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Prognostic value of the atrial pulsed Doppler recordings of transmitral flow in the assessment of left ventricular diastolic dysfunction

Ventricular diastolic dysfunction is a common finding among patients with heart failure but is often recognized in asymptomatic patients with systemic hypertension or ischaemic heart disease (1, 5, 6, 7, 11, 15, 16). Doppler echocardiography is the most valuable method providing non-invasive insight into ventricular diastolic performance. Diastolic flows through mitral or tricuspid valves with an additional assessment of pulmonary venous flow profiles reveal wide spectrum of ventricular diastolic dysfunction (10). Doppler echocardiographic recordings are influenced by several factors including respiration, heart-rate and body position (12, 17). It is also well evidenced that recorded values of ventricular filling wave velocities depend on volume sample location. Doppler recordings are usually obtained at the tips of the mitral valve leaflets. Recordings obtained from the left atrial volume sample location are characterized by lower early and late diastolic filling velocities. Nevertheless, independently of volume sample location early to late filling velocities ratio (E/A) remains unchanged and thus it has become the most useful index of ventricular diastolic function (4, 8).

Some patients, however, demonstrate different patterns of transmitral diastolic flow: normal, with E/A above 1 measured between the tips of the mitral leaflets and similar to the pattern of delayed ventricular relaxation with E/A below 1 recorded in the left atrium. The aim of our study was to compare M-mode echocardiographic measurements between patients with E/A ratio>1 recorded both at the tips of the mitral valve leaflets and in the left atrium and patients with E/A ratio >1 at the tips of the mitral valve leaflets and E/A<1 in the left atrium.

MATERIAL AND METHODS

96 consecutive patients without clinical symptoms of heart failure with sinus rhythm and normal atrio-ventricular conduction in standard electrocardiogram were enrolled to the study. On the day of examination patients did not take medications that might affect cardiac performance. Echocardiographic examinations were performed using commercially available ultrasonograph Hitachi EUB-450 equipped with 3.5 MHz transducer. During the examinations patients were in left decubitus position. M-mode presentation in the parasternal long axis view was used to measure interventricular septum diastolic diameter, posterior wall diastolic diameter, left ventricular end-diastolic diameter and left atrium diameter. Left ventricular mass was calculated using Devereaux formula (2). M-mode measurements were used for calculation of relative wall thickness and left ventricular ejection fraction by Teichholz formula.

The apical four chamber view was used to obtain pulsed Doppler recordings. Doppler volume sample was positioned at the tips of the mitral valve leaflets. Peak early (E_{vent}) and late (A_{vent}) diastolic filling velocities, LV diastolic filling time, early mitral wave deceleration time and E_{vent}:A_{vent} (E/A_{vent}) ratio were measured. Then, volume sample was moved toward the left atrium and placed approximately 1 cm above mitral annulus. Peak early and late filling velocities (E_{atr} and A_{atr}, respectively), LV diastolic filling time, LV early filling deceleration time E_{atr}:A_{atr} ratio (E/A_{atr}) were recorded. All recordings were obtained during quiet breathing at the end of expiration and measurements used for calculations represented averaged values of two consecutive beats recorded from atrial and ventricular volume sample locations.

Pulmonary venous flows were recorded and peak reverse flow velocities exceeding 0.35 m/s were used as a criterion to discriminate pseudonormalized from normal filling patterns.[8]

All pulsed Doppler recordings were analyzed and the following patients were excluded from the original group: 11 patients with mitral or aortic regurgitation, 23 patients with delayed relaxation and 11 patients with pseudonormalized filling pattern recorded in LV. Finally, the study population composed of 51 patients with $E/A_{vent} > 1$ was divided into two groups based on Doppler profile of diastolic flow recorded in the left atrium: group A - 26 patients with $E/A_{atr} < 1$ and group B – 25 patients with $E/A_{atr} > 1$. In group A 12 patients suffered from mild to moderate systemic hypertension and 9 suffered from ischaemic heart disease, in group B 9 patients were hypertensive and 5 demonstrated clinical signs of myocardial ischaemia.

STATISTICAL ANALYSIS

Statistica 5.0 package was used to perform statistical analysis. Data are expressed as mean ±SD. 95% confidence intervals were calculated for all examined parameters except those without normal distribution. Two-sample t-tests and nonparametric Mann--Whitney U tests were used to assess differences in M-mode and pulsed Doppler echocardiography parameters for subjects with E/A_{atr} <1 and E/A_{atr} >1. Pearson's r coefficients were calculated in order to assess associations between atrial and ventricular Doppler recordings and M-mode measurements.

RESULTS

General characteristics, M-mode and pulsed Doppler echocardiographic measurements of the studied population are listed in Table 1.

Table 1. General characteristics and echocardiographic parameters of study population

	Mean	SD	MIN	MAX	-95%CI	+95%CI
Age (yrs)	49.4	13.1	19	76	45.7	53.1
Height (cm)	168.8	8.5	150	182	166.4	171.2
Weight (kg)	76.8	15.7	47	115	72.4	81.2
BMI (kg/m^2)	26.9	4.6	18.5	38.4	25.6	28.2
RR (ms)	980	137	730	1310	942	1019
M-mode echocardiographic examinati on						
LVID (mm)	51.6	6.8	42	76	*	*
PWD (mm)	10.4	2.1	5	14	*	*
IVSD (mm)	11.6	3	6	19	10.7	12.4
LAD (mm)	41	5.8	29	56	39.4	42.7
RWT	0.43	0.12	0.22	0.79	0.4	0.47
LVM (g)	264.1	94.7	92.5	509	237.5	290.7
EF (%)	64.1	8.5	44	87	61.7	66.5
Pulsed Doppler echoc ardiographic examination						
E_{vent} (cm/s)	67.8	11.1	46.5	93.5	64.7	71
A_{vent} (cm/s)	47.9	8.5	32.5	70	45.6	50.4
E/A_{vent}	1.45	0.34	1.02	2.54	*	*
FT_{vent} (ms)	594	152	365	965	*	*
DT_{vent} (ms)	194.4	49.9	115	305	*	*
E_{atr} (cm/s)	45.3	10.4	23.5	74.5	42.4	48.2

A_{atr} (cm/s)	45.4	10.4	26.5	82	42.5	48.3
E/A_{atr}	1.05	0.38	0.48	2.39	*	*
FT_{atr} (ms)	550.2	135	335	855	*	*
DT_{atr} (ms)	143.5	33.4	95	235	*	*

* Not calculated.

BMI – body mass index, DT – early filling wave deceleration time, FT – LV diastolic filling time, EF – LV ejection fraction, IVSD – intraventricular septum diastolic diameter, LAD – left atrium diameter, LVID – LV end-diastolic diameter, LVM – LV mass, PWD – posterior wall diastolic diameter, RR – R-R wave interval, RWT – relative wall thickness.

CLINICAL AND ECHOCARDIOGRAPHIC FEATURES IN SUBJECTS WITH $E/A_{ATR}<1$ (GROUP A) AND $E/A_{ATR}>1$ (GROUP B)

Patients from group A were significantly older and had an increased body mass index as compared with patients from group B. There were no differences in resting heart rate. M-mode study revealed significant differences between the examined groups. The average thickness of interventricular septum was 9.7 ± 1.6 mm in group B and 13.5 ± 2.8 mm in group A ($p<0.001$), the average thickness of LV posterior wall was 9.2 ± 1.8 mm and 11.6 ± 1.7 mm, respectively ($p<0.001$). LV end-diastolic diameter and LV ejection fraction were similar in both groups. Relative wall thickness, LV mass and the left atrium diameters were significantly increased in group A.

PULSED DOPPLER ECHOCARDIOGRAPHIC MEASUREMENTS AT THE TIPS OF MITRAL VALVE LEAFLETS

E_{vent} velocity was significantly higher in group B as compared to group A (71.3 ± 10.6 cm/s vs 64.2 ± 10.6 cm/s; $p<0.05$), while A_{vent} velocity was significantly lower in group B (44.8 ± 6.7 cm/s vs 51.3 ± 9 cm/s). As a result, calculated E/A_{vent} in group B was greater than in group A (1.63 ± 0.37 vs 1.26 ± 0.17, $p<0.001$). Patients in group A demonstrated prolonged deceleration and LV filling time, however, these differences did not reach statistical significance.

DOPPLER PROFILES OF DIASTOLIC FLOWS RECORDED IN THE LEFT ATRIUM

In patients from group B recorded values of early and late filling velocities were lower than those measured at the tips of the mitral valve leaflets. E_{atr} velocity was 51 ±

9.1 cm/s, A_{atr} wave velocity was 38.6 ± 6.9 cm/s. Mean velocity of E_{atr} was 39.4 ± 8.3 cm/s in patients classified as group A and this value was also lower than E_{vent}. In these subjects A_{atr} was higher than A wave velocity recorded at the tips of the mitral valve leaflets (52.5 ± 8.5 vs 51.3 ± 9 cm/s). LV filling time and early filling wave deceleration time were also prolonged in group A, but differences were not statistically significant. E/A in group B calculated from the left atrial recordings was diminished in comparison with ventricular recordings (1.34 ± 0.3 vs 1.63 ± 0.37). The results of M-mode and pulsed Doppler study are listed in Table 2.

Table 2. Comparison of M-mode and pulsed Doppler echocardiographic data in subjects with $E/A_{atr}<1$ (group A) and $E/A_{atr}>1$ (group B)

	Group A		Group B		p value	-95%CI	+95% CI
Age (yrs)	55.6	12.8	43.5	10.5	<0.001	5.5	18.7
Height (cm)	168	7	169	10	NS	*	*
Weight (kg)	82	15	72	15	<0.05	0.9	17.9
BMI (kg/m^2)	28.8	4.4	25	4.1	0.01	1.3	6.1
RR (ms)	1004	125	956	145	NS	*	*
M mode echocardiographic examination							
LVID (mm)	51.1	8	52.1	5.6	NS	*	*
PWD (mm)	11.6	1.7	9.2	1.8	<0.001	*	*
IVSD (mm)	13.5	2.8	9.7	1.6	<0.001	2.6	5.1
LAD (mm)	43.5	5.7	38.7	4.8	<0.01	1.8	7.7
RWT	0.5	1.2	0.37	0.1	<0.001	0.04	0.19
LVM (g)	311	82	219	85	<0.001	45.4	139.1
EF (%)	64.4	9.7	63.8	7.4	NS	*	*
Pulsed Doppler profiles od diastolic flows recorded in left ventricle							
E_{vent} (cm/s)	64.2	10.6	71.3	10.6	<0.05	-13	-1,1
A_{vent} (cm/s)	51.3	9	44.8	6.7	<0.01	2	10.9
E/A_{vent}	1.26	0.17	1.63	0.37	<0.001	*	*
FT_{vent} (ms)	613	138	575	164	NS	*	*
DT_{vent} (ms)	207	50	182	47	NS	*	*
Pulsed Doppler profiles of diastolic flows recorded in left atrium							
E_{atr} (cm/s)	39.4	8.3	51	9.1	<0.001	-16.5	-6.7
A_{atr} (cm/s)	52.5	8.5	38.6	6.9	<0.001	9.5	18.2

E/A_{atr}	0.75	0.11	1.34	0.3	<0.001	*	*
FT_{atr} (ms)	572	126	529	143	NS	*	*
DT_{atr} (ms)	149	33	138	33	NS	*	*

* Not calculated.
Explanation as in Table 1.

E/A ratio calculated from both ventricular and atrial recordings correlated with age, body mass index, ventricular mass and relative wall thickness. The strongest negative correlation was found for E/A measured from the left atrial recordings. It should be emphasized that in both groups a significant negative correlation between E/A and left atrial dimension was demonstrated only for atrial recordings.

DISCUSSION

Volume sample location is one of the most important factors influencing pulsed Doppler recordings of diastolic flows. Measurements obtained at the level or just below mitral and tricuspid valve annulus are recommended for the echocardiographic analysis of ventricular diastolic properties because of relatively high dispersion of diastolic filling velocities due to volume sample position (4, 8, 9). Sniderman et al. compared recordings of diastolic flows obtained at the mitral orifice and at midventricular level. The average value of E/A ratio increased from 1.6 at mitral orifice level up to 2.1 measured in LV cavity (13). It is also well established that diastolic flows measured between the tips of mitral valve leaflets are higher than those obtained from the left atrial volume sample location. E wave velocities measured from the left atrial location are on average 25% lower (43 ± 12 cm/s vs 57 ± 12 cm/s), A wave velocities 22% lower (36 ± 7 cm/s vs 46 ± 11 cm/s) than those measured at the tips of the mitral valve leaflets. Nevertheless, unlike intraventricular recordings, in normal subjects there is no significant difference between late to early filling velocities ratio (A/E) measured at the tips of mitral valve leaflets and in the left atrium (0.91 ± 0.3 vs 0.87 ± 0.3, respectively) (4).

In our study, however, we showed that E/A ratios recorded in the left atrium above mitral valve annulus are lower than those measured at the tips of the mitral valve leaflets. Moreover, in the group composed of 51 patients with $E/A_{vent}>1$ we found 26 subjects with quite different patterns recorded in the left atrium, with predominant A wave velocity, and as a result, with decreased $E/A_{atr}<1$. These patients demonstrated an increased LV wall thickness, LV mass and relative wall thickness, whereas LV end-diastolic diameter and LV systolic performance were similar in both groups. Thus, the presence of ventricular diastolic dysfunction is more likely in these subjects than in those with normal M-mode examination.

The results of our study suggest that in asymptomatic patients with $E/A_{vent}>1$ the presence of abnormal diastolic flow profiles in the left atrium, similar to the pattern of delayed LV relaxation, may be the earliest sign of ventricular diastolic dysfunction. It should be emphasized, however, that there were also differences between E/A ratios recorded at the tips of mitral valve leaflets and patients from group A demonstrated significantly lower ratio than patients from group B; however, even in group A E/A_{vent} remained within normal range.

Ventricular hypertrophy is a common finding among patients with diastolic filling abnormalities, but obviously, there is no direct interdependence between the degree of ventricular hypertrophy and LV diastolic performance. Our findings can be explained by the presence of mitral orifice dysfunction in subjects with $E/A_{atr} < 1$.

The influence of mitral orifice function on ventricular diastolic filling profiles is still underestimated. Abnormal mitral orifice geometry and inappropriate motion can be observed when ventricular hypertrophy develops. Patients with sinus rhythm show two distinct movements of the mitral annulus. Early mitral annulus diastolic movement period begins simultaneously with LV inflow and is followed by late diastolic mitral annulus motion. Sohn et al. observed in their tissue Doppler study decreasing with age both early diastolic mitral annulus motion velocity and E velocity recorded in ventricle (14). Based on E/A ratio the profile of delayed relaxation (E/A<1) was found in patients aged 60 to 69, whereas peak early to late mitral annulus motion velocities below 1 were found in younger patients, aged 40 to 49. This study clearly demonstrates that the earliest stages of diastolic dysfunction are probably not detected using standard pulsed Doppler echocardiograpy. It is noteworthy that patterns of mitral annulus motion velocity differentiate patients with all types of diastolic filling abnormalities. In that case, it is possible that pulsed Doppler atrial recordings are mostly influenced by mitral annulus motion, while ventricular recordings depend more on LV performance.

STUDY LIMITATIONS

The population examined in our study us was heterogeneous, comprising both healthy subjects and patients with cardiovascular disorders. All patients with inappropriate diastolic filling profiles were excluded from the study. The exclusion of pseudonormalized pattern was based on the assessment of peak reverse pulmonary venous flow velocities; however, the quality of recordings of the pulmonary venous flows obtained by transthoracic echocardiography is usually not satisfactory (3). Moreover, in some patients the pattern of the pulmonary venous flow does not reflect actual atrial pressures, so the reliability of this method is questioned. In our study invasive measurements of LV and the left atrial pressures have not been performed. Thus, it is possible that in some, if not in all patients from group A, the pseudonormalized pattern of LV filling was recorded. Considering the above the question remains, if the results obtained in our study indicate that distinct atrial and ventricular recordings of diastolic flows precede the development of impaired LV relaxation or if these findings reflect the presence of pseudonormalized filling pattern. If the latter is true, pulsed Doppler atrial recordings could be applied as a simple method differentiating normal from pseudonormalized filling patterns. In that case it seems obvious that further studies involving invasive techniques should be performed to support or criticize our finding. It is also necessary to compare atrial and ventricular Doppler recordings in patients with different patterns of LV diastolic filling abnormalities. We hope that the nearest future let all these doubts be explained.

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SUMMARY

Volume sample location is the most important factor influencing pulsed Doppler recordings of left ventricular (LV) diastolic filling. Transmitral diastolic flow velocities measured at the tips of mitral valve leaflets are usually higher than those obtained from atrial location. Nevertheless, independently of volume sample location, differences between early to late velocities ratio (E/A) are nonsignificant, so E/A became the most useful index of ventricular diastolic performance. In some patients, however, with E/A>1 measured between the tips of mitral leaflets, the pattern of delayed LV relaxation, with diminished E and predominant A wave (E/A<1), is often obtained from left atrial volume sample location. The aim of our study was to compare LV dimensions and wall thickness between patients with E/A >1 recorded both at the tips of mitral valve leaflets and in the left atrium and patients with E/A>1 at the tips of mitral valve leaflets and E/A<1 in the left atrium. The study population consisted of 51 patients with E/A>1 recorded between the tips of mitral valve (E/A_{vent}) and excluded pseudonormalized filling pattern. The study population was divided into two groups based on Doppler profile recorded in the left atrium: group A– 26 patients with E/A<1 (E/A_{atr}) and group B– 25 patients with E/A_{atr}>1. Patients from group A were significantly older (55.6 ± 12.8 vs 43.5 ± 10.5 yrs, p<0.001) and had increased body mass index (28.8 ± 4.4 vs 25 ± 4.1 kg/m^2,

$p<0.01$) compared to subjects from group B. The average thickness of intraventricular septum was 13.5 ± 2.8 mm in group A and 9.7 ± 1.6 mm in group B, the average thickness of LV posterior wall was 11.6 ± 1.7 and 9.2 ± 1.8 mm, respectively. The results of this study suggest that abnormal atrial recordings of diastolic flows may reflect the earliest stage of left ventricular diastolic dysfunction in asymptomatic patients with echocardiographic signs of mild cardiac damage.

Wartość prognostyczna oceny czynności rozkurczowej lewej komory serca w oparciu o rejestrację napływu mitralnego z przedsionkowej lokalizacji bramki dopplerowskiej

Lokalizacja bramki dopplerowskiej jest jednym z wielu czynników wpływających w istotny sposób na wartości pomiarów rozkurczowego napływu do lewej komory. Średnie prędkości fal napływu mitralnego uzyskiwane z przedsionkowej lokalizacji bramki są niższe w porównaniu z wartościami rejestrowanymi na szczycie płatków zastawki mitralnej (lokalizacja komorowa). Niezależnie od lokalizacji bramki stosunek fal wczesnego (E) do późnego (A) napływu mitralnego (E/A) pozostaje stały, stąd E/A stanowi bardzo użyteczny wskaźnik oceny czynności rozkurczowej komory. U części chorych stwierdza się jednakże współistnienie odmiennych profili napływu mitralnego, z E/A>1 rejestrowanym w komorze i E/A<1 w obrębie przedsionka, odpowiadającym profilowi upośledzonej relaksacji komory.

C e l p r a c y: Porównanie wyników badania echokardiograficznego lewej komory i lewego przedsionka u chorych z E/A>1, rejestrowanych zarówno z lokalizacji przedsionkowej, jak i komorowej, z chorymi reprezentującymi odmienne profile napływu mitralnego. M a t e r i a ł i m e t o d y k a: 51 pacjentów z E/A>1 w komorze, wykluczonym pseudonormalnym profilem napływu mitralnego, bez cech niewydolności serca, podzielono na dwie grupy. Grupa A - 26 chorych z E/A<1 w przedsionku i grupa B - 25 pacjentów z E/A>1 w przedsionku. U wszystkich chorych wykonano badanie M-mode lewej komory i lewego przedsionka. W y n i k i: Chorzy z grupy A byli istotnie statystycznie starsi (55,5 ± 12,8 vs. 43,5 ± 10,5; $p<0,001$) oraz cechowali się istotnie wyższym wskaźnikiem BMI (28,8 ± 4,4 vs. 25 ± 4,1 kg/m^2; $p<0,01$). Średnia grubość przegrody międzykomorowej wynosiła 13,5 ± 2,8 mm w grupie A i 9,7 ± 1,6 mm w grupie B, grubość tylnej ściany odpowiednio 11,6 ± 1,7 mm i 9,2 ± 1,8 mm. W n i o s k i: Profile napływu mitralnego o typie upośledzonej relaksacji, rejestrowane w obrębie przedsionka u chorych z prawidłowym profilem w obrębie komory, mogą odzwierciedlać najwcześniejsze stadium dysfunkcji rozkurczowej lewej komory serca.