Regional Myocardial Function in Healthy Adults. Assessment Through Tissue Doppler Echocardiography

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Objective – *To characterize left ventricular regional myocardial function through tissue Doppler echocardiography in healthy adults and to assess the influence of aging in this function.*

Methods *– In 45 healthy volunteers divided in two groups (≤ 45 and > 45 years old) we assessed longitudinal and radial regional function (velocities, times intervals and velocity-time integrals). Data were compared in each group and between groups.*

Results – *Systolic function: a) longitudinal: higher velocities and integrals in lateral and inferior walls and in basal segments, with a trend to reduction of these parameters with aging; b) radial: higher basal velocities, no significant change with aging. Diastolic function: a) longitudinal: higher velocities in lateral and inferior walls and in basal segments. With aging* e *and* e/a *velocities and integrals decreased,* a *increased and older individuals showed lower percentage of segments with* e/a *>1; b) radial: aging was associated with lower* e *and higher* a *velocities.*

Conclusion*: 1) Tissue Doppler echocardiography detects physiological differences between regional myocardial function of different ventricular segments, in velocities, times intervals and integrals, with physiological heterogeneity and asynchrony; 2) Many of these data are age dependent; 3) Our data contribute to define normal values, and may become useful when compared with data from populations with heart diseases.*

Key words: longitudinal and radial regional myocardial function, tissue Doppler echocardiography

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The correct evaluation of myocardial function is an important challenge for modern cardiology. While global function [1-3] has been intensely investigated, and the value of each method (diagnostic capacity, accuracy, and reproducibility) has been well established, the same has not happened with regional myocardial function, whose importance results from the segmentary character of several cardiac diseases. In clinical practice, segmentary analysis is usually performed qualitatively or semiquantitatively with two-dimensional echocardiography, which, despite its usefulness, has some disadvantages, such as the influence of the operator's experience and dependence on technical conditions [4].

The quantitative analysis of regional myocardial function may be performed with invasive and noninvasive methods, each of which has advantages and disadvantages. Among the ultrasound methods, tissue Doppler echocardiography stands out. This technique, which complements the conventional study, allows, through the analysis of the signals originating in the myocardium, quantification of regional myocardial function with little dependence on load conditions. In the pulsed tissue Doppler echocardiography modality, regional myocardial function is characterized by the direction of movement, velocities, and time intervals. Another advantage of tissue Doppler echocardiography is that it allows the selective study of longitudinal regional myocardial function, evaluated in the apical view (subendocardial sample composed essentially of longitudinal fibers), and of radial regional myocardial function, evaluated in the parasternal view (intramyocardial sample composed predominantly of circumferential fibers). This approach may be useful in clinical practice because certain diseases, which affect the subendocardium in particular, such as small vessel disease, may mainly affect longitudinal function. On the other hand, other diseases involving the endomyocardial region, such as some infiltrating diseases or transplant rejection, may mainly affect radial function. Other details about tissue Doppler echocardiography and its clinical applications have been reported in other studies

regarding regional function [5-35] and longitudinal global function (mitral annulus kinetics) [36-47].

The objectives of this study were to characterize left ventricular regional myocardial function by tissue Doppler echocardiography in a population of healthy adult volunteers and to assess the influence of age on regional myocardial function. The study comprised healthy asymptomatic volunteers with normal objective examinations, no history of cardiac disease, and no risk factors for coronary artery disease. The inclusion criteria comprised normal findings in high-quality electrocardiography, M-mode echocardiography, two-dimensional echocardiography, and conventional Doppler echocardiography. All patients older than 45 years had negative noninvasive tests for ischemia detection. No volunteer was receiving cardiovascular medication. Our hospital ethics committee approved the study protocol, and every volunteer provided consent.

The population was stratified according to age groups, below and above 45 years, to assess the effect of age and its functional alterations in the variables studied (G1: group 1- individuals aged 45 years or less; G2: group 2 - individuals above the age of 45 years).

Methods

All examinations were performed using a Toshiba SSA 380A - Powervision echocardiographic device (Toshiba Corp, Tokyo, Japan) and a 3.75-mHz probe, phased array with 64 elements, fundamental imaging, frame rate > 100/s using the conventional echocardiographic views, with the individuals in the left lateral decubitus position. The scanning velocity used in the measurements was 100 mm/s with video recording for later review.

Table I - Clinical and echocardiographic data

	Group 1	Group 2
Age (years)	27± 9	60± 10§§
Male/female	15/7	11/12
Weight (kg)	66± 12	71± 14
Height (cm)	169± 6	165± 8
Body surface (m^2)	1.75± 0.18	1.78± 0.21
Systolic BP (mm Hg)	127± 14	138± 14
Diastolic BP (mm Hg)	75± 7	72± 8
Heart rate (min^{-1})	68± 5	71± 9
LV mass index	60± 12	71± 14**
LV hypertrophy index	60± 11	65± 8
LA diameter (mm)	30± 3	32± 4
LV diastolic diameter (mm)	48± 3	50± 3
LV systolic diameter (mm)	28± 3	28± 4
Shortening fraction (%)	41± 4	43± 6
Time of isovolumetric contraction (ms)	78± 20	75± 23
Ejection time (ms)	283± 17	290± 22
Time of isovolumetric relaxation (ms)	81± 7	92± 9§§
E/A	1.89± 0.43	1.14± 0.33§§

Values presented as mean ± standard deviation. **p<0.01; §§p<0.001; BP – blood pressure; LV – left ventricle; LA – left atrium.

According to the recommendations of the American Society of Echocardiography, the parameters usually assessed with this methods were measured in M-mode, two-dimensional, and continuous-wave and pulsed Doppler echocardiography (tab. I).

In the pulsed tissue Doppler echocardiographic modality, a sample was placed in the region of interest, and the velocity-time spectral Doppler profile referring to the area of interest was presented on the screen. Based on the several deflections recorded, measurements of the parameters of velocity and time domain, which characterized the regional myocardial function of the area studied, could be performed. Whenever possible, maximal alignment between the ultrasound beam and parietal movement was attempted. The gains and filters were optimized to obtain the best signal-to-noise ratio, with a Nyquist limit of 15-20 cm/s. In each segment analyzed, 5 consecutive cycles were studied at the end of expiration, and the respective mean was calculated.

Assessing longitudinal regional myocardial function, a 5-mm volume sample was placed in the subendocardial region of 8 segments of the 4 left ventricular walls: basal and medial segment of the interventricular septum, lateral wall (apical view of 4 chambers), inferior and anterior walls (apical view of 2 chambers). The apical segments were excluded from the study, because, as the apex is relatively fixed throughout the cardiac cycle, the velocities obtained are very low, sometimes with poor resolution and technical quality insufficient for analysis.

Assessing radial regional myocardial function, the volume sample was placed in the endomyocardial region of the basal and medial segment of the inferior wall in the left parasternal view, short axis. Given the perpendicularity of the inferior septum and lateral wall movement in regard to the ultrasound beam, these walls were not included in the analysis. The anterior septum was also excluded, given the poor technical quality of the images obtained.

In each of the segments analyzed, the maximum velocities (cm/s) of the systolic wave (*s*), of the rapid filling wave (*e*), and of the atrial contraction wave (*a*) were measured, and the *e/a* ratio was calculated (fig. 1). For each parameter in the longitudinal axis, the respective heterogeneity index

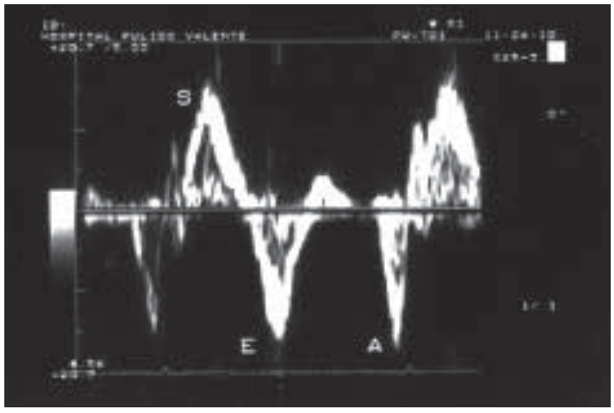

Fig. 1 - Regional myocardial velocities. S- systolic wave; E- rapid filling wave; A- atrial contraction wave.

was calculated. The heterogeneity index represents the physiological variation of the velocities in the 8 ventricular segments analyzed (heterogeneity index HI= $\Sigma |x-m|/8$), in which "x" is the maximal velocity of the wave in each segment studied and "m" is the mean of the velocities in these sites. In each group, the percentage of the longitudinal segments in which the *e/a* ratio was greater than 1 was also calculated, as was the mean number of segments with the *e/a* ratio greater than 1 per individual. The meridional gradient in the longitudinal and radial axes, which consists of the differences in velocities between the basal and median left ventricular segments, was also calculated.

The duration of each wave (ms) was extrapolated, prolonging the respective acceleration/deceleration pendent as far as the base line. Recording was performed with simultaneous electro- and phonocardiographic monitoring, and 9 time intervals (t1 to t9) were measured based on the electrocardiographic R wave (S1 of phono) as follows (fig. 2 and 3): t1 – from R (S1 of phono) to the beginning of *s* – isovolumic contraction time = PEP (preejection period); t2 – until the peak of *s*; t3 – until the end of *s* – time of systole; t4 – until the beginning of *e*; t5 – until the peak of *e*; t6 – until the end of *e*; t7 – until the beginning of *a*; t8 – until the peak of *a*; t9 – until the end of *a*.

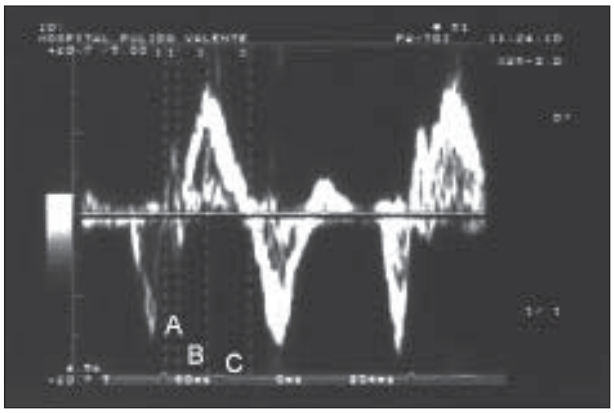

Fig. 2 - Regional systolic times. A- time of isovolumetric contraction; B- time to reach the peak of S; C- time of systole.

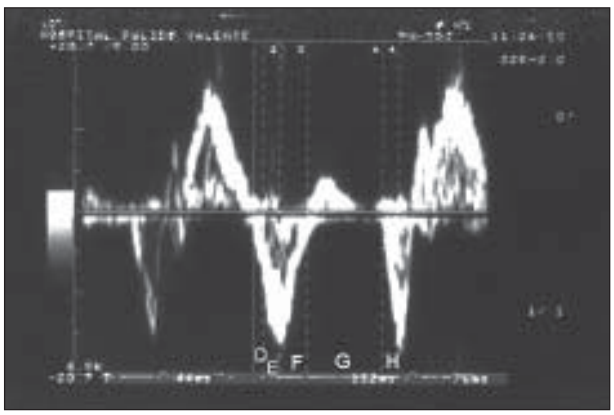

Fig. 3 - Regional diastolic times. D- time of isovolumetric relaxation; E- time to reach the peak of E; F- time until the end of E; G- diastasis; H- time to reach the peak of Aa.

Based on these intervals, other time intervals were calculated as follows: ejection time = t3 - t1 = LVET (left ventricular ejection time); PEP/LVET = t1/t3-t1; IRT (isovolumic relaxation time) = t4-t3; time for reaching the peak of *e* = A2-e = t5-t3; diastole time = t9-t3. Through the coefficient of variation of the several time intervals in the different segments in the longitudinal plane, the indices of physiological systolic diastolic asynchrony were calculated for each time interval.

For each wave, its velocity-time integral, which represents a measure of the amplitude of movement, was measured and expressed in mm.

The results are shown as mean and standard deviation. The Student *t* test and the chi-square test were used to compare the clinical and echocardiographic data in the 2 groups. To investigate the longitudinal myocardial function, the values of each variable were compared between the 4 basal ventricular segments and the 4 medial segments in the same individuals, using the analysis of variance with 2 factors. In the cases in which the analysis showed the existence of a difference between locations for a significance level of 5%, a post hoc analysis of the differences between every 2 locations was performed with the Student *t* test for paired samples with a Bonferroni correction.

Then, the hypothesis of nonexistent differences between the groups in the set of measurements in the 4 locations of every cardiac structure in each individual was investigated with analysis of variance with 2 factors and repeated measurements in 1 factor. The adjusted model was that of an analysis of variance of mixed effects with 3 factors, in which the groups of individuals and the locations represented the fixed factors and the individuals represented the random factor. In this analysis, 2 hypotheses were simultaneously tested: the hypothesis that the groups did not differ in regard to the mean values tested through the different locations of the measurements, and the hypothesis that the differences between the groups were not constant in all the 4 locations. This latter hypothesis was tested by the inclusion of a term for interaction between the groups and the locations in the model. Due to questions of potency, a significant test for a bilateral level of 10% was accepted as evidence of difference. In all other cases, the differences were tested for a significance level of 5% for bilateral tests.

The reproducibility of measurements was tested in 10 consecutive healthy volunteers, 5 from each group, through linear regression and the Bland-Altman plot [48]. The calculations were performed with STATA software version 7.0 (Stata Corporation, College Station, TX, USA).

Results

The study comprised 45 healthy volunteers, who, according to the methodological criteria reported, were divided into 2 groups as follows: group 1 - age < 45 years (n=22, 15 males and 7 females, mean age of 27 ± 9 years); group 2 - age > 45 years (n=23, 11 males and 12 females, mean age of 60±10 years). In regard to clinical data, the 2 groups were observed to differ only in regard to age, the distribution

according to sex, weight, height, body surface, blood pressure, and heart rate being similar (tab I).

The conventional echocardiographic data revealed that G2 compared with G1 had higher left ventricular mass indexes (71±14 vs 60±12g/m^2, p<0.01), a longer isovolumic relaxation time (92±9 vs 81±7ms, p<0.001), and shorter *e/a* (1.14±0.33 vs 1.89±0.43, p<0.001). The remaining parameters analyzed were similar, particularly the global systolic function indices (tab I).

Regional systolic function, myocardial velocities (tab. II) - Longitudinal function. The systolic velocities were more elevated in the lateral and inferior walls in both segments. The meridional gradient was greater in the anterior and inferior wall in G1, and in the inferior wall in G2. This gradient diminished with age (p <0.05), mainly in the anterior wall. A reduction in *s* was observed with age (p <0.001), with statistical significance in the anterobasal segment and in the mean value of the 8 segments (G1: 8.5±0.7; G2: 8.1±1.1, p<0.05). The heterogeneity of *s* did not change with age (G1: 1.36±0.54; G2: 1.12±0.49).

Radial function - The velocities and the radial meridional gradient did not significantly change with age.

Regional systolic function, time intervals (tab. III) - Longitudinal function. Isovolumic contraction time (ICT) - This interval had a shorter duration in the septum and anterior wall, with no significant differences with aging, except for the inferobasal segment, in which a reduction in this time interval was observed with age. The asynchrony index did not change with age (G1: 0.16±0.04; G2: 0.19±0.07).

Time until the peak of *s* - This interval also had a shorter

Table II – Regional systolic function, myocardial velocities

	Basal segments		Medial segments		Meridional gradient	
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
IVS	7.9 ± 0.7	82± 1.1	7.3 ± 0.8	7.3 ±1.3	0.68±0.89	0.91±1.04
LW	9.4 ± 1.8	8.6± 2	8.6 ± 2.6	7.6 ±1.9	0.77±1.45	0.96±1.4
IW	10.2 ± 1.5	9.4± 2.3	7.8 ± 1.1	7.6 ±1.2	2.45±1.41	1.83±1.59
AW	9.2 ± 2.2	7.6± 1.4§	7.2 ± 1.2	7.0 ±1.2	2.05±1.84	0.57±1.12§
Radial function	8.0 ± 1.2	8.6± 1.2	7.2 ± 1	7.8 ±1	0.8 ±1.1	0.8 ±1.1

Values presented as mean ± standard deviation. § p<0.005; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall.

Table III - Regional systolic function, temporal intervals

		Basal segments		Medial segments	
		Group 1	Group 2	Group 1	Group 2
ICT	IVS	59 ± 9	60 ± 13	63 ± 11	60 ± 13
	LW	69 ± 20	71 ± 17	65 ± 13	73 ± 24
	IW	73 ± 13	65 ± 13*	66 ± 11	69 ± 11
	AW	63 ± 10	64 ± 9	62 ± 12	54 ± 16
	RF	70 ± 17	64 ± 15	65 ± 16	64 ± 17
T peak of s	IVS	173 ± 20	167 ± 31	181 ± 24	165 ± 40
	LW	165 ± 83	1764 ± 46	166 ± 60	180 ± 63
	IW	167 ± 48	180 ± 33	176 ± 35	174 ± 34
	AW	152 ± 60	146 ± 36	153 ± 56	137 ± 32
	RF	163 ± 24	144 ± 39	162 ± 31	154 ± 44
Ejection time	IVS	275 ± 21	289 ± 23*	283 ± 41	316 ± 33§
	LW	294 ± 26	280 ± 48	316 ± 39	290 ± 56
	IW	290 ± 21	294 ± 29	304 ± 20	303 ± 33
	AW	282 ± 30	292 ± 35	283 ± 29	300 ± 26
	RF	295 ± 25	302 ± 35	301 ± 28	307 ± 32
PEP/LVET	IVS	0.22 ± 0.04	0.21 ± 0.05	0.23 ± 0.05	0.19 ± 0.05*
	LW	0.23 ± 0.07	0.26 ± 0.09	0.21 ± 0.05	0.26 ± 0.11*
	IW	0.25 ± 0.05	0.22 ± 0.04 *	0.22 ± 0.04	0.23 ± 0.04
	AW	0.23 ± 0.05	0.22 ± 0.05	0.22 ± 0.05	0.22 ± 0.06
	RF	0.24 ± 0.05	0.21 ± 0.05 *	0.22 ± 0.06	0.21 ± 0.05
Time of systole	IVS	334 ± 22	348 ± 30	346 ± 43	376 ± 32*
	LW	362 ± 34	351 ± 48	382 ± 42	362 ± 59
	IW	363 ± 23	359 ± 35	370 ± 22	372 ± 36
	AW	346 ± 29	356 ± 37	345 ± 31	364 ± 28*
	RF	365 ± 26	365 ± 40	367 ± 29	370 ± 41

Values presented as mean ± standard deviation; *p<0.05; § p<0.005; TIC- time of isovolumetric contraction; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall; RF- radial function.

duration in the septum and anterior wall, with no significant differences with aging. The asynchrony index did not change with age (G1: 0.20±0.06; G2: 0.21±0.05).

Ejection time - The duration of this interval was shorter in the septum and anterior wall only in G1 (basal interaction < 0.10, median < 0.0005). No significant differences were observed with aging, except for the septum, where a longer duration of this time interval was observed with age. The asynchrony index did not change with age (G1: 0.08±0.03; G2: 0.10±0.06).

PEP/LVET - Only in G2 did the septum have the lowest value and the lateral wall the greatest value of this ratio in both segments (basal interaction < 0.10, medial < 0.005). This ratio diminished with age in the inferobasal and septal-medial segment and increased with age in the lateromedial segment. The asynchrony index did not change with age (G1: 0.19±0.04; G2: 0.25±0.09).

Time of systole - Systole was significantly shorter in the septum and the anterior wall only in G1 (medial interaction < 0.01). The duration of systole was longer in the older group only in the septal-medial and anteromedial segment. The index of asynchrony did not change with age (G1: 0.07±0.03; G2: 0.08±0.05).

Radial function - No significant differences were observed between the 2 groups in regard to isovolumic contraction time, time to reach peak of *s*, ejection time, and time of systole. The PEP/LVET ratio decreased with age in the basal segment.

Regional systolic function, velocity-time integrals (tab. IV) - Longitudinal function – In the basal segments, this parameter had a greater value in the inferior wall and a lower value in the anterior wall only in G2. In the medial segments, the lowest value was observed in the anterior wall in both groups. In these segments, a reduction in the integral of *s* was observed with age ($p < 0.05$). The heterogeneity index did not change with age (G1: 1.34±0.62; G2: 1.09±0.31).

Radial function - No differences were observed between the 2 groups with age.

Regional diastolic function, myocardial velocities (tab. V) – Longitudinal function. *e* wave: the velocities of the *e* wave were more elevated in the lateral and inferior walls in both groups and segments. The meridional gradient was always positive, greater in the inferior wall and lower in the septum (negative in G2). This gradient did not change with age. A reduction in *e* was observed with age in all walls and mean values (G1: 14.3±1.5; G2: 11.1±1.8; $p<0.0001$), and a nonsignificant tendency towards reduction in heterogeneity was observed (G1: 2.1±0.8; G2: 1.6±0.7).

a wave - The velocities of *a* were more elevated in the inferior wall and lower in the anterior wall in both groups and segments. The meridional gradient was similar between the 4 walls in the 2 groups. A significant increase in *a* in all walls, segments, and mean values was observed with age (G1: 7.3±1.1; G2: 10.2±1.9; $p<0.0001$), with no difference in the meridional gradient. The index of heterogeneity of the *a* wave increased with age (G1: 1.07±0.31; G2: 1.53±0.47; $p<0.0005$).

e/a: In G1, *e/a* was greater in the lateral wall and lower in the septum in both segments, while, in G2, *e/a* was greater in the anterior wall and lower in the septum (basal segments)

Table IV - Regional systolic function, integral of *s*

		Basal segments		Medial segments	
		Group 1	Group 2	Group 1	Group 2
Integral of *s*	IVS	4.5±0.8	4.4±1.2	4.3±0.9	3.7±1.1
	LW	4.5±2.4	4.4±1.9	3.9±2.3	3.8±1.6
	IW	5±0.6	5.3±1	4.2±1.5	3.9±1.1
	AW	4.3±0.6	3±1.1	3.3±1.8	2.6±1.2
	RF	3.7±1.2	3.4±1.6	3.5±1.2	3.5±1.4

Values presented as mean ± standard deviation; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall; RF- radial function.

Table V – Regional diastolic function, myocardial velocities

		Basal segments		Medial segments		Meridional gradient	
		Group 1	Group 2	Group 1	Group 2	Group 1	Group 2
e	IVS	12.7 ± 2.1	10.3 ± 2.6 §	12.2 ± 2.2	10.4 ± 1.9**	0.5 ± 2.82	-0.13 ± 2.16
	LW	15.1 ± 3.6	11.6 ± 2.7§§	13.9 ± 2.9	10.6 ± 2.7 ¶	1.27 ± 1.86	1 ± 2.2
	IW	16.7 ± 2.2	12.2 ± 4 ¶¶	13.8 ± 2.1	9.8 ± 2.4¶¶	2.91 ± 2.69	2.35 ± 3.02
	AW	12.5 ± 1.6	10 ± 2.3 ¶	116 ± 2.7	9.6 ± 1.9 **	0.95 ± 1.81	0.43 ± 1.34
	RF	13 ± 2.8	11 ± 3.3 *	12.9 ± 2.8	10.9 ± 2.5 *	0.1 ± 2.4	0.1 ± 2.8
a	IVS	8.4 ± 1.1	11.1 ± 2.2¶¶	7.2 ± 1.4	10.4 ± 2.2¶¶	1.18 ± 0.80	0.70 ± 1.61
	LW	7.2 ± 1.9	10.9 ± 3.1¶¶	6.6 ± 2.1	10 ± 3.1 ¶	0.59 ± 1.50	0.83 ± 1.37
	IW	9.1 ± 1.8	11.9 ± 2 ¶¶	7.9 ± 1.3	10.4 ± 2.1¶¶	1.14 ± 1.21	1.48 ± 1.53
	AW	6.8 ± 1.4	9.1 ± 3.1 §	6.2 ± 1.1	88 ± 24 ¶	0.55 ± 0.86	0.30 ± 1.69
	RF	6.4 ± 1.6	9.3 ± 2.6 ¶	5.9 ± 1.7	8.6 ± 2.1 ¶¶	0.5 ± 1.4	0.7 ± 2.2
e/a	IVS	1.5 ± 0.3	0.96 ± 0.3¶¶	1.8 ± 0.4	1 ± 0.3 ¶¶	-0.22 ± 0.46	-0.08 ± 0.24
	LW	2.2 ± 0.6	1.1 ± 0.4 ¶¶	2.2 ± 0.6	1.2 ± 0.5 ¶¶	-0.04 ± 0.47	-0.045± 0.27
	IW	1.9 ± 0.4	1.1 ± 0.4 ¶¶	1.8 ± 0.4	0.98 ± 0.3¶¶	0.13 ± 0.45	0.09 ± 0.28
	AW	1.9 ± 0.5	1.2 ± 0.5 ¶¶	1.9 ± 0.6	1.2 ± 0.4 ¶¶	0.02 ± 0.35	0.06 ± 0.21
	RF	2.2 ± 0.9	1.3 ± 0.5 ¶	2.3 ± 0.7	1.26 ± 0.5¶	-0.1 ± 0.8	0.04 ± 0.4

Values presented as mean ± standard deviation; *p<0.05; **p<0.01; §p<0.005; §§p<0.001; ¶ p<0.0005; ¶¶ p<0.0001; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall; RF- radial function.

and greater in the lateral and anterior wall (medial segments). These differences explain the interaction observed (basal < 0.01, median <0.10). The meridional gradient was, in both groups, similar for the 4 walls and slightly negative in the septum and lateral wall, with no changes with age. A significant reduction in the *e/a* ratio was observed with age in all walls, segments, and mean values (G1: 2.1±0.4; G2: 1.2±0.3; p<0.0001), with a reduction in the heterogeneity index (G1: 0.37±0.14; G2: 0.23±0.; p<0.0005). The percentage of segments with *e/a* >1 was significantly higher in group 1 (G1: 99%; G2: 56%; p<0.01), in which, of the 176 segments analyzed, only 1 segment in the basal septum did not have an *e/a* >1. The mean number of segments with *e/a* >1 per individual was also greater in group 1 (G1: 7.9; G2: 4.5). In group 2, the wall with the lowest percentage of *e/a* >1 (41%) was the septum, followed by the inferior (52%), lateral (63%), and anterior (69%) walls.

Radial function - A reduction in *e*, an increase in *a*, and a reduction in *e/a* were observed with age, the meridional gradient being similar in the 2 groups.

Regional diastolic function, time intervals (tab. VI) – Longitudinal function. Isovolumic relaxation time (IRT) - No significant differences were observed between the isovolumic relaxation time in the several walls in both groups and segments. In the basal segments, this interval significantly increased in the interventricular septum with age, while, in the medial segments, this increase was observed in the lateral wall with a significant p between (< 0.05). An increase in asynchrony of IRT was observed with age (G1: 0.24±0.09; G2: 0.28±0.09; p< 0.05).

Time until the peak of *e* - The duration of this interval was shorter in the inferior and lateral wall, only in the basal segments of G1. No significant alterations in this parameter or in its asynchrony were observed with age (G1: 0.16±0.08; G2: 0.16±0.06).

Time of diastole – Only in the basal segment of G1 was this interval longer in the inferior wall and shorter in the lateral wall (interaction < 0.1). With age, a reduction in this interval was observed in the basal segments (p between <0.0005), mainly in the inferobasal segment. Asynchrony did not change with age (G1: 0.1±0.04; G2: 0.07±0.04).

Radial function - No significant temporal differences were observed between the 2 groups in any of the segments analyzed.

Regional diastolic function, velocity-time integrals (tab. VII) – Longitudinal function - integral of *e* - no differences were observed between the various walls, in both groups and segments. This integral decreased with age in all segments, as did its mean (G1: 5.7±0.9; G2: 3.9±0.9; p<0.0001) with a reduction in its heterogeneity (G1: 1.5±0.4; G2: 0.9±0.3; p<0.0005).

Integral of *a* - No differences were observed between the various walls in the medial segments. In the basal segments, the most elevated value was observed in the inferior wall and the lowest in the anterior wall. This parameter and its mean value (G1: 1.8±0.4; G2: 2.5±0.6; p<0.0005) increased with age in all segments, but with no statistical significance in the anterobasal and lateromedial segment. The heterogeneity index did not change with age (G1: 0.56±0.47; G2: 0.75±0.25).

Radial function – A nonsignificant reduction in the integral of *e* and a significant increase in the integral of *a* were observed with age.

The reproducibility of the measurements was tested in 10 consecutive healthy volunteers, 5 in each group; intraobserver and interobserver correlation coefficients of 0.94 and 0.92, respectively, were obtained for the velocities. In the temporal domain, the intraobserver and interobserver correlation coefficients were 0.92 and 0.90, respectively. Based on the Bland-Altman plot, the mean difference between the observations was found to be smaller than 5% of the mean values for velocity and time.

Discussion

The asymmetries in regional myocardial function of

Table VI – Regional diastolic function, temporal intervals

		Basal segments		Medial segments	
		Group 1	Group 2	Group 1	Group 2
IRT	IVS	65± 16	79± 23*	64± 16	73± 26
	LW	64± 32	74± 25	62± 27	76± 20*
	IW	66± 23	68± 21	75± 23	77± 25
	AW	71± 18	70± 19	68± 23	72± 25
	RF	57± 20	52± 19	69± 19	59± 23
T peak of *e*	IVS	155± 22	157± 23	155± 31	150± 34
	LW	146± 26	145± 40	145± 54	141± 31
	IW	140± 24	142± 19	150± 25	150± 24
	AW	160± 29	152± 31	158± 15	151± 26
	RF	117± 18	119± 24	132± 21	122± 29
Time of diastole	IVS	574± 84	546±153	624±154	526±114
	LW	548±105	542±146	533± 94	546±121
	IW	620±111	543±117*	534± 83	545±131
	AW	590± 96	556±151	537± 69	550±135
	RF	535± 64	549±148	523± 73	541±127

Values presented as mean ± standard deviation; *p<0.05; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall; RF- radial function.

Table VII - Regional diastolic function, integral of *e* and of *a*

		Basal segments		Medial segments	
		Group 1	Group 2	Group 1	Group 2
Integral of *e*	IVS	5.7±1.2	4.1±1.4¶	5.7±2.2	4.1±1.9*
	LW	6.1±2.1	4.1±1.8§	5.9±3.3	3.5±1.6§
	IW	6.1±1.2	4.5±1.9*	5.1±2.1	3.6±1.5*
	AW	5.6±1.8	4.0±1.0§§	5.2±2.2	3.7±0.9§
	RF	4±1.9	3.6±1.3	4.2±1.9	3.9±1.9
Integral of *a*	IVS	2±0.6	2.7±1.1**	1.5±0.5	2.3±0.8¶
	LW	1.9±0.8	2.9±1.4**	2.1±2.6	2.4±1.1
	IW	2.3±0.6	3.1±1§	1.7±0.5	2.7±1¶¶
	AW	1.8±0.6	2.2±1,3	1.3±0.5	2.1±0.9§
	RF	1.4±0.6	2.2±1§	1.2±0.6	2.4±1.2¶

Values presented as mean ± standard deviation; *p<0.05; **p<0.01; §p<0.005; §§p<0.001; ¶ p<0.0005; ¶¶ p<0.0001; IVS- interventricular septum; LW- lateral wall; IW- inferior wall; AW- anterior wall; RF- radial function.

the different ventricular zones were reported in experimental studies [49] and invasive methods [50] with off line and frame-by-frame analysis of ventriculographies, which, due to the complexity of the analysis and time consumption, has little clinical applicability. Of the noninvasive methods, the isotopic ones [51-56] (despite the deficient temporal resolution and the fact that they are not performed in real time), tagging magnetic resonance imaging [57-60] (with the disadvantages of having poor temporal resolution, of not being acquired in real time, of being expensive, and of being of difficult accessibility) and ultrafast computerized axial tomography stand out [61]. In regard to ultrasound methods, M-mode echocardiography [62-66], despite its high temporal resolution, has the disadvantage of limiting the analysis to segments with movement parallel to the ultrasound beam, which is a limitation that can be potentially overcome with the "anatomic M-mode". In two-dimensional studies [67-71], quantification of regional myocardial function is based on the measurement of the endocardial movement between systole and diastole, the technological advances being digital subtraction high frame rate echocardiography and segmental analysis of color kinesis images [72,73]. The also promising three-dimensional echocardiography [45-47] has not yet entered daily clinical practice.

Most tissue Doppler studies in healthy individuals [13,17,18,20,22,24,26] have only analyzed myocardial velocities and concluded that a physiological heterogeneity exists between the ventricular walls. Therefore, the velocities of *s* and *e* are usually greater in the lateral wall and lower in the septum as a consequence of the "sandwich" position of the septum in between ventricles, of its greater physiological parietal stress, of the fact that the septal cytoarchitecture is rich in circumferential fibers, and of its different proportion between the number of myocytes/beta-adrenergic receptors and the degree of interstitial fibrosis. These studies also report heterogeneity of velocities in the same wall, more elevated in the basal segments, producing a positive meridional gradient that reflects the importance of these segments in myocardial function. Most studies do not perform a systematic analysis of temporal parameters, measuring usually only 1 or 2 intervals. The regional isovolumic relaxation time is shorter in the basal segments on apical view (reflecting myocardial electric activation) and longer in the anterior septum on the parasternal view [18]. With aging [28-30], a slight reduction in the velocities of *s* is observed, as are a significant reduction in the velocity of *e,* an increase in *a*, and an inversion in *e/a*. According to a recent study [30] with healthy volunteers under the age of 40 years, regional *e/a* was always > 1, and the number of segments with *e/a* <1 increased with age initially in the basal segments and in the longitudinal axis.

In regard to velocities and meridional gradients, our results are in accordance with those reported [13,17,18,20,22,24,26], revealing physiological heterogeneity and greater systolic and diastolic velocities in the lateral and inferior walls. The analysis of temporal intervals reveals physiological systolic asynchrony, suggesting a better septal and anterior systolic performance (shorter isovolumic contraction time and PEP/LVET). These data, which seem contradictory to the better velocity profile of these walls, may result from the shorter duration of systole in the inferior wall or the fact that depolarization occurs first in the septum. In regard to diastolic intervals, the fact that no significant differences were found between the various segments points to a small degree of physiological diastolic asynchrony. In our study, isovolumic relaxation time had a variable duration, although it was not significantly shorter in the basal segments. The fact that most systolic parameters did not change with age is in accordance with the little deterioration in systolic function with aging [28-30]. In regard to diastole, a reduction in *e*, an increase in *a*, and an inversion in *e/a* have been observed with age, coinciding with those reported. Also as reported [30], *e/a* was always > 1 in younger individuals (except for 1 segment with *e/a* =1), but it varied in the older group. However, in this group, the inversion in *e/a* did not preferably occur in the basal segments, which may be related to methodological differences, mainly to the number of segments studied with the tissue Doppler modality used or with the age cut off chosen.

Some of the major limitations in this study are the general limitations of tissue Doppler echocardiography previously reported, such as the influence of the global cardiac movement and adjacent structures, time consumption, and the dependence on the angle of incidence. Many of these limitations will be overcome with strain-rate imaging techniques [74,75].

On the other hand, the echocardiographic ejection fraction was not measured on purpose, because the correlations with fundamental imaging reported in the literature are not the best. Data regarding systolic function were not equally assessed on conventional Doppler echocardiography, mainly stroke volume, cardiac output, and cardiac index. Another limitation on longitudinal analysis is the exclusion of the apical segments, and, on radial analysis, the fact that the study is limited to 1 wall. However, these aspects are similar to those of the MYDISE multicenter study [76]. The fact that the time intervals were not normalized for systole and diastole duration may have influenced some results.

Finally, although the presence of subclinical coronary artery disease may not be excluded, the likelihood of its existence is very low, given the sensitivity of the noninvasive methods used.

In conclusion, is tissue Doppler echocardiography the ideal ultrasound technique or simply a new approach providing known data in a new perspective? The ideal technique for analyzing regional myocardial function does not exist, but tissue Doppler echocardiography has many of its requirements and approaches the ideal [15]. One of its great advantages is not the introduction of new concepts, but the capacity to obtain high-resolution images for quantitative analysis. According to Hatle and Sutherland [17], tissue Doppler echocardiography is strong enough for investigation and routine clinical studies, providing greatly accurate

data and value in terms of radial and longitudinal, systolic and diastolic direction, time, and velocity.

This study reveals that physiological differences exist between the regional myocardial function of different segments, in terms of velocities, times, and velocity-time integrals, with heterogeneity and physiological asynchrony, and that some of these parameters are significantly changed with age. Our data contribute to the definition of parameters of normality and may be useful for comparing populations with heart disease.

References

1. Oh J. Echocardiography for the evaluation of systolic and diastolic functions. ACC Curr J Rev 2000: 2: 74-6.
2. Schmidt M, Starling M. Physiological assessment of left ventricular systolic and diastolic performance. Curr Prob Cardiol 2000; 12: 833-908.
3. Van der Wall E, Bax J. Different imaging approaches in the assessment of left ventricular dysfunctional things equal? Eur Heart J 2000; 21: 1295-7.
4. Picano E, Lattanzi F, Orlandini A, Marini C, L'Abbate A. Stress echocardiography and the human factor: the importance of being an expert. J Am Coll Cardiol 1991; 17: 666-9.
5. D'Hooge J, Bijnens B, Jamal F, Hatle L, Sutherland G. High frame rate, myocardial integrated backscatter: does this change our understanding of this acoustic parameter? Eur J Echocardiogr 2000; 1: 32-41.
6. Kvitting J, Wigstrom L, Strotmann J, Sutherland G. How accurate is visual assessment of synchronicity in myocardial motion: an in vitro study with computer simulated regional delay in myocardial motion. Clinical implications for rest and stress echocardiography studies. J Am Soc Echocardogr 1999; 12: 698-705.
7. Isaaz K, Thompson A, Ethevenot G, Cloez J, Brembilla B, Pernor C. Doppler echocardiography measurement of low velocity motion of the left ventricular posterior wall. Am J Cardiol 1989; 64: 66-75.
8. Mc Dicken W, Sutherland G, Moran C. Color Doppler velocity imaging of the myocardium. Ultrasound Med Biol 1992; 18: 651-4.
9. Sutherland G, Stewart M, Groundstream K, et al. Color Doppler myocardium imaging, a new technique for the assessment of myocardial function. J Am Soc Echocardiography 1994; 7: 441-58.
10. Miyatake K, Yamagishi M, Tanaka M, Uematsu M, Yamazaki N, Mine Y. A new method for evaluation of left ventricular wall motion by color coded tissue Doppler echocardiography: in vitro and in vivo studies. J Am Coll Cardiol 1995; 25: 717-24.
11. Drodz J, Schon F, Nesser J, Erbel R. Tissue Doppler echocardiography: new promising method in cardiovascular diagnoses. Essener Kardiologische Kardiovaskul Nachrichten 1994; 3(suppl.): 1-3.
12. Zamorano J, Wallbridge D, Ge J, Drodz J, Nesser J, Erbel R. Non invasive assessment of cardiac physiology by tissue Doppler echocardiography: a comparison with invasive haemodynamics. Eur Heart J 1997; 18: 330-9.
13. Galiuto L, Ignone G, de Maria A. Contraction and relaxation velocities of the normal left ventricle using pulsed wave tissue Doppler echocardiography. J Am Coll Cardiol 1998; 81: 609-14.
14. Cardim N, Erbel R. Tissue Doppler echocardiography: a new method in the assessment of myocardial function. Rev Port Cardiol 1995; 14: 609-18.
15. Sutherland G. Doppler myocardial imaging: rationale, principles and instrumentation. In: Garcia Fernandez M, Delcan J. Ed. Proceedings of the International Summit in Doppler Tissue Imaging, 1997: 17-24.
16. Zamorano J. Is tissue Doppler echocardiography ready for clinical application? Eur Heart J 1998; 20: 558-60.
17. Hatle L, Sutherland G. Regional myocardial function-a new approach. Eur Heart J 2000; 21: 1337-57.
18. Garcia Fernandez M, Azevedo J, Moreno M, Arroja I, Zamorano J, Caso P. Doppler tissue imaging. Rev Port Cardiol 2001; (Supl I): 33-47.
19. Tonti G, Salustri A, Fedele F, Sutherland G. New insights into regional systolic and diastolic left ventricular function with tissue Doppler echocardiography:from qualitative analysis to a quantitative approach. J Am Soc Echocardiog 2001; 14: 85-96.
20. Shan K, Bick R, Poindexter B, et al. Relation of tissue Doppler derived myocardial velocities to myocardial structure and beta adrenergic receptors density in humans. J Am Coll Cardiol 2000; 36: 891-6.
21. Uematsu M, Myiatake K, Tanaka N, et al. Myocardial velocity gradient as a new indicator of regional left ventricular contraction: detection by a two dimensional tissue Doppler imaging technique. J Am Coll Cardiol 1995; 26: 217-23.
22. Gorcsan III J, Gulati V, Mandarino W, Katz W. Color coded measures of myocardial velocity throughout the cardiac cycle by tissue Doppler imaging to quantify regional left ventricular function. Am Heart J 1996; 6: 1204-13.
23. Gorcsan III J, Deswall A, Mankad S, et al. Quantification of the myocardial response to low dose dobutamine using tissue Doppler echocardiography measures of velocity and gradient. Am J Cardiol 1998; 81: 615-23.
24. Donovan C, Armstrong W, Bach D. Quantitative Doppler tissue imaging of the left ventricular myocardium: validation in normal subjects. Am Heart J 1995; 130: 100-4.
25. Farias C, Rodriguez L, Garcia M, Sun J, Klein A, Thomas J. Assessment of diastolic function by tissue Doppler echocardiography:comparison with standard transmitral and pulmonary venous flow. J Am Som Cardiol 1999; 12: 609-17.
26. Oki T, Tabata T, Mishiro Y, et al. Pulsed tissue Doppler imaging of left ventricular systolic and diastolic wall motion velocities to evaluate differences between long and short axes in healthy subjects. J Am Soc Echocardiogr 1999; 12: 308-13.
27. Vinereanu D, Khokhar A, Fraser A. Reproductibility of pulsed wave tissue Doppler echocardiography 1999; 12: 492-9.
28. Edner M, Jarnert C, Muller B, Malmquist K, Ring M. Influence of age and cardiovascular factors on regional pulsed wave Doppler myocardial imaging indexes. Eur J Echocardiogr 2000; 1: 87-95.
29. Palka P, Lange A, Fleming D, et al. Age related transmural peak mean velocity gradients by Doppler myocardial imaging in normal subjects. Eur Heart J 1996; 17: 940-50.
30. Wilkenshoff U, Hatle L, Sovany A, Wranne B, Sutherland G. Age dependent changes in regional diastolic function by color Doppler myocardial imaging: a comparison with pulsed Doppler indexes of global function. J Am Soc Echocardiogr 2001; 14: 959-69.
31. Kukulski T, Wilkenshoff U, Strotmann J. A comparison of segmental myocardial velocity information derived by either pulsed or color Doppler myocardial imaging: are they interchangeable data sets? A normal subject study. Eur Heart J 1998; 19(Suppl): 440.
32. Isaaz K, Munoz del Romeral L, Lee E, Schiller N. Quantitation of the motion of the cardiac base in normal subjects by Doppler echocardiography. J Am Soc Echocardiogr 1993; 6: 166-76.
33. Garcia M, Rodriguez L, Ares M, et al. Myocardial wall velocity assessment by pulsed Doppler tissue imaging: characteristics findings in normal subjects. Am Heart J 1996; 132: 648-56.
34. Wilkenshoff U, Sovany A, Kukulski T, Strptmann J, Wranne B, Sutherland G. When, where and to what extent does left ventricular regional function become abnormal with age in normal individuals? A color Doppler myocardial study. Eur Heart J 1998; 19(Suppl): 440.
35. Yamada H, Oki T, Mishiro Y, et al. Effect of aging on diastolic left ventricular myocardial velocity measured by pulsed tissue Doppler imaging in healthy subjects. J Am Soc Echocardiogr 1999; 12: 574-81.
36. Henein M, Gibson D. Normal long axis function. Heart 1999; 81: 111-3.
37. Wandt B. Long-axis contraction of the ventricles: a modern approach, but described already by Leonardo da Vinci. J Am Soc Echocardiogr 2000; 7: 699-706.
38. Greenbaum R, Siew Y, Gibson D, Becker A. Left ventricular fibre architecture in man. Br Heart J 1981; 45: 248-63.
39. Jones C, Raposo L, Gibson D. Functional importance of the long axis dynamics of the human left ventricle. Br Heart J 1990; 63: 215-20.
40. Heng M, Janz R, Jobin J. Estimation of regional stress in the left ventricular septum and free wall: an echocardiograph study suggesting a mechanism for asymmetric septal hypertrophy. Am Heart J 1985; 1: 84-90.
41. Ingels N, Daughters G, Stinson E, Alderman E. Evaluation of methods for quantating left ventricular segmental wall motion in man using myocardial markers as a standard. Circulation 1980; 61: 966-72.
42. Emilsson K, Alam M, Wandt B. The relation between mitral annulus motion and ejection fraction: a non linear function J Am Soc Echocardiogr 2000; 10: 896-904.
43. Bruch C, Schmermund A, Marin D, et al. M-Mode analysis of mitral annulus motion for detection of pseudonormalization of the mitral inflow pattern. Am J Cardiol 1999; 84: 692-7.
44. Ormiston J, Shah P, Tei C, Wong M. Size and motion of the mitral valve annulus in man: I-A two dimensional echocardiograph method and findings in normal subjects. Circulation 1981; 64: 113-20.

45. Flachskampf F, Chandra S, Gaddipatti A, et al. Analysis of shape and motion of the mitral annulus in subjects with and without cardiomyopathy by echocardiograph 3-dimensional reconstruction. J Am Soc Echocardiogr 2000; 4: 277-87.
46. Salustri A, Becker A, Van Herwerden L, Vletter W, Ten Cate F, Roelandt J. Three dimensional echocardiography of normal and pathological mitral valve: a comparison with two dimensional transesophageal echocardiography. J Am Coll Cardiol 1996; 27: 1502-10.
47. Komoda T, Hetzer R, Uyama C, et al. Mitral annular function assessed by 3D imaging for mitral valve surgery. J Heart Valve Disease 1994; 3: 483-90.
48. Bland J, Altman D. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; 1: 307-10.
49. Ingels N, Daughters G, Stinson E, Alderman E. Evaluation of methods for quantating left ventricular segmental wall motion in man using myocardial markeres as a standard. Circulation 1980; 61: 966-72.
50. Gibson D, Prewitt T, Brown D. Analysis of left ventricular wall movement during isovolumic relaxation and its relation to coronary artery disease. Br Heart J 1976; 38: 1010-9.
51. Bonow R, Vitale D, Bacharach S, Frederick T, Kent K, Green M. Asynchronous left ventricular regional function and impaired global diastolic filling in patients with coronary artery disease: reversal after coronary angioplasty. Circulation 1985; 71: 297-307.
52. Perrone-Filardi P, Bacharach S, Dilsizian V, Bonow R. Impaired left ventricular filling and regional diastolic asynchrony at rest in coronary artery disease and relation to exercise induced myocardial ischemia. Am J Cardiol 1991; 67: 356-60.
53. Hayashida W, Kumada T, Kohno F, et al. Left ventricular regional relaxation and its nonuniformity in hypertrophic obstructive cardiomyopathy. Circulation 1991; 84: 1496-504.
54. Bonow R, Vitale D, Bacharach S, Maron B, Green M. Effects of aging on asynchronous left ventricular regional function and global ventricular filling in normal human subjects. J Am Coll Cardiol 1988; 11: 50-8.
55. Perrone-Filardi P, Bacharach S, Dilsizian V, Bonow R. Effects of regional systolic asynchrony on left ventricular global diastolic function in patients with coronary artery disease. J Am Coll Cardiol 1992; 19: 739-44.
56. Bonow R, Vitale D, Maron B, Bacharach S, Frederick T, Green M. Regional left ventricular asynchrony and impaired global left ventricular filling in hypertrophic cardiomyopathy: effect of verapamil. J Am Coll Cardiol 1987; 1108-16.
57. Rademakers F, Rogers W, Guier W, et al. Relation of regional cross-fiber shortening to wall thickening in the intact heart: three-dimensional strain analysis by NMR. Circulation 1994; 89: 1174-82.
58. Young A, Imai H, Chang C, Axel L. Two dimensional left ventricular deformation during systole using magnetic resonance imaging with spatial modulation of magnetization. Circulation 1994; 89: 740-52.
59. Pattyanama P, Roos A, Van der Wall, Van Voorthuisen A. Evaluation of cardiac function with magnetic resonance imaging. Am Heart J 1994:128: 595-607.
60. Karwatoski S, Mohiaddin R, Yang G, Firmin D, Sutton M, Underwood S. Regional myocardial velocity imaged by magnetic resonance in patients with ischemic heart disease. Br Heart J 1994;72: 332-8.
61. Rumberger J, Weiss R, Feiring A, Stanford W, Hajduczock Z, Rezai K, Marcus M.. Patterns of regional diastolic function in the normal left ventricle: an ultrafast computed tomography study. J Am Coll Cardiol 1989; 14: 119-26.
62. Kerber R, Abbound F. Echocardiographic detection of regional myocardial infarction. An experimental study. Circulation 1973; 47: 997-1005.
63. Heikkilä J, Nieminen M. Echoventriculographic detection, localization and quantification of left ventricular asynergy in acute myocardial infarction. Br Heart J 1975; 37: 46-59.
64. Strotmann J, Kvitting J, Wilkenshoff U, Wranne B, Hatle L, Sutherland G. Anatomic M-mode echocardiography: a new approach to assess regional myocardial function – a comparative in vivo and in vitro study of both fundamental and second harmonic imaging modes. J Am Soc Echocardiogr 1999; 12: 300-7.
65. Boudoulas H. Systolic time intervals. Eur Heart J, 11 (Supplement I), 1990; 93-104.
66. Burwash I, Otto C, Pearlman A. Use of Doppler-Derived Left Ventricular Time Intervals for Noninvasive Assessment of Systolic Function. Am J Cardiol, 1993; 1331-3.
67. Haendchen R, Wyatt H, Maurer G, et al. Quantitation of regional cardiac function by two-dimensional echocardiography: patterns of contraction in the normal left ventricle. Circulation 1983; 67: 1234-45.
68. Weiss J, Bulkley B, Hutschins G, Mason S. Two-dimensional echocardiograph recognition of myocardial injury in man: comparison with postmortem studies. Circulation 1981; 63: 401-8.
69. Parisi A, Moyniban P, Folland E, Feldman C. Quantitative detection of regional left ventricular contraction abnormalities by two-dimensional echocardiography. Circulation 1981; 63: 761-7.
70. Gillam L, Hogan R, Foale R, et al. A comparison of quantitative echocardiograph methods for delineating infarct-induced abnormal wall motion. Circulation 1984; 70: 113-22.
71. Kondo H, Masuyama T, Ishihara K, et al. Digital subtraction high frame rate echocardiography in detecting delayed onset of regional left ventricular relaxation in ischemic heart disease. Circulation 1995; 91: 304-12.
72. Lang R, Vignon P, Weinert L, et al. Echocardiograph quantification of regional left ventricular wall motion with color kinesis. Circulation 1996; 93: 1877-85.
73. Koch R, Lang RM, Garcia M, et al. Objective evaluation of regional left ventricular wall motion during dobutamine stress echocardiograph studies using segmental analysis of color kinesis images. J Am Coll Cardiol 1999; 34: 409-19.
74. Heimdal A, Stoylen A, Torp H, Skjærpe T. Real-time strain rate imaging of the left ventricle by ultrasound. J Am Soc Echocardiogr 1998, 11: 1013-9.
75. D'hooge J, Heimdal A, Jamal F, et al. Regional strain and strain rate measurements by cardiac ultrasound: principles, implementation and limitations. Eur J Echocardiogr 2000; 1: 154-70.
76. Grocott Mason R, Payne N, Wilkenshoff U, et al. Can off line tissue Doppler echocardiography make dobutamine stress echocardiography objective? (abstract) Eur Heart J 1999; 20 (Suppl): 687.