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Regional diastolic function in ischaemic heart disease using pulsed wave Doppler tissue imaging

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Aims The aim of this study was to determine the utility of pulsed wave Doppler tissue imaging in the evaluation of regional left ventricular diastolic function in patients with ischaemic heart disease.

Methods and Results In 30 normal subjects and 43 patients with ischaemic heart disease, Doppler tissue imaging was performed in each of the 16 segments of the myocardium. The following diastolic pulsed wave Doppler tissue imaging parameters were obtained for each segment: (1) regional early diastolic peak velocity (regional e wave cm . s^{-1}); (2) regional late diastolic peak velocity (regional a wave cm . s^{-1}); (3) regional diastolic e/a velocity ratio; and (4) the regional isovolumic relaxation time, defined as the time interval from the second heart sound to the onset of the diastolic E wave. In patients with ischaemic heart disease, each of these parameters was evaluated and compared in ischaemic and normally perfused segments, based on the presence or absence of obstructive lesions of the supplying coronary artery. In patients with coronary artery disease, several differences were observed between diseased and normal wall segments: the mean segmental peak early diastolic velocity (e wave) was reduced (mean ± SD: $6{\cdot}4 \pm 2{\cdot}1$ cm . s^{-1} vs $8{\cdot}5 \pm 2{\cdot}8$ cm . s^{-1}; $P<0{\cdot}01$); the e/a diastolic velocity ratio was decreased ($0{\cdot}95 \pm 0{\cdot}3$ vs $1{\cdot}5 \pm 0{\cdot}6$, respectively; $P<0{\cdot}01$) and the regional isovolumic relaxation time was prolonged ($104 \pm 36{\cdot}7$ ms vs $69{\cdot}6 \pm 30$ ms; $P<0{\cdot}01$. No differences were observed in any of these parameters between the normally perfused segments of ischaemic patients and normal subjects. Patients with a normal transmitral diastolic Doppler inflow pattern had a mean of $3{\cdot}7 \pm 2{\cdot}7$ myocardial segments with a local e/a pulsed wave Doppler tissue imaging velocity ratio <1, fewer than those with an inverted diastolic transmitral Doppler inflow pattern ($10{\cdot}3 \pm 3$ segments; $P<0{\cdot}001$). Overall sensitivity and specificity for an inverted local e/a ratio and a local isovolumetric relaxation time ≥85 ms were of 62% and 72% and 69% and 80%, respectively.

Conclusion Regional diastolic wall motion is impaired at baseline in ischaemic myocardial segments, even when systolic contraction is preserved. Pulsed wave Doppler tissue imaging is a useful non-invasive technique which allows the assessment of regional diastolic performance and dynamics of the left ventricular myocardium. Further studies are required to define this role in the evaluation of coronary heart disease.
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Key Words: Doppler tissue imaging, diastole, coronary artery disease.

See page 476 for the Editorial comment on this article.

Introduction

Due to the focal distribution of coronary atherosclerosis and arterial wall plaque lesions, ischaemic heart disease characteristically involves the heart regionally. Ischaemia is also known to impair the diastolic myocardial wall motion of the left ventricle earlier than systolic contraction. Based on this concept, clinical studies have demonstrated that the evaluation of regional left ventricular diastolic function could be a good strategy with which to identify myocardial regions with impaired coronary artery flow and reduced myocardial perfusion[1–10]. Regional diastolic function has previously been analysed by radionuclide methods and angiography[3–9], demonstrating that the beginning of the outward left ventricular wall motion in the

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isovolumic relaxation phase is delayed in ischaemic left ventricular myocardial wall segments[7–8]. With echocardiography, analysis of regional diastolic function used to be performed by means of digital post-processing of M-mode recordings[9]; however, this technique is rarely used in current clinical practice due to the complexity of image processing and the few left ventricular regions available for M-mode scanning. Recently, digital subtraction high-frame-rate echocardiography has been successfully applied in the detection of regional left ventricular diastolic abnormalities in patients with ischaemic heart disease[10]. The prolongation of the time interval from the second heart sound to the onset of the outward motion of each left ventricular wall segment in early diastole showed that this parameter could be a sensitive index with which to detect ischaemic areas and abnormal segments related to haemodynamically significant coronary artery lesions and obstruction.

Recent technical developments in the field of Doppler echocardiography, such as myocardial wall motion analysis by pulsed-wave and colour[11–14] Doppler tissue imaging are useful non-invasive methods with which to quantify regional left ventricular wall dynamics. Because of its temporal resolution, pulsed wave Doppler tissue imaging may be an easy and reliable method with which to quantify patterns of segmental left ventricular myocardial relaxation.

Therefore, our present study was designed to assess whether regional abnormalities in left ventricular myocardial wall dynamics due to ischaemic heart disease can be detected by pulsed wave Doppler tissue imaging. This study was also designed to analyse the relationship between pulsed wave Doppler tissue imaging findings and conventional Doppler indices of global left ventricular filling patterns and diastolic performance.

Methods

Principles of pulsed wave Doppler tissue imaging

Doppler tissue imaging has been developed to display and assess the velocity of myocardial structures instead of blood flow. Basically, the system is derived from conventional Doppler imaging, while avoiding the high pass filter, to allow the Doppler signal originated in the myocardium to enter the auto-correlation. The rejection of high frequencies can be achieved by low pass filtering. Scaling is set to encode velocities in the range of 3 to 24 cm . s^{-1}, much lower than the velocities used typically for blood flow analysis. Post-processing of this pulsed wave Doppler signal may then be performed to obtain either colour-mapped images or spectral time-velocity recordings after Fourier transformation.

For the present study, all images were acquired with a commercially available phased-array ultrasound scanner equipped with a pulsed wave Doppler tissue imaging programme (Accuson XP 128/10C Mountain View, CA, U.S.A.) using a 2·5 to 4·5 MHz multi-frequency transducer. All images were recorded on a conventional VHS PAL videotape for subsequent data analysis.

Validation of pulsed wave Doppler tissue imaging velocities

Initially, the accuracy of spectral pulsed wave Doppler tissue imaging velocity measurements was experimentally evaluated and validated using a spinning phantom. A 5 cm cylindrical sponge was attached by a mechanical arm to an electric motor and reduction gear. Rotational speed was manipulated in order to obtain linear velocities within the interval from -10 cm . s^{-1} to 12 cm . s^{-1} as measured by a stroboscopic light device. Pulsed wave Doppler tissue imaging velocities were registered locating multiple sample volumes on the positive and negative linear velocity fields of the rotational sponge and afterwards comparing them with corresponding stroboscopic-derived linear velocity.

Study population

The study population consisted of two different groups; (1) 43 consecutive patients with the clinical diagnosis of ischaemic heart disease referred to our institution for coronary angiography, and (2) 30 normal subjects without any previous history of cardiovascular disease. The following exclusion criteria were adopted in both groups: prior myocardial infarction, intraventricular conduction disturbances, any type of valvular heart disease, systemic hypertension, hypertrophic, dilated or restrictive cardiomyopathies, arrhythmias, pulmonary hypertension and congestive heart failure. The study was approved by the Investigation Committee of our institution and informed consent was obtained from all patients. Clinical and echocardiographic data of both groups are shown in Table 1.

Echocardiography and pulsed wave Doppler tissue imaging

Initially, a conventional transthoracic Doppler echocardiographic examination was performed according to A.S.E. guidelines, in order to rule out concomitant cardiovascular diseases and to obtain the conventional indexes of global left ventricular diastolic function[15]. The transmitral flow was recorded at end expiration from the transthoracic apical four-chamber view, using a 2·5 MHz transducer, and locating a 0·5 cm pulsed wave Doppler sample volume at a position equidistant between the mitral leaflet tips, at the maximal diastolic excursion point. The following parameters of global left ventricular diastolic performance were obtained:

Table 1 Clinical and diastolic pulsed wave Doppler tissue imaging characteristics

	Patients with ischaemic heart disease	Normal subjects
Number	43	30
Age (years)	54 ± 9	49 ± 8
Heart rate (beats . min^{-1})	70 ± 4	74 ± 10
LVSD (mm)	29 ± 4	28 ± 6
LVDD (mm)	49 ± 4	44 ± 9
EF (%)	59 ± 6	64 ± 7
E mitral flow	66+12	77+15
A mitral flow	67 ± 14*	41 ± 12
Global isovolumic time	92 ± 15*	76 ± 19
IVRT normal segment (ms)	69·6 ± 30·0	59 ± 22
IVRT ischaemic segment (ms)	104 ± 36·7	
e normal segment (cm . s^{-1})	8·5 ± 2·8	10·3 ± 2
e Ischaemic segment (cm . s^{-1})	6·4 ± 2·1†	
a Normal segment (cm . s^{-1})	5·9 ± 1·7	5·8+1·6
a Ischaemic segment (cm . s^{-1})	7·1 ± 4·5†	
e/a Normal segment (cm . s^{-1})	1·5 ± 0·6	2·1 ± 0·90
e/a Ischaemic segment	0·95 ± 0·3†	

LVSD=left ventricular systolic dimension; LVDD=left ventricular diastolic dimension; EF=ejection fraction; IVRT=regional isovolumic relaxation time; e=peak early diastolic velocity of relaxation of the myocardium; a=peak late diastolic velocity; e/a=ratio of early diastolic velocity of relaxation of the myocardium to late diastolic velocity; *E*=peak early diastolic left ventricular filling velocity; *A*=peak left ventricular filling velocity at atrial contraction.
Values are reported as mean ± SD.
*Statistical significance of $P<0·05$ vs normal subjects. †Statistical significance of $P<0·01$ compared with segments of normal subjects and normal segment of patients.

early diastolic filling peak velocity (E wave cm . s^{-1}), late diastolic filling peak velocity (A wave cm . s^{-1}) and the diastolic transmitral E/A velocity ratio[16,17]. In this pulsed wave Doppler method, the left ventricular isovolumic relaxation time was determined as the interval from the end of aortic outward flow until the onset of transmitral inflow of the left ventricular cavity.

For the purpose of segmental analysis of contraction and relaxation, the left ventricle was divided into a conventional 16-segment model, with a mean number of three to five wall segments per coronary artery. Systolic left ventricular wall contraction was scored by a conventional echocardiogram as normal, hypokinetic or akinetic. Pulsed wave Doppler tissue imaging velocities were recorded from conventional transthoracic parasternal long axis, two-, and four-chamber apical views. Two-dimensional echocardiographic images were obtained, and colour-coded Doppler tissue imaging was optimized to improve maximal colour codification of the left ventricular myocardium. Then, pulsed wave Doppler tissue imaging was performed in each left ventricular segment. The Doppler sample volume was placed equidistant between the endocardial and epicardial borders and pulsed wave Doppler tissue imaging spectral recordings were obtained. Three stable and well defined consecutive cardiac cycles were captured and recorded for analysis of left ventricular segmental relaxation and calculation of quantitative pulsed wave Doppler tissue imaging parameters. A microphone was set on the right second intercostal space to record the phonocardiogram simultaneously. The beginning of the second heart sound was registered as the reference of diastolic onset. Four pulsed wave Doppler tissue imaging diastolic parameters were obtained for each left ventricular wall segment: (1) regional early diastolic peak velocity (regional e wave); (2) regional late diastolic peak velocity (regional a wave); (3) regional e/a velocity ratio; and (4) the regional isovolumic relaxation time, defined as the time interval from the second heart sound on the phonocardiogram to the onset of each segmental pulsed wave Doppler tissue imaging e wave (Fig. 1).

Coronary angiography and the assessment of coronary involved segments

Selective coronary angiography was performed by the percutaneous femoral approach. Coronary arteriograms were obtained in at least two projections and recorded on 35 mm film at 12·5 frames per second. Coronary stenoses were measured by an on-line automatic edge detection system from the projection showing the most severe lumen obstruction (Phillips DCI). Coronary stenoses were considered significant when a reduction of $\geq 50\%$ in the vessel diameter was found. On the basis of angiographic distribution and location of the coronary artery stenosis, each left ventricular myocardial segment was classified either as normally perfused or ischaemic, if supplied by an involved coronary artery.

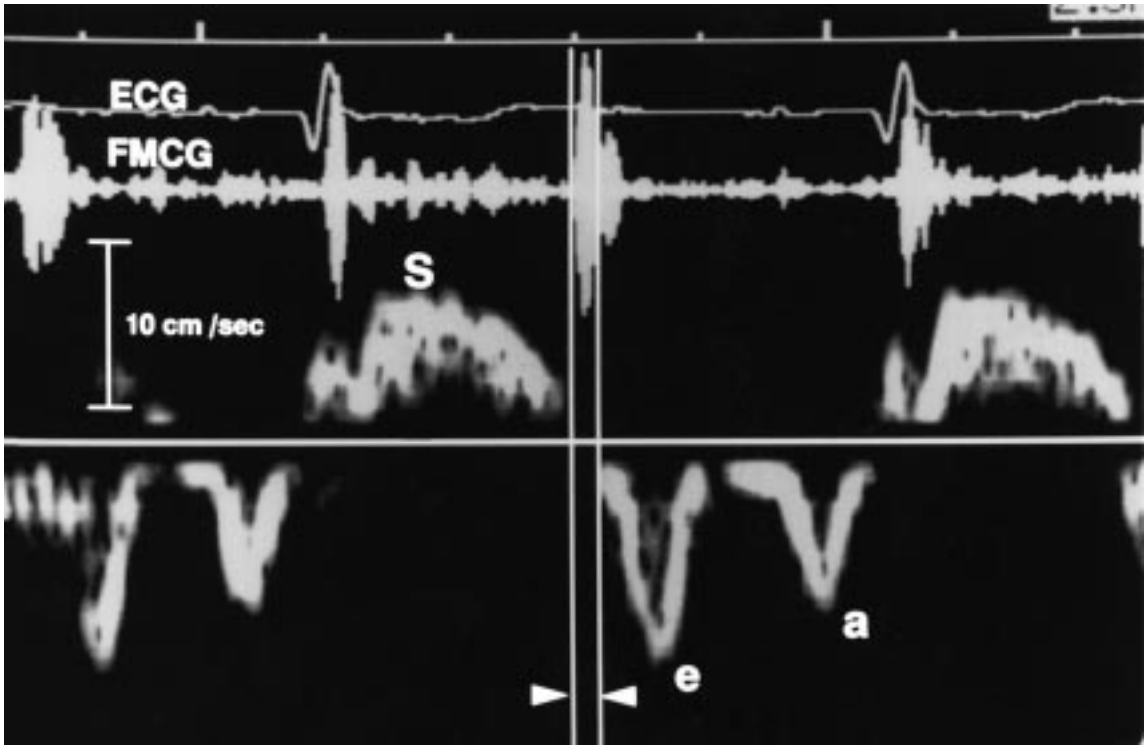

Figure 1 **Normal pulsed wave Doppler tissue imaging pattern. The sample volume is located in the left ventricular inferior wall. S=systolic wave; e=early diastolic velocity of relaxation; a=late diastolic velocity of relaxation. The local isovolumetric relaxation time was measured as the interval from the second heart sound to the onset of the early diastolic velocity of relaxation (arrows).**

Reproducibility of measurements

Five healthy subjects and five patients with coronary artery disease were selected to determine the reproducibility of the measurements of all pulsed wave Doppler tissue imaging parameters, the isovolumetric relaxation time, diastolic e and a wave velocities. Pulsed wave Doppler tissue imaging measurements were analysed by two independent observers (inter-observer variability) and by the same observer on two distinct occasions (intra-observer variability). Mean values ± SD of the difference in the measurement of the pulsed wave Doppler tissue imaging regional isovolumetric relaxation time were 6 ± 8 ms (inter-observer variability) and 4 ± 8 ms (intra-observer variability), for the pulsed wave Doppler tissue imaging regional diastolic e wave 0·6 ± 0·2 cm . s^{-1} (inter-observer variability) and 0·5 ± 0·3 cm . s^{-1} (intra-observer variability), for the pulsed wave Doppler tissue imaging regional diastolic a wave 0·4 ± 0·2 cm . s^{-1} (inter observer variability) and 0·3 ± 0·3 cm . s^{-1} (intra-observer variability).

Statistical analysis

Quantitative variables are expressed as mean values ± one standard deviation. Chi-square, non-paired t-tests and one-way ANOVA followed by Scheffé tests were used when appropriate. A P value <0·05 was considered significant to reject the null hypothesis. Optimal cut-off values of isovolumetric relaxation time, and the e/a ratio for discriminating normal from ischaemic left ventricular wall segments were obtained from ROC curves. The 95% confidence intervals of the best cut-off values were then computed.

Results

Pulsed wave Doppler tissue imaging 'in vitro' validation

The accuracy of measurements and results derived from the experimental protocol with the rotational sponge model described before showed that the real velocities (velocity interval from -10 cm . s^{-1} to 12 cm . s^{-1}) correlated well with the measurement determined by pulsed wave Doppler tissue imaging (velocity interval from $-9{\cdot}6$ cm . s^{-1} to 12 cm . s^{-1}) with a regression equation of $y=0{\cdot}96x+0{\cdot}007$; $r^2=0{\cdot}99$. These data showed that pulsed wave Doppler tissue imaging enables the correct analysis of left ventricular tissue wall motion velocities (Fig. 2).

Regional left ventricular myocardial relaxation in normal subjects

In normal subjects, adequate pulsed wave Doppler tissue imaging recordings were obtained in 467 of the 480 left

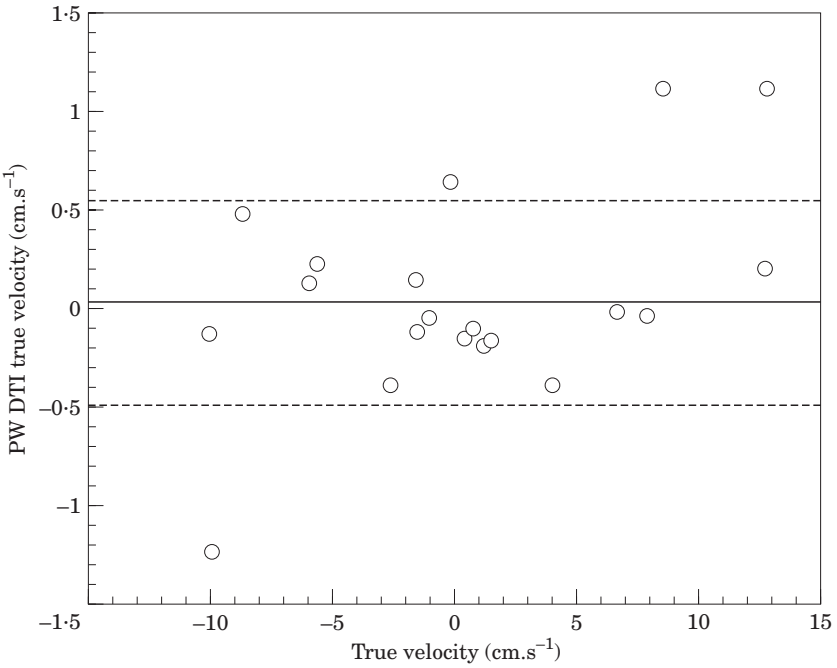

Figure 2 **Validation of measurements in the experimental study of the rotating sponge phantom. Bland-Altman plot, with true velocity in the horizontal axis and the difference between pulsed wave Doppler tissue imaging and true velocity in the vertical axis. Mean ± SD difference between methods expressed as thick and dotted lines.**

ventricular wall segments (97%). Mean values of regional left ventricular peak diastolic early (e wave) and late (a wave) pulsed wave Doppler tissue imaging velocities were $10{\cdot}3 \pm 2{\cdot}0$ cm . s^{-1} and $5{\cdot}8 \pm 1{\cdot}6$ cm . s^{-1}, respectively. The regional left ventricular e/a pulsed wave Doppler tissue imaging diastolic velocity ratio was $2{\cdot}1 \pm 0{\cdot}9$ and the mean isovolumetric relaxation time was 59 ± 22 ms (range: 0–110 ms). The regional e/a pulsed wave Doppler tissue imaging diastolic velocity ratio was >1 in 450 left ventricular segments (96%). Some differences were observed in some regional pulsed wave Doppler tissue imaging parameters of relaxation among different left ventricular myocardial wall segments. Significant differences were obtained for the mean values of the left ventricular myocardial diastolic pulsed wave Doppler tissue imaging e wave peak velocity in the comparison between the mid-interventricular septal segment and the basal and mid segments of the left ventricular lateral wall obtained from the apical four chamber view (Table 2). There were no significant differences in the mean values of the diastolic peak a wave, and the e/a velocity ratio among the remaining left ventricular myocardial wall segments.

Regional left ventricular myocardial relaxation in patients with ischemic heart disease

Regional parameters of left ventricular diastolic function were obtained adequately in 589 of 688 wall segments (86%). Mean values of regional parameters of diastolic function in these patients were: $7{\cdot}1 \pm 2{\cdot}91$ for the pulsed wave Doppler tissue imaging diastolic e wave peak velocity, $7{\cdot}1 \pm 2{\cdot}1$ for the diastolic pulsed wave Doppler tissue imaging a wave peak velocity, $1{\cdot}1 \pm 0{\cdot}5$ for the diastolic e/a diastolic velocity ratio and 89 ± 13 ms for the regional left ventricular myocardial isovolumetric relaxation time. According to angiographic classification, 368 of these segments were identified as located in the left ventricular ischaemic territory. In these patients, significant differences in regional parameters of left ventricular relaxation were observed between ischaemic and normally perfused myocardial wall segments. In ischaemic left ventricular segments, the pulsed wave Doppler tissue imaging diastolic e wave peak velocity and the pulsed wave Doppler tissue imaging e/a velocity ratio were smaller ($6{\cdot}4 \pm 2{\cdot}1$ cm . s^{-1} vs $8{\cdot}5 \pm 2{\cdot}8$ cm . s^{-1}; $P<0{\cdot}01$ and $0{\cdot}95 \pm 0{\cdot}3$ vs $1{\cdot}4 \pm 0{\cdot}6$; $P<0{\cdot}01$, respectively), while the regional pulsed wave Doppler tissue imaging isovolumetric relaxation time was prolonged (104 ± 37 ms vs 70 ± 30 ms; $P<0{\cdot}05$; Fig. 3). No differences were observed concerning the regional pulsed wave Doppler tissue imaging diastolic a wave peak velocity. A cut-off level of regional pulsed wave Doppler tissue imaging isovolumetric relaxation time longer than 85 ms (as determined by ROC analysis) disclosed a sensitivity of 69% and a specificity of 80% in identifying left ventricular ischaemic segments, while these values were 62% and 72% for a regional e/a velocity ratio<1. Normal left ventricular myocardial wall segments from patients with ischaemic heart disease

Table 2 Values of the regional diastolic parameters in healthy subjects

Ventricular segment	Regional isovolumic relaxation time, ms		e velocity cm . s^{-1}		a velocity cm . s^{-1}	e/a ratio	n
Basal septum	43·7 ± 12·6		12·6 ± 2·8		7·3 ± 1·7	1·8 ± 0·5	29
Mid septum	45·3 ± 16·9		11·6 ± 2·03		6·4 ± 1·8	1·9 ± 0·5	30
Apical septum	54·7 ± 24·6		8·3 ± 2·1		4·4 ± 1·7	1·9 ± 0·6	25
Basal anterior septum	76·3 ± 25·03	┐	8·5 ± 1·9		4·9 ± 1·1	1·6 ± 0·5	28
Mid anterior septum	69·4 ± 27·5	┤	7·8 ± 2·1	┐	5 ± 0·9	1·5 ± 0·4	28
Basal anterior	46·3 ± 17·4	┤	12·9 ± 2·5	┤	5·9 ± 1·8	2·4 ± 0·9	30
Mid anterior	49·6 ± 23·4	┤	11·6 ± 2·3	*	5·3 ± 1·6	2·3 ± 0·7	28
Apical anterior	60·8 ± 26·1	┤	9·3 ± 2·5	┤	4·8 ± 1·5	2 ± 0·6	27
Basal lateral	44·6 ± 17·9	*	16·1 ± 1·2	┘	7·8 ± 3·1	2·3 ± 0·8	25
Mid lateral	43·8 ± 20·3	┤	15·1 ± 3·2		6·6 ± 2·7	2·6 ± 1·1	29
Apical lateral	50 ± 25·5	┤	11·2 ± 3·1		5·5 ± 2	2·2 ± 1·1	28
Basal posterior	47·1 ± 17·8	┤	11·1 ± 3		5·8 ± 1·3	2·3 ± 1	30
Mid inferolateral	64·1 ± 25·6	┤	11·6 ± 2·3		5·3 ± 1·6	2 ± 0·6	30
Basal inferior	35·3 ± 14·9	┘	11·8 ± 1·8		5·3 ± 1·6	2·2 ± 1·1	28
Mid inferior	56·3 ± 20·6		12·1 ± 2·5		6·6 ± 1·3	2 ± 0·86	29
Apical inferior	59·7 ± 28·3		8·9 ± 1·8		5·1 ± 1·2	1·7 ± 0·5	28

The different values are reported as mean ± SD.
*Statistical significance of $P<0·01$ between segments.

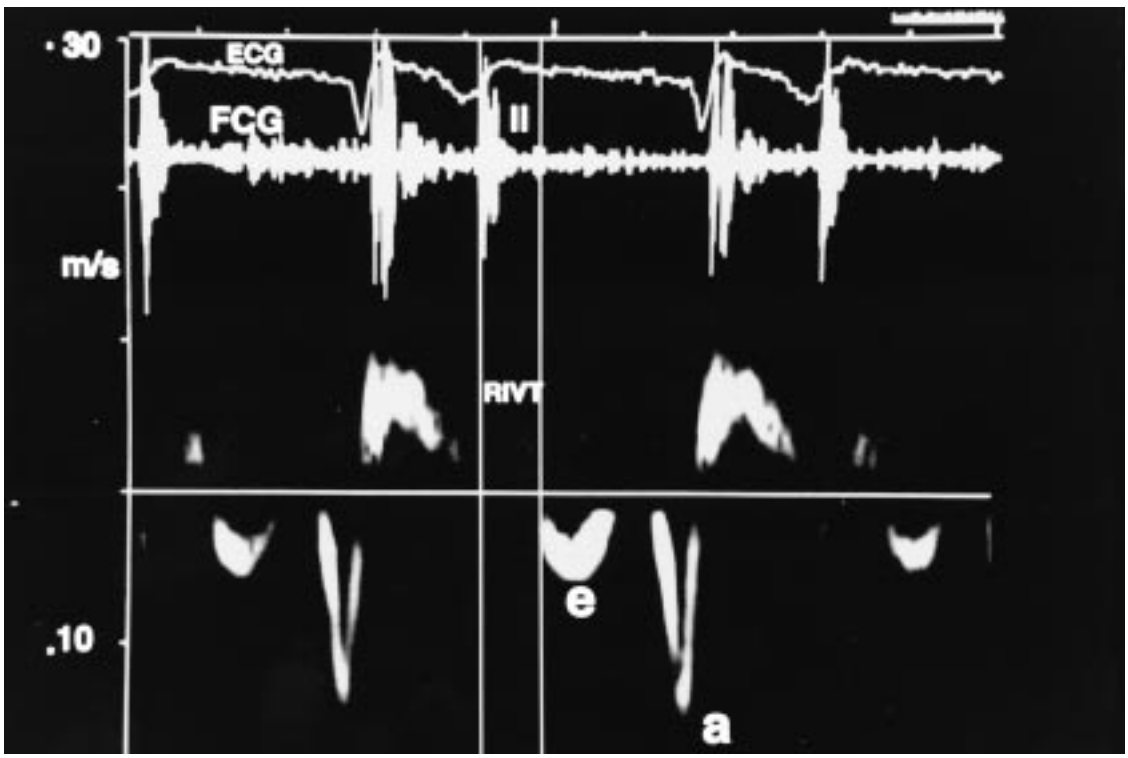

Figure 3 **Pulsed wave Doppler tissue imaging of the left ventricular inferior wall in a patient with abnormal regional diastolic function. The sample volume is located in the basal segment of the inferior wall. The pulsed wave Doppler tissue imaging e diastolic wave is decreased and there is an increase of the a wave; the local isovolumetric relaxation time is enlarged.**

showed similar values of pulsed wave Doppler tissue imaging isovolumetric relaxation time when compared with normal patients (P=ns).

Regional parameters of left ventricular diastolic function were associated with the presence of systolic wall motion abnormalities. A pulsed wave Doppler tissue imaging e/a diastolic velocity ratio<1 was found in four out of six akinetic left ventricular wall segments (67%), 48 of 66 hypokinetic left ventricular wall segments (73%) and 141 of 517 normokinetic left

ventricular wall segments (27%; $P<0{\cdot}001$). Similar differences were also observed in regional pulsed wave Doppler tissue imaging isovolumetric relaxation time ($P<0{\cdot}0001$ for the whole model ANOVA), with normally contracting left ventricular wall segments showing shorter intervals than hypokinetic (79 ± 14 ms vs 109 ± 24 ms respectively; $P<0{\cdot}0001$) and akinetic segments (104 ± 12 ms; $P<0{\cdot}0001$).

Relationship of regional and global left ventricular myocardial relaxation

The global E/A velocity ratio of the left ventricular filling pattern could be compared and was related to the regional pulsed wave Doppler tissue imaging e/a diastolic velocity ratio. Patients with an abnormal transmitral left ventricular inflow pattern (pulsed wave E/A<1) had more left ventricular segments with an abnormal left ventricular relaxation (pulsed wave Doppler tissue imaging e/a<1) than patients with a normal diastolic left ventricular inflow profile ($10{\cdot}3 \pm 3{\cdot}0$ vs $3{\cdot}7 \pm 2{\cdot}7$ abnormal (pulsed wave Doppler tissue imaging <1) left ventricular myocardial wall segments; $P<0{\cdot}001$.

In normal subjects, the regional pulsed wave Doppler tissue imaging isovolumetric relaxation time was shorter than the global isovolumetric relaxation time in 94% of the subjects. In patients with ischaemic heart disease, significant differences were observed among normal and coronary involved left ventricular myocardial wall segments: regional pulsed wave Doppler tissue imaging isovolumetric relaxation time was longer than global isovolumetric relaxation time in 54% of the ischaemic segments and only in 8% of those segments normally perfused ($P<0{\cdot}01$).

Discussion

The results of our present study demonstrate that regional myocardial relaxation of the left ventricle can be adequately studied by transthorathic echocardiography using the new pulsed wave Doppler tissue imaging technique. Differences in left ventricular myocardial relaxation are observed between normal and poorly perfused myocardial wall segments, a fact that seems to have an impact on the conventional parameters of the global left ventricular diastolic filling pattern.

Regional diastolic function analysis in normal subjects

With pulsed wave Doppler tissue imaging, regional left ventricular wall motion dynamics can be sequentially analysed throughout the cardiac cycle. This emerging non-invasive technique offers the possibility of describing the evaluating new regional myocardial parameters to provide a new assessment of the left ventricular relaxation pathophysiology, process and dynamics. The diastolic phase profile analysed using the pulsed wave Doppler tissue imaging system is complex (Fig. 1). An initial diastolic wave follows the T wave of the ECG and the isovolumetric relaxation time, corresponding to the rapid filling period of the left ventricular cavity, after mitral valve opening. This first dominant negative wave of left ventricular myocardial relaxation is simultaneous with the early wave (E wave) of the transmitral pulsed Doppler profile, and therefore we have designated it the regional diastolic e wave. Thereafter, an intermediate period without left ventricular myocardial wall motion can be observed corresponding to diastasis. No myocardial wall motion is registered during this period using pulsed wave Doppler tissue imaging. A second diastolic pulsed wave Doppler tissue imaging wave is obtained after the P wave of the ECG. This second diastolic wave is due to late myocardial wall relaxation which follows mechanical left atrial contraction. Left atrial contraction increases the pressure gradient between the left atria and the left ventricle, increasing the transmitral blood flow and forcing the myocardial wall to expand outwards during the late period of diastole. This late pulsed wave Doppler tissue imaging diastolic wave is coincident with the A wave of the transmitral pulsed Doppler inflow and therefore we have designated it the regional diastolic a wave.

In the left ventricular wall segments of normal subjects, no differences were found in respect of the mean values of pulsed wave Doppler tissue imaging diastolic peak regional velocities (regional pulsed wave Doppler tissue imaging e and a diastolic waves) or in the local isovolumetric relaxation time. These findings confirm that the normal left ventricle relaxes homogeneously. The regional isovolumetric relaxation time was larger than the global isovolumetric relaxation time in only 6% of the myocardial wall segments of healthy subjects. These data support the findings of Kondo *et al.*[10] using digital subtraction high frame rate echocardiography, who suggested that the diastolic motion of left ventricular myocardium started before global isovolumetric relaxation time was over. Other authors have found a heterogeneous regional relaxation pattern in the left ventricular myocardium in normal hearts[18]. The different techniques used to assess regional diastole, as well as the great number of factors which interact with left ventricular diastolic relaxation, may be responsible for these discrepancies.

An E/A diastolic ratio <1 measured by conventional transmitral pulsed wave Doppler interrogation is a well known parameter of abnormal left ventricular relaxation. The data of our present study suggests that a regional pulsed wave Doppler tissue imaging diastolic e/a ratio inversion may similarly reflect local diastolic impairment, since the mean values of the pulsed wave Doppler tissue imaging e/a diastolic velocity ratio were >1 in almost all 16 left ventricular myocardial wall segments of a normal population.

Regional diastolic function analysis in ischaemic heart disease

Myocardial diastolic function is impaired early in patients with ischaemic heart disease and a delay in the regional left ventricular myocardium outward wall motion is frequently observed during ischaemia[6–8,19]. Although there are numerous imaging techniques which allow these changes to be evaluated, their methods are technically complex or require invasive interventions[2,5]. The ischaemic impairment of regional isovolumetric relaxation time, representative of ventricular incoordination, was initially demonstrated by digital processing of M-mode echocardiograms and of left ventriculography[9]. Recently, high frame rate echocardiography has been used for non-invasive assessment of regional ventricular diastolic function[10]. A delay in the initial left ventricular outward motion was observed in patients with significant coronary artery disease, beyond the isovolumetric relaxation time in coronary involved segments. However, this method was not free of technical limitations, such as temporal resolution, noisy images, the necessity of a reference system to minimize the effect of the left ventricular myocardium translation, and the difficulty of detecting changes in endocardial location when the absolute movement is small[10,20–23]. In the present study, regional isovolumetric relaxation time, as assessed by pulsed wave Doppler tissue imaging, was also prolonged in poorly perfused segments, frequently over the global isovolumetric relaxation time. These findings indicate that diastolic outward wall motion may start after mitral valve opening in ischaemic left ventricular wall segments.

A reduced regional pulsed wave Doppler tissue imaging peak early diastolic velocity was also observed in ischaemic wall segments and is in accordance with previous findings using magnetic resonance imaging[24]. The observation of an inverted e/a diastolic ratio in ischaemic left ventricular wall segments corroborates previous experimental studies performed in our laboratory[25,26]. In an animal model of induced ischaemia, we observed decreased peak early diastolic velocity of the myocardial wall motion measured with pulsed wave Doppler tissue imaging. Pulsed wave Doppler tissue imaging peak late diastolic velocity increased simultaneously and therefore an inverted e/a ratio was present. All values returned to baselines after the occluded coronary artery was opened and blood flow and myocardial perfusion restored.

Early diastolic relaxation is known to be an active phenomenon which takes place at a higher energetic expenditure than passive late diastolic motion. This may constitute the physiological basis underlying our findings of a low e-wave velocity and an inverse e/a ratio as the most sensitive signs of hypoperfusion. Of these two indices, the e/a ratio offers the advantage of being expressed in an adimensional relationship to myocardial velocities and therefore is not influenced by the Doppler limitation of angle-dependence.

The presence of abnormal diastolic relaxation in ischaemic left ventricular wall segments is a complex phenomenon which depends on a variety of factors. Coronary flow, loading conditions and metabolic disorders such as intracellular phosphate depletion, myofilament disruption and action potential disturbances all modify diastole[31–34]. Moreover, diastolic relaxation is more sensitive to ischaemia than systolic contraction, and may motivate subtle relaxation abnormalities without systolic impairment. On this basis, ischaemia may be detected at rest, without the need of stress interventions[27–30].

Relationship of global and regional Doppler diastolic function

The number of segments with an abnormal pulsed wave Doppler tissue imaging regional e/a diastolic ratio was higher in ischaemic patients with an impaired transmitral Doppler E/A ratio. This finding suggests a direct correlation between conventional Doppler echocardiographic diastolic indices and integrated segmental wall motion diastolic abnormalities. It may be hypothesized that the magnitude and extension of regional diastolic impairment modulates the global left ventricular diastolic function, at the initial stages of ischaemic heart disease. A similar interaction between regional and global left ventricular myocardial systolic performance is well known[35].

Study limitations

The present study suggests that pulsed wave Doppler tissue imaging is a useful method to evaluate regional diastolic function, which may allow us to detect ischaemic myocardial wall segments. However, this technique has several technical limitations. First, due to the angle-dependence of all Doppler-based methods, accurate determination of myocardial velocities needs an adequate alignment between the ultrasound beam and the main vector direction of the left ventricular segmental wall motion. Myocardial wall motion is complex and does not take place in a single direction. Systolic and diastolic excursions of the left ventricular myocardium follow both the left ventricular longitudinal and transverse axes, as well as the rotation and displacement of the whole heart. We have found that the best recordings were obtained mainly in apical views, in which we obtained the smallest angle of incidence between the Doppler beam and the longitudinal left ventricular wall motion. Further studies to investigate the several components of segmental myocardial dynamics using various transthorathic views are warranted. We believe the potential bias in recording maximal velocities of diastolic excursions was solved by using the regional e/a diastolic ratio and the regional isovolumetric relaxation time rather than absolute pulsed wave Doppler tissue imaging peak e or a diastolic wave velocities.

A delayed diastolic relaxation of the left ventricle is not a specific signal of myocardial ischaemia and may be due to other pathological conditions often associated with myocardial ischaemia, such as old age, ventricular hypertrophy, heart failure, fibrosis, loading conditions, intraventricular conduction disturbances and others. The effect of all these factors on the diastolic properties and parameters of the left ventricle measured by pulsed wave Doppler tissue imaging may further reduce the specificity of this technique to detect ischaemic myocardial wall segments and limit its clinical usefulness.

The classification of left ventricular myocardial wall segments in ischaemic and normal hearts based on coronary angiography is also limited. On the one hand, the correlation between the distribution of the coronary arterial anatomy and the echocardiographic myocardial wall segment location is not completely accurate. On the other hand, the presence of angiographic and anatomical coronary arterial stenosis is not necessarily associated with the presence of left ventricular myocardial ischaemia in the wall segments supplied by such an artery. Radionuclide methods would be more accurate than coronary angiography in defining ischaemic left ventricular myocardial segments and the accuracy of pulsed wave Doppler tissue imaging may be different when compared with this perfusion technique.

The pulsed wave Doppler tissue imaging examination was performed with the patient at rest. Whether the combination of this technique with stress interventions improves diagnostic accuracy remains also to be determined. As with any echocardiographic technique, a low quality echo image limits the generalized use of the pulsed wave Doppler tissue imaging technique to screen ischaemic left ventricular segments in patients with coronary artery disease.

Conclusions and clinical implications

Doppler tissue imaging is a new echocardiographic technique that can be used to examine the regional diastolic motion of the left ventricular myocardial wall and may allow the detection of ischaemic segments by the presence of abnormal relaxation. This method, as opposed to others evaluating diastolic function, is technically simple and may be easily performed in daily clinical practice. Pulsed wave Doppler tissue imaging allows a detailed analysis of regional left ventricular diastolic dynamics such as the assessment of regional isovolumetric relaxation time and early and late diastolic velocities.

Pulsed wave Doppler tissue imaging could be clinically useful as a non-invasive test to detect ischaemic myocardial left ventricular segments and to estimate the severity of coronary disease in patients with proven or suspected ischaemic heart disease. In our study, a prolonged isovolumetric relaxation time and an inverted E/A diastolic velocity ratio measured by pulsed wave Doppler tissue imaging showed a 69% sensitivity and a 80% specificity to detect involved segments, values lower than those expected for stress echocardiography. Further studies using modifications of this technique (different views, pharmacological or stress interventions, etc.) are therefore warranted.

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