [16]. Inability to obtain cardiac flows related to atrial function was the only cardiac criterion for exclusion from own study, whereas Roselló et al. [16] excluded patients with clinical symptoms of heart failure, cardiac valve diseases, dysarythmias or history

of myocardial infarction. Ischemic heart disease, cardiac valve disease and administration of ACEI/ARB and β-blockers independently influenced in own study results of echo parameters. Additionally, own patients were approximately 14 years older than peritoneal dialysis patients. As cardiac diseases and advanced age obviously contribute to impairment of left ventricle function, it has to be expected that diastolic dysfunction frequency and its severity will be greater in older patients with cardiac diseases than in younger ones without heart illnesses. This analysis indicates that E/A ratio could not differentiate these both groups, but it was possible with the use of E/E` ratio > 10 as an indicator of diastolic malfunction.

Systolic dysfunction (LVEF < 50%) was present in approximately 11% of own HD patients. Gagliardi et al. [17] showed systolic dysfunction (LVEF < 50%) in 9.7% of patients treated with HD or peritoneal dialysis. This corresponds with lower prevalence of diastolic dysfunction in this dialysis group (77.4%) than in own group (92.9%). Barberato et al. [6] showed systolic dysfunction in 20% of HD patients, but LVEF < 65% was considered as diagnostic for this malfunction.

A reduced preload resulted in a significant change of echo pattern: moderate diastolic dysfunction converted to mild dysfunction in 46.2% of patients with pseudonormal filling. It was shown that patients with moderate dysfunction were not uniform group. Among them there were persons whose pattern of diastolic dysfunction converted from moderate to mild pattern in response to reduced preload, and patients with more advanced dysfunction whose echo parameters could not change sufficiently to show mild pattern.

LVEF also improved after HD session, but prevalence of systolic dysfunction did not change significantly as compared to evaluation before HD session. Earlier studies also indicated beneficial effect of HD session on systolic function of the left ventricle [6, 20], but not all [3]. The difference in pre- and post-HD global LVEF did not reach statistical significance in 16 patients assessed by radionuclide ventriculography, but the peak ejection rate was increased following HD session [20].

Residual renal volume is of great importance in maintenance of cardiac function, because helps in keeping more stable interdialytic body weight and avoiding extreme overhydration. In peritoneal dialysis patients, Roselló et al. [16] found positive correlation between residual renal function and ejection fraction. In own study, post-HD echo examination revealed positive association between systolic pulmonary vein velocity (S), S/D and residual urine volume. Higher pre-HD and post-HD values of S were associated with higher LVEF. Additionally, pre-HD and post-HD differences in LVEDd, E, S/D and IVC diameter were smaller in patients with greater urine volume, indicating more stable cardiac function in this respect.

Own results, showing better cardiac function after HD than before HD session, indicate that echo evaluation of the heart of HD patients should be done with preload reduced by effective ultrafiltration.

Efficacy of single HD session, measured by online Kt/V, did not correlate in own study with echo parameters. Uremic retention products add to cardiovascular damage, but exactly which of these substances are cardiotoxic and due to what mechanisms is largely unclear [21]. Routinely examined small molecule uremic toxins (urea, creatinine, uric acid) seem not influence cardiac function. Despite this, in own study, patients showing higher serum uric acid concentration revealed a greater HD-induced difference in LVESd and LA surface.

Inflammation is commonly accepted cardiovascular risk factor. However, in studies of Baýes et al. [22] serum concentration of CRP was not a good predictive factor of cardiovascular mortality during 4 years follow-up, possibly because of the slight positive correlation that existed between CRP and age. In our previous study adjustment of results for age did not reveal significant difference in serum CRP level between patients with CHF and without it [23]. In this study positive correlation between serum CRP concentration and dimensions of LA before and after HD session was shown. Moreover, CRP was independent predictor of pre-HD LA diameter. LVEF was negatively related to CRP, but only before HD session, when increased preload occurred due to interdialytic weight gain. E/A ratio and CRP did not correlate in own study, unlike in other studies [16].

Own study indicates lower LVEF at pre-HD and post-HD session as well as lower post-HD systolic superior pulmonary vein velocity (S) with increased hematocrit, red blood cell count and hemoglobin level. These negative correlations may indicate a beneficial effect of anemia reduction on hyperkinetic circulation caused in HD patients by anemia, arteriovenous fistula, and overhydration [24]. Additionally, in own study patients with higher hematocrit and hemoglobin showed greater decrease in LA diameter after HD session. Differences in pre-HD and post-HD pulsed and tissue Doppler parameters positively correlated with hematocrit, hemoglobin and red blood cell count, indicating their contribution to changes in cardiac function occurring during HD session.

An association between WBC count and mortality in end-stage renal disease has been suggested in the past [25]. Own study showed that CHF in

dialyzed patients is associated with higher WBC count (but usually not increased) as compared to values observed in dialyzed persons without CHF [23]. The present study indicates that WBC count negatively correlated with post-HD E` wave velocity and positively with pre-HD and post-HD difference in deceleration time (DT), what means that with higher WBC count HD-related prolongation of DT is smaller. The post-HD E/E` ratio positively correlates with WBC count, what suggests that higher WBC count is related to diastolic dysfunction.

Higher serum concentrations of total calcium were associated with smaller E/A differences induced by HD session, but a difference in HD-induced LA surface was more pronounced with higher both serum phosphate levels and values of Ca and P product. However, in own study positive correlation was shown between serum concentration of intact PTH and LVEF in pre-HD and post-HD examination. Interestingly, there are studies indicating decreased LVEF after parathyroidectomy [26, 27]. Additionally, in patients with CHF (NYHA functional class III or IV) elevated PTH was associated with better LVEF [28]. These facts are explained by elevated blood pressure coexisting with hyperparathyroidism [26] or by an inotropic influence exerted by PTH [27].

Although numerous echo indices correlated with patients` demographic, clinical and laboratory data, some of which being even their independent predictors, the authors were able to show only cardiac valve disease as a predictor for systolic dysfunction of the left ventricle, and age as a risk factor for diastolic dysfunction. Etiology of left ventricle dysfunction was obviously multifactor, and different factors could play a main pathological role in each individual HD patient.

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