European Heart Journal (1997) **18**, 330–339

Non-invasive assessment of cardiac physiology by tissue Doppler echocardiography

A comparison with invasive haemodynamics

J. Zamorano*, D. R. Wallbridge, J. Ge, J. Drozd, J. Nesser and R. Erbel

*University Clinic, Essen, Germany; *University Clinic, Madrid, Spain*

Background Tissue Doppler echocardiography reveals characteristic patterns of myocardial velocities within systole and diastole which are not well understood.

Aim The purpose of this study was to determine the relationship of myocardial velocity patterns, as assessed by tissue Doppler echocardiography, to the contraction and relaxation phases of the cardiac cycle, as determined during cardiac catheterization.

Methods Recordings of left ventricular/aortic and left ventricular/pulmonary wedge pressures were obtained simultaneously with apical tissue Doppler echocardiographic images of the left ventricle. A total of 210 cardiac cycles from 22 patients (mean age 58 years, 18 male) undergoing cardiac catheterization were analysed. The time intervals of the different phases of the cardiac cycle were measured from the pressure tracings. These time intervals were correlated to the interfaces of colour myocardial velocity patterns obtained by M-mode tissue Doppler echocardiography.

Results There was a good correlation between the time intervals assessed haemodynamically and those based on the different velocity interfaces obtained with M-mode tissue Doppler echocardiography. Comparable time intervals (from the R wave) obtained by pressure recordings and tissue Doppler echocardiography were, respectively: isovolumic contraction (70 ± 14 vs 67 ± 9 ms, $r=0.79$); rapid ejection (206 ± 54 vs 202 ± 49 ms; $r=0.95$); late ejection (357 ± 36 vs 346 ± 42 ms, $r=0.93$); isovolumic relaxation (405 ± 43 vs 409 ± 56 ms; $r=0.95$); rapid filling (514 ± 67 vs 523 ± 64 ms, $r=0.91$); diastasis (697 ± 153 vs 709 ± 146 ms, $r=0.98$); atrial contraction (890 ± 128 vs 899 ± 132 ms, $r=0.96$).

Conclusion Tissue Doppler echocardiography has the potential to accurately measure the different phases of the cardiac cycle which until now could only be determined invasively. It may provide a sensitive method for the assessment of changes in both cardiac contraction and relaxation in different clinical settings.
(Eur Heart J 1997; 18: 330–339)

Key Words: Tissue Doppler, cardiac physiology.

Introduction

Knowledge about cardiac contraction and relaxation is mainly based on haemodynamic studies[1]. Diastole starts with closure of the aortic valve and ends with closure of the mitral valve, and is classically divided into four phases (isovolumic relaxation, rapid filling, diastasis, and atrial contraction). Systole commences with closure of the mitral valve and is divided into three phases (isovolumic contraction, rapid ejection, and slow ejection). Assessment of physiological phases of the cardiac cycle may be a better way to evaluate clinical disorders than global measurements of left ventricular function. For example, it is known that changes in rapid ventricular filling may be an early marker of cardiac dysfunction in hypertension and acute coronary syndromes, even in the absence of changes in systolic function[2,3].

In contrast to detailed haemodynamic studies, precise Doppler echocardiographic assessment of the cardiac cycle has not been available to date [4–6]. Spirito *et al.* found considerable day to day variability in Doppler indexes of diastolic function[7]. The isovolumic contraction time can be determined from the beginning of QRS to the rise in aortic pressure, as shown on

Revision submitted 26 February 1996, and accepted 28 March 1996.

Dr Zamorano was supported by a grant from Fondo De Investigaciones Sanitarias (FIS). Dr Wallbridge was supported by a British Heart Foundation International Research Fellowship.

Correspondence: Jose Zamorano, MD, Hospital Clinico, Servicio Cardiologia, Plaza Cristo Rey, 28040 Madrid, Spain.

0195-668X/97/020330+10 $18.00/0

electrocardiographic and pressure tracings. Using Doppler derived systolic time intervals, this is defined as the pre-ejection period: the interval between the beginning of ventricular depolarization and ventricular ejection[8]. With this technique, left ventricular ejection is taken to be from when the aortic pressure starts to rise to the anacrotic notch[9].

Diastolic time intervals have been analysed by M-mode echocardiography. In combination with Doppler echocardiography, isovolumic relaxation is measured as the time from when the aortic valve closes to when the mitral valve opens[10,11]. Differentiation of rapid, slow and atrial filling phases of diastole were first attempted using digitized M-mode recordings[12]. More recently, the combination of 2-D echocardiography and acoustic quantification for automatic border detection has facilitated analysis of systole and diastole, but assessment of the different phases has not been attempted[13].

Tissue Doppler echocardiography is a new non-invasive method capable of quantifying the velocity of tissue motion and preliminary reports have suggested its usefulness in different clinical settings[14–18]. However, although constant (in all cardiac segments) and characteristic patterns of tissue velocities within systole and diastole have been reported, there is still no clear understanding of them[14]. We hypothesize that the individual phases of the cardiac cycle are reflected in changes in wall motion, which could be determined by tissue Doppler echocardiography measurements of tissue velocity. Thus, the purpose of this study was to determine whether changes in tissue velocity, as detected by tissue Doppler echocardiography, are related to the different phases of the cardiac cycle.

Methods

Subjects

The study group comprised 22 consecutive patients undergoing diagnostic cardiac catheterization. The mean age was 58 ± 9 years and 18 patients were male. Informed consent was obtained from all patients before cardiac catheterization and tissue Doppler echocardiography was performed. Patients with prior myocardial infarction were excluded.

Cardiac catheterization

Cardiac catheterization was performed with either a Siemens (Erlangen, Germany) Coroskop U or a Siemens BICOR system. Each patient was fitted with an 8F arterial and venous femoral sheath. A fluid-filled double-lumen pig-tail catheter (Cordis, U.S.A.) was used to obtain simultaneous recordings of left ventricular and aortic pressures. In patients without valvular heart disease and normal pulmonary arterial pressure, an indirect measure of left atrial pressure was obtained by pulmonary wedge pressure recordings from a Swan–Ganz catheter. In patients with valvular heart disease, left atrial pressure was registered directly after transeptal puncture using the Brockenbrough technique[19]. To assess the different physiological phases during systole and diastole, simultaneous pressures from the left ventricle/aorta and left ventricle/left atrium were recorded at a paper speed 100 mm . s^{-1}. To correct the time delay of pulmonary wedge pressure, the wedge tracing was realigned, so that the V wave peak was bisected by the downstroke of left ventricular pressure[20,21]. Pressure recordings were always obtained before coronary and ventricular angiography. Tissue Doppler echocardiographics were obtained during the pressure recordings at cardiac catheterization.

Tissue Doppler echocardiography

Tissue Doppler echocardiography enables tissue velocities to be measured (according to the pulsed Doppler principle) and identifies the direction of tissue motion. Tissue velocity toward the transducer is colour coded red and away from the transducer blue, with yellow–red and white–blue, respectively, being used to display higher velocities (Fig. 1). Although the aim of this study was to compare the time intervals obtained by colour tissue Doppler echocardiography M-mode with the different phases of the cardiac cycle, the myocardial velocities of the different phases were also measured by tissue Doppler echocardiography. Using a computer system they were measured off-line from the colour tissue Doppler echocardiography M-mode recordings. Calibration was achieved using the colour scale of the M-mode tracings.

Tissue Doppler echocardiography studies were performed with Powervision equipment (Toshiba, Nasu, Japan) incorporating both 2·5 and 3·75 MHz transducers and facilities for pulsed, continuous, colour and tissue Doppler. Recordings of tissue Doppler echocardiographic images, two pressure channels, an ECG, and a phonocardiogram were made simultaneously. During the tissue Doppler echocardiography studies, appropriate gain settings and filters were used to maintain optimal colouring of the myocardium. The Doppler velocity range (0–14 cm . s^{-1}) was adjusted to encompass all myocardial colour velocities, and because the shades are dependent on the set up of the tissue Doppler echocardiographic velocity, we always used the lower velocity range that encompasses all myocardial velocities (so all the colour interfaces can be seen). Pulsed repetition frequency was 3–6 KHz and the frame rate could reach 103 s^{-1}. The echocardiographic studies were stored on S-VHS videotape to enable frame-by-frame analysis. All studies were subsequently reviewed independently by two cardiologists experienced in tissue Doppler echocardiographic imaging. In the case of discrepancies, a consensus decision was achieved by joint review of the videotape.

Analysis of the data

Haemodynamic data

The end of the different phases of the cardiac cycle used were as previously defined: (a) the point at which aortic

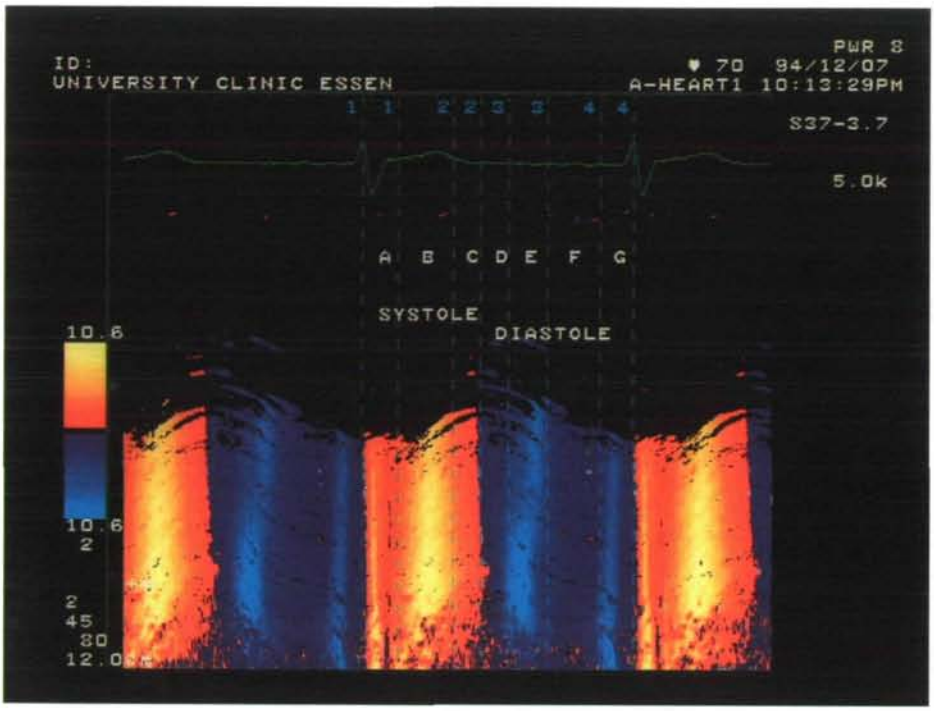

Figure 1

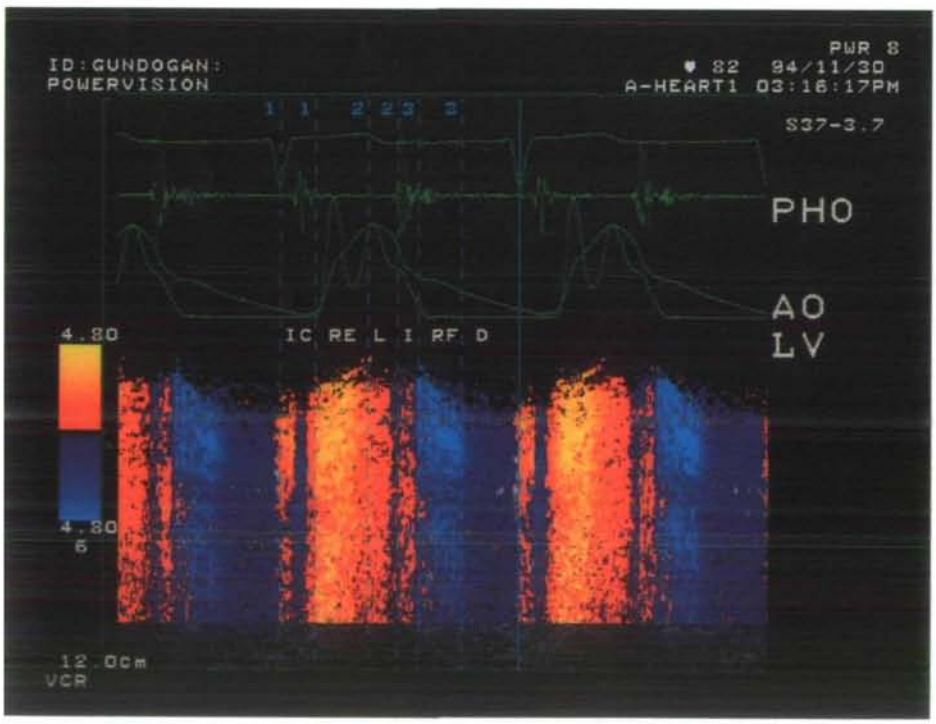

Figure 2

and left ventricular pressure becomes equal (aortic valve opening; isovolumic contraction); (b) peak left ventricular pressure (rapid ejection); (c) the anacrotic notch (aortic valve closure; reduced ejection); (d) the point at which left atrial and left ventricular pressures become equal (mitral valve opening; isovolumic relaxation) (e) the point when the left ventricular filling rate plateaus and equilibrates its pressure to that of the left atrium (rapid filling); (f) the peak of the P wave on the ECG (diastasis); (g) the peak of the following R wave (atrial contraction).

Tissue Doppler echocardiography data

Conventional echocardiographic studies were performed according to the recommendations of the American Society of Echocardiography[22]. In all patients, the colour M-mode of the mid-septum (2 cm above the aortic valve) was obtained from the parasternal and apical five-chamber view. The time intervals of the different colour interfaces were measured and compared from both views. Due to the patient's position in the catheterization laboratory, simultaneous tissue Doppler echocardiographic recordings obtained from the apical view were compared with haemodynamic recordings. The method used for analysing tissue Doppler echocardiographic images is shown in Fig. 1. Using the ECG as a reference, several distinct colour phases of the M-mode tissue Doppler echocardiographic image were detected. Systole is represented by a red band and diastole by a blue one. Higher velocities within systole are represented as yellow–red and white–blue (Fig. 1). Time intervals were measured according to the different colour interfaces in the colour tissue Doppler echocardiographic M-mode. The end of the different phases of the cardiac cycle were defined by the following colour interfaces: (a) the start of the yellow–red band (isovolumic contraction phase); (b) the end of the yellow–red band (rapid ejection phase); (c) the end of the red band (late ejection phase); (d) the start of the white–blue band (isovolumic relaxation phase); (e) the end of the white–blue band (rapid filling phase); (f) the end of the dark blue band and the start of the second white–blue band (diastasis); (g) the start of the red band (atrial contraction).

To assess the potential of M-mode tissue Doppler echocardiography to identify the different phases of the cardiac cycle, these time intervals were compared to those obtained by invasive haemodynamics (measured from the pressure tracings) in the same cardiac cycles. Measurements obtained by both techniques (tissue Doppler echocardiography and pressure tracings) were performed by two different blinded observers.

Statistical analysis

All the data were analysed by the Excel 5·0 program (Microsoft, U.S.A.). Results of measurements of time intervals (ms) and wall velocities ($cm \cdot s^{-1}$) are expressed as mean ± standard deviation. Haemodynamic determinations of left ventricular, left atrial and aortic pressures are expressed in mmHg. Time intervals obtained by invasive haemodynamic and tissue Doppler echocardiographic techniques were compared using the Student t-test. A probability value less than 0·05 was considered statistically significant. In order to determine if there was a linear correlation between the measurements performed by both techniques, the correlation coefficients (r) were calculated. The agreement between tissue Doppler echocardiography and invasive haemodynamics in assessing the different phases of the cardiac cycle is represented by the Bland and Altman plot[23].

To assess inter-observer variability of time intervals between the different phases of the cardiac cycle, all the studies were examined by a second observer who was unaware of previous measurements. To determine intra-observer variability a random subset of 30 cardiac cycles were later reviewed by the first observer. Variability was determined as the difference between measurements divided by the mean value of the two observations and expressed as percent.

Results

Patient profile

A total of 210 cardiac cycles from 22 patients were analysed (19 patients with suspected coronary artery disease). In 12 patients the indication for cardiac catheterization was stable angina with a positive exercise stress test and in eight patients unstable angina. However, during the tissue Doppler echocardiography studies none of them had angina and were stable for at

Figure 1 **M-mode tissue Doppler echocardiographic pattern obtained from the septum in the apical view. Systole is represented by a red band and diastole by a blue one. Systole starts with a phase of low velocity coloured in red (A), followed by a phase of higher velocity (yellow–red); B) and ends with another slow velocity phase (C). Diastole showed two phases of low velocity coloured blue (D and F) that separated two high velocities phases coloured white–blue (E and G).**

Figure 2 **Simultaneous recordings of tissue Doppler echocardiographic images of the septum, left ventricular and aortic pressure. Following the opening of the aortic valve, the upstroke of the aortic volume (rapid ejection) is marked by a transition of high velocity (yellow–red). This phase is followed by a lower velocity period (red) that corresponds to the late ejection phase after the peak of the aortic pressure. Ao=aortic pressure; D=diastasis; I=isovolumic relaxation; IC=isovolumic contraction; L=late ejection; LV=left ventricular pressure; Pho=phonocardiogram; RE=rapid ejection; RF=rapid filling.**

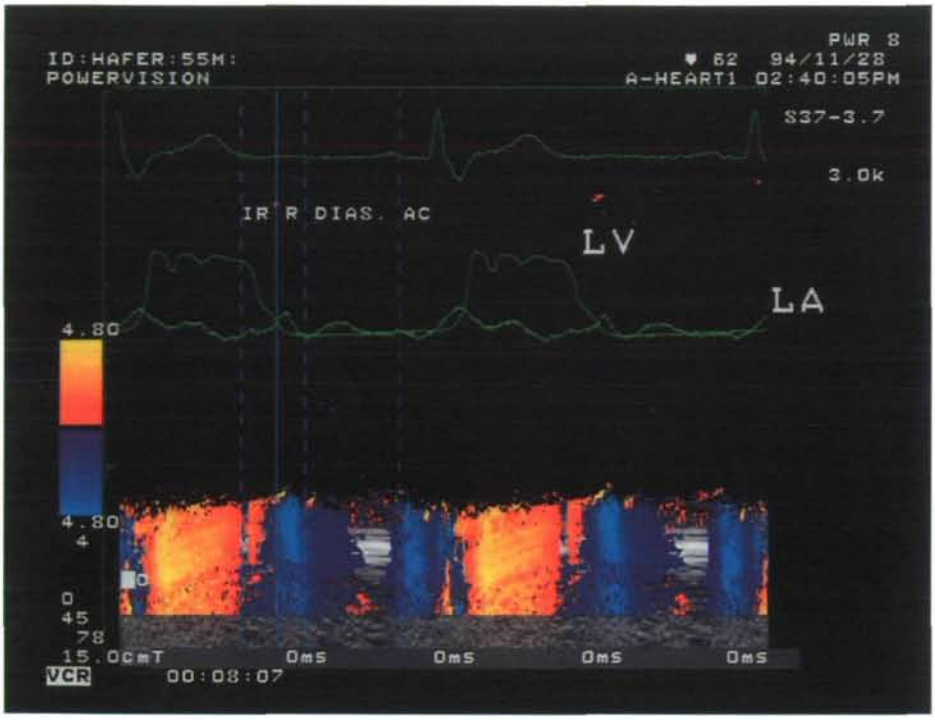

Figure 3

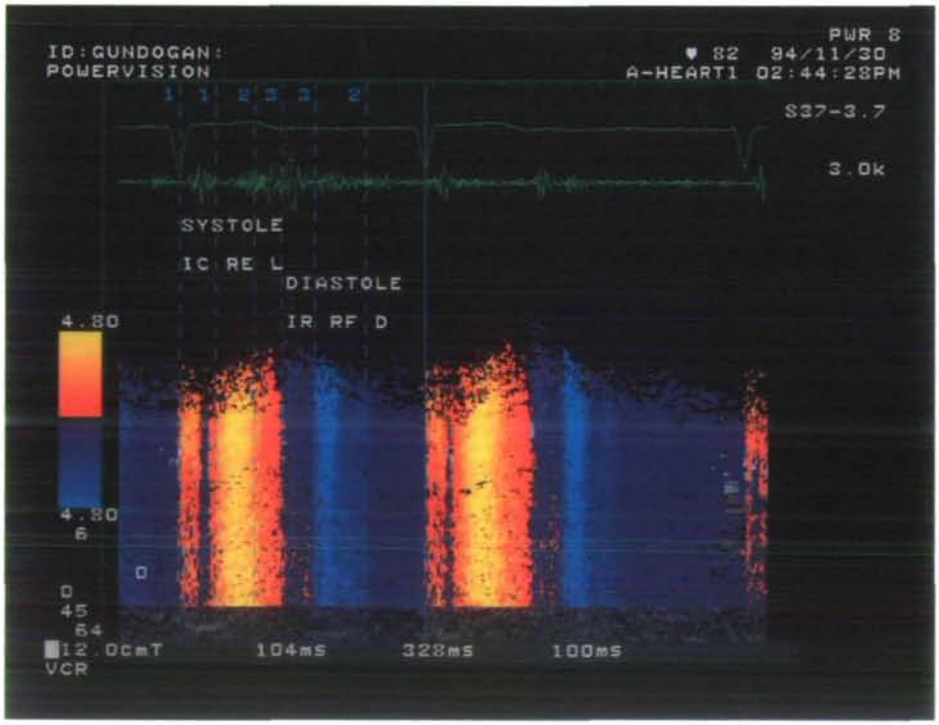

Figure 5

Table 1 Comparison of the different time intervals (ms) obtained by invasive haemodynamics and mid-septum tissue Doppler echocardiographic images for the different phases of the cardiac cycle

Cardiac phase	Haemodynamic		Tissue Doppler echocardiography		r
	TI	range	TI	range	
Isovolumic contraction	70 ± 17	40–95	67 ± 9	45–89	0·79
Rapid ejection	136 ± 34	100–150	127 ± 22	112–151	0·95
Late ejection	151 ± 37	132–182	140 ± 32	120–165	0·93
Isovolumic relaxation	60 ± 18	45–88	65 ± 16	43–80	0·95
Rapid filling	109 ± 27	91–146	123 ± 44	105–161	0·91
Diastasis	183 ± 35	156–209	197 ± 31	160–235	0·98
Atrial contraction	189 ± 22	177–262	179 ± 23	155–202	0·96

Differences were not significant.
TI=time interval; r=correlation coefficient.

least 48 h prior to the examination. Sixteen of these 19 patients had significant coronary stenosis (>70%) in at least one major coronary artery. However, none of them showed a lesion in the proximal left anterior descending artery (before the first septal branch). Two patients had mitral stenosis. None of the patients had had a prior myocardial infarction. Seven patients (30%) were in New York Heart Association functional class I; 11 (50%) in class II, and four (20%) in class III. During the examination 19 patients (85%) were in sinus rhythm and three (15%) in atrial fibrillation.

Haemodynamic assessment of the cardiac cycle

The mean intervals (ms) in the different phases of the cardiac cycle, as determined according to haemodynamic parameters (measured from the pressure tracings), are shown and compared to those obtained with tissue Doppler echocardiography in Table 1.

Assessment of the cardiac cycle by tissue Doppler echocardiography

In all our patients, a cyclic and constant pattern of tissue velocities in all cardiac segments was seen. This pattern consists of two negative (away from the transducer) velocity peaks during diastole and one positive (toward the transducer) during systole. Between these peaks, areas of lower velocity rate were also seen (Fig. 1). In M-mode tissue Doppler echocardiographic recordings, systole started with a phase of low velocity (mean $1{\cdot}4 \pm 0{\cdot}67$ cm . s^{-1}); followed by a phase of high velocity (mean $4{\cdot}9 \pm 0{\cdot}63$ cm . s^{-1}); and ended with another slow velocity phase (mean $1{\cdot}7 \pm 0{\cdot}29$ cm . s^{-1}) (Table 1). Analysis of diastole showed two phases of low velocity (mean $1{\cdot}3 \pm 0{\cdot}44$ and $1{\cdot}1 \pm 0{\cdot}62$ cm . s^{-1}, respectively) separating two high velocity phases (mean $4{\cdot}3 \pm 0{\cdot}88$ and $4{\cdot}4 \pm 0{\cdot}69$ cm . s^{-1}, respectively). Although myocardial velocity was not the same in different cardiac segments, the time intervals of the different colour interfaces were the same, regardless of the segment analysed. The mean intervals (ms) in these phases are shown in Table 1. The wide scatter of values pertaining to diastasis and atrial contraction relates to the inclusion of a wide range of RR intervals (range of heart rate 48–123).

Haemodynamic vs tissue Doppler echocardiography data

The temporal relationship of invasive haemodynamics and the interfaces in the colour myocardial velocity pattern obtained by M-mode tissue Doppler echocardiography is more easily appreciated when the pressure

Figure 3 **Simultaneous recording of tissue Doppler echocardiographic images of the septum, left ventricular and left atrial pressure. Rapid filling commences when left atrial pressure exceeds left ventricular pressure, and this corresponds to a transition to high myocardial velocities (white–blue). As left atrial and left ventricular pressure equalize, diastasis commences, and myocardial velocities become dark blue. Atrial contraction following the P wave, is shown in tissue Doppler echocardiographic M-mode by an increase in myocardial velocities (white–blue). AC=atrial contraction; Diast=Diastasis; IR=isovolumic relaxation; LA=left atrial pressure; LV=left ventricular pressure; R=rapid filling.**

Figure 5 **M-mode tissue Doppler echocardiographic image of the septum (apical view) in a patient in atrial fibrillation. There is a loss of the last high velocity phase, consistent with the absence of atrial contraction. Comparing the two cycles showed in the figure, major differences are only seen in the second diastolic low velocity phase that corresponds to diastasis. D=diastasis; IC=isovolumic contraction; IR=isovolumic relaxation; L=late ejection; RE=rapid ejection; RF=rapid filling.**

tracings are simultaneously displayed on the Powervision equipment. In Fig. 2, aortic and left ventricular pressures demonstrate the timing of systolic events. The upstroke of the aortic pressure tracing, corresponding to the start of rapid ejection, is marked by a transition to high myocardial velocity (yellow–red). The lower myocardial velocities (red) of late ejection follow the peak of the aortic pressure. Systole ends with the start of the second phonocardiographic heart sound, and the myocardial colour velocity pattern is marked by the end of the red band (Fig. 2). In Fig. 3, left ventricular and left atrial pressure tracings are recorded to demonstrate the timing of diastolic events. Rapid filling commences when left atrial pressure exceeds left ventricular pressure, and this corresponds to a transition to high myocardial velocities (white–blue). As left atrial and left ventricular pressure equalize, filling is reduced, diastasis commences, and myocardial velocities become dark blue. Atrial contraction following the P wave further augments ventricular filling, and myocardial velocities again increase (white–blue).

There was good correlation between the time intervals of the different phases of systole assessed by heart catheterization and M-mode tissue Doppler echocardiography (isovolumic contraction, r=0·79; rapid ejection, r=0·95; late ejection, r=0·93) (Table 1). Similarly, a good correlation was found between both techniques when diastolic intervals were analysed (isovolumic relaxation, r=0·95; rapid filling, r=0·91; diastasis, r=0·98; atrial contraction, r=0·96) (Table 1). The level of agreement between both techniques is displayed in Fig. 4.

Atrial fibrillation

Twenty-four beats were analysed from the three patients in atrial fibrillation. The colour velocity pattern in patients with atrial fibrillation was characterized by loss of the last high velocity phase, consistent with the absence of atrial contraction (Fig. 5). Despite extreme variation in RR intervals in these patients, systolic and early diastolic time intervals did not change significantly (Table 2). Major differences from one cardiac cycle to the next were only seen for diastasis (Fig. 5). Both these observations, which are consistent with known physiology, highlight the reliability of tissue Doppler echocardiography as a non-invasive technique for assessing cardiac physiology.

Reproducibility

Correlation between observers and variability in measurements in the different phases of the cardiac cycle assessed non-invasively (tissue Doppler echocardiography) were, respectively: isovolumic contraction (r=0·91; 4%); rapid ejection (r=0·85; 5%); late ejection (r=0·92; 5%); isovolumic relaxation (r=0·92; 6%); rapid filling (r=0·88; 7%); diastasis (r=0·90; 5%); atrial contraction (r=0·94; 10%). Correlation between observers and variability in measurements in the different phases of the cardiac cycle assessed by invasive haemodynamics (pressure tracings) were, respectively: isovolumic contraction (r=0·93; 6%); rapid ejection (r=0·91; 4%); late ejection (r=0·94; 7%); isovolumic relaxation (r=0·89; 6%); rapid filling (r=0·90; 7%); diastasis (r=0·91; 6%); atrial contraction (r=0·92; 8%).

The correlation and intra-observer variability for the non-invasive (tissue Doppler echocardiography) assessment of the different phases of the cardiac cycle were, respectively: isovolumic contraction (r=0·88; 4%); rapid ejection (r=0·92; 3%); late ejection (r=0·93; 5%); isovolumic relaxation (r=0·92; 7%); rapid filling (r=0·91; 4%); diastasis (r=0·90; 5%); atrial contraction (r=0·94; 5%).

Discussion

Our study demonstrates for the first time that tissue Doppler echocardiography accurately determines different cardiac phases recorded by M-mode. The duration of isovolumic contraction, ejection, isovolumic relaxation and diastolic phases could be assessed and the velocities within these phases measured. The tissue Doppler echocardiographic recordings obtained during atrial fibrillation demonstrate the accuracy of the technique on a beat-to-beat basis.

It is known that the different phases of the cardiac cycle may be influenced by common clinical disorders and therapeutic interventions, and intervals derived from echocardiographic measurements have been shown to be sensitive in detecting changes in myocardial function[24–26]. Although conventional assessment of cardiac physiology by haemodynamic measurements is accurate, it has limited application due to its invasive nature and unsuitability for serial evaluation. The potential use of M-mode tissue Doppler echocardiography to accurately assess in one scan plane the different phases of the cardiac cycle may open new methodological fields for physiology, clinical pharmacology and clinical research.

Limitations of conventional echocardiography

Current echocardiographic techniques assess global systolic and diastolic function, but are unable to distinguish, in one single scan, the individual phases of the cardiac cycle[27,29]. Moreover, regional myocardial abnormalities in these phases cannot be identified.

Systolic time intervals have been used for 50 years and are very reliable in determining the pre-ejection period, left ventricular ejection time, and mechanical systole (QS2)[29]. QS2 in particular has been shown to be a sensitive marker of changes in cardiac

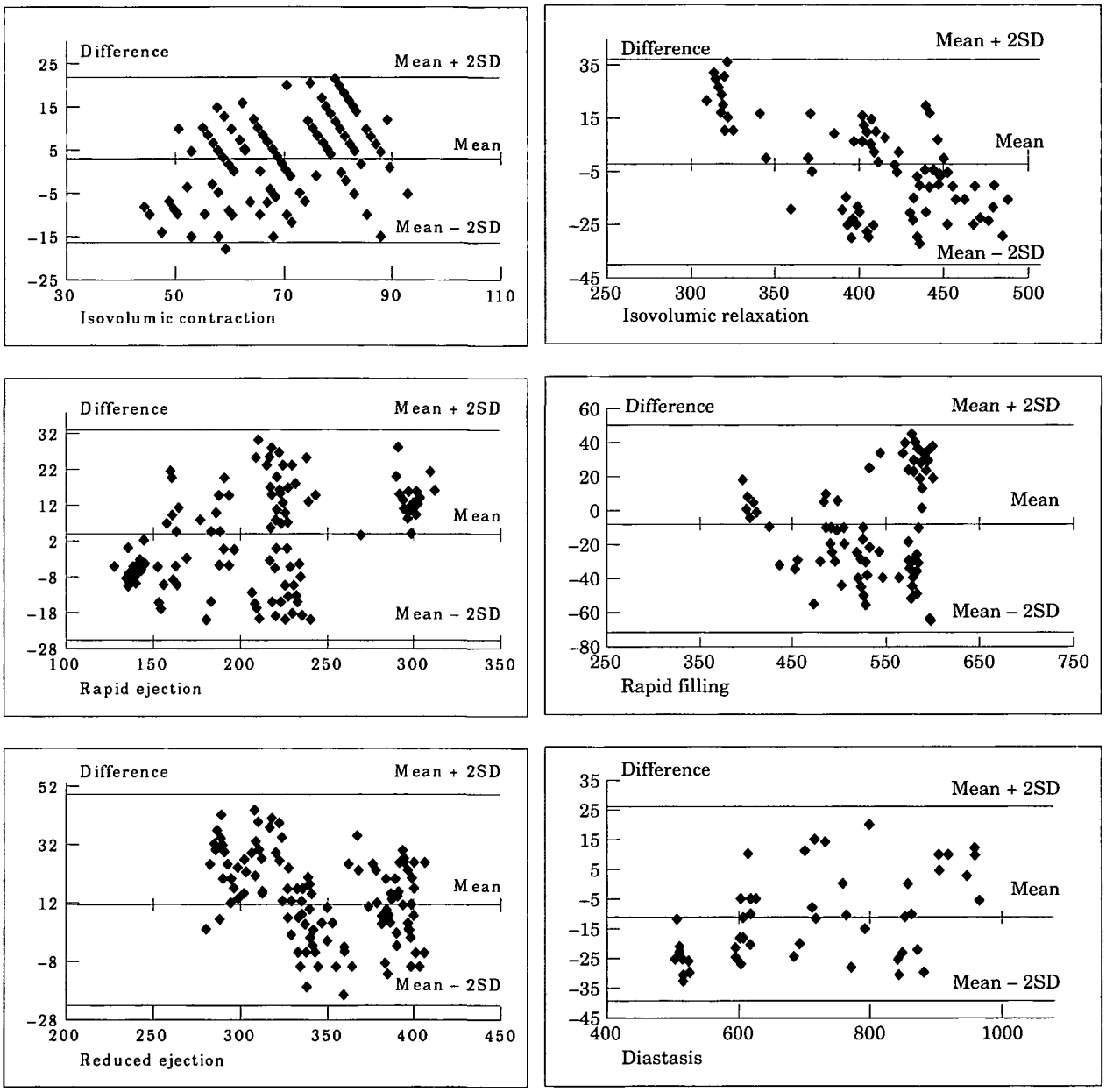

Figure 4 **The agreement between time intervals measured by invasive haemodynamic and tissue Doppler echocardiographic methods shown as Bland and Altman plots. A uniform style is used for all plots, with the X-axis depicting the mean time interval (ms) derived from both methods, and the Y-axis the difference between time intervals (ms) obtained by each method.**

function[24]. This technique has been used in clinical pharmacology to determine the dose response curve of digoxin/digitoxin and the influence of inotropic agents in dilated cardiomyopathies[31]. In patients undergoing treatment with potential cardiotoxic agents (for example, adriamycin) systolic time intervals can be used to detect early signs of myocardial dysfunction[8]. This technique requires high quality recordings, is restricted to observations of systole, and is limited by the fact that the pre-ejection period is derived indirectly[8]. M-mode echocardiography has been used to analyse cardiac function by assessing intervals in simultaneous recordings of aortic and mitral valves[10,11]. In clinical pharmacology, such measures have been shown to be less accurate than systolic time intervals[31,32]. The use of the digitized M-mode to assess isovolumic relaxation and early diastolic filling is limited by the fact that only recordings of high technical quality can be reliably digitized. In addition, specific indices of left ventricular filling determined by Doppler and the digitized M-mode have demonstrated a weak correlation[12].

Pulsed Doppler mitral inflow has certain limitations and some studies have failed to demonstrate a correlation between Doppler and haemodynamic

Table 2 Different time intervals (ms) and velocities (cm . s^{-1}) obtained in patients with atrial fibrillation

Cardiac phase	Haemodynamic		Tissue Doppler echocardiography		Mean velocity
	TI	range	TI	range	
Isovolumic contraction	81 ± 5	75–90	72 ± 4	72–84	1·32 ± 0·23
Rapid ejection	134 ± 4	112–155	142 ± 7	125–155	4·69 ± 0·51
Late ejection	167 ± 10	144–176	189 ± 12	168–210	1 86 ± 0·31
Isovolumic relaxation	66 ± 9	59–87	74 ± 7	64–89	1·22 ± 0·37
Rapid filling	121 ± 14	101–140	119 ± 10	101–137	4·73 ± 0 82
Diastasis	198 ± 71	147–241	212 ± 76	154–234	1·1 ± 0·84

Differences were not significant.
TDE=Tissue Doppler Echocardiography; TI=time interval; r=correlation coefficient.

parameters of diastolic function[33]. Moreover, a normal pattern of Doppler mitral inflow certainly does not exclude diastolic dysfunction because of the possibility of pseudonormalization of the Doppler tracing.

Precise differentiation of the different phases of the cardiac cycle is now possible with tissue Doppler echocardiography.

The normal cardiac cycle by tissue Doppler echocardiography

Because the intervals measured by tissue Doppler echocardiography and haemodynamics agreed we were able describe the different phases of the cardiac cycle by assessing tissue velocities. While the velocity pattern appears consistent between different myocardial segments, the precise colour coding (red or blue) depends on the echocardiographic view. In the present study the interventricular septum was viewed from the apex. Following the R wave, the initial low velocity red colour indicates isovolumic contraction. The start of rapid ejection is marked by an increase in velocity, represented by the red–yellow interface. Late ejection is indicated as a reduction in velocity, represented by a further red band.

The isovolumic relaxation period is defined by a low velocity phase from the end of the red systolic band to the start of a high velocity phase, coloured white–blue, that represents rapid filling. Diastasis commences with the transition from white–blue to blue, as tissue velocities decrease. Another high velocity phase (white–blue), occurring late in diastole, corresponds with atrial contraction. The latter phase was absent in subjects with atrial fibrillation (Fig. 5).

Potentials of tissue Doppler echocardiography

The tissue Doppler echocardiographic images provided a quantitative measure of tissue velocity. With this technique, different tissue velocity patterns can be detected during and within systole and diastole (Fig. 1). The current study has demonstrated that colour velocity patterns with tissue Doppler echocardiographic imaging correlate with the different phases of the cardiac cycle as assessed by invasive haemodynamics. Whether changes in myocardial velocity patterns are apparent in the early stages of different cardiac pathologies remains to be determined. Certainly, in the early stages of coronary artery disease there is a decrease in the duration of rapid filling, although total ventricular filling appears normal due to the contribution of atrial contraction. Such changes have been observed in the presence of normal systolic function[2]. The possibility of regional assessment by tissue Doppler echocardiography has been pointed out by some authors[34]. It seems that diastolic regional changes (regional isovolumic relaxation time obtained by tissue Doppler echocardiography) is an early marker of ischaemia, even before the development of regional systolic dysfunction.

Limitations

This study was undertaken in the catheterization laboratory, which limited the echocardiographic views available. While only images of the septum could be obtained during catheterization, it was possible to demonstrate a similar velocity colour pattern in other myocardial segments at separate examinations.

A further limitation may be the indirect measurement of left atrial pressure by pulmonary wedge pressure. However, direct measurement by transeptal catheterization was performed in all patients with valvular heart disease or pulmonary hypertension. For time delay correction between pulmonary wedge and left atrial pressure, previously validated methods were used (see methods).

Tissue Doppler echocardiography gives a good representation of myocardial velocities, possibly related to the rate of wall thickening. The contribution of whole heart motion within the chest to tissue velocities is not fully understood. Unlike pressure tracings and systolic time intervals, it is uncertain whether regional M-mode tissue Doppler echocardiographic analysis represents

whole heart contraction and relaxation. For this reason, in the present study, patients with regional wall motion abnormalities were specifically excluded.

Conclusions

Tissue Doppler echocardiography appears to be a simple, non-invasive, and reproducible method for assessing cardiac physiology. This may afford the opportunity to study regional systolic and diastolic function. Further studies are needed in order to establish the potential clinical applications of this new method.

References

[1] Karliner JS, Bouchard RJ, Gault JH. Dimensional changes of the human left ventricle prior to aortic valve opening: A cineangiographic study in patients with and without left heart disease. Circulation 1971; 44: 312.

[2] Bonow R, Bacharach S, Green M *et al.* Impaired left ventricular diastolic filling in patients with coronary artery disease: Assessment with radionuclide angiography. Circulation 1981; 64: 315–23.

[3] Hatle J. Doppler echocardiographic evaluation of diastolic function in hypertensive cardiomyopathies. Eur Heart J 1993; 14. 88–94.

[4] Erbel R, Brennecke R, Görge G, Meyer J. Accuracy and limitations of two-dimensional echocardiography in quantitative evaluation of left ventricular function. Z Kardiol 1989; 78: 131–42.

[5] Shapiro SM, Bersohn MM, Laks MM. In search of the holy grail: the study of diastolic ventricular function by the use of Doppler echocardiography. J Am Coll Cardiol 1991; 17: 1517–19.

[6] Lee CH, Hogan JC, Gibson DG. Diastolic disease in left ventricular hypertrophy: comparison of M mode and Doppler echocardiography for the assessment of rapid ventricular filling Br Heart J 1991; 65. 194–200.

[7] Spirito P, Maron JB, Verter I, Merril JS. Reproducibility of Doppler echocardiographic measurements of left ventricular diastolic function. Eur Heart J 1988; 9: 879–86.

[8] Li Q, Belz GG. Systolic time intervals on clinical pharmacology. Eur J Clin Pharmacol 1993; 44: 415–21.

[9] Ahmed SS, Levinson GE, Schwartz CJ, Ettinger PO. Systolic time intervals as measures of the contractile state of the left ventricle myocardium in man. Circulation 1972; 46: 559–71.

[10] Burckhardt CB. Comparison between spectrum and time interval histogram of ultrasound Doppler signals. Ultrasound Med Biol 1981; 7: 79–82.

[11] Sahn DJ, DeMaria A, Kisslo J, Weymann A. Recommendations regarding quantitation in M-mode echocardiography: Results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–9.

[12] Spirito P, Maron B, Bellotti P, Chapella F, Vecchio C. Noninvasive assessment of left ventricular diastolic function: Comparative analysis of pulsed Doppler ultrasound and digitized M-mode echocardiography. Am J Cardiol 1986; 68: 337–48.

[13] Vandenberg B, Rath L, Stuhmuller P, Melton HE, Skarton DJ. Estimation of left ventricular cavity area with an on line semiautomatic echocardiographic edge detection system. Circulation 1992; 86: 159–66.

[14] Sutherland GR, Stewart J, Groundstroem WE *et al.* Color Doppler myocardial imaging: A new technique for the assessment of myocardial function. J Am Soc Echocardiogr 1994; 7: 441–58.

[15] Bach D, Armstrong W, Donovan C, Hummel J, Bolling S, Muller D. Quantitative assessment of regional systolic and diastolic myocardial velocities during transient ischemia and reperfusion (Abstr). Circulation 1994; 90: I-326.

[16] Nakayama K, Uematsu M, Tanaka N *et al.* An enhanced method for evaluation of results after radio frequency catheter ablation in Wolf–Parkinson–White (WPW) Syndrome: Application of tissue Doppler imaging technique (Abstr). Circulation 1994; 90: I-327

[17] Miyatake K, Yamagishi M, Tanaka N *et al.* New method for evaluating left ventricular wall motion by color coded tissue Doppler imaging: In vitro and in vivo studies. J Am Coll Cardiol 1995; 25: 717–24.

[18] Palka P, Lange A, Flemming A, Sutherland G, Fenn L. Doppler tissue imaging: Myocardial wall motion velocities in normal subjects. J Am Soc Echocardiogr 1995; 8: 659–68.

[19] Brockenbrough EC, Braunwald E A new technique for left ventricular angiography and transeptal left heart catheterization. Am J Cardiol 1960; 6: 1062–9.

[20] Grossman W. Cardiac catheterization and angiography, 3rd edn. Philadelphia: Lea & Febiger, 1986: 145–8.

[21] Lange R, Moore D, Ciggaroa R, Hillis D. Use of pulmonary capillary wedge pressure to assess severity of mitral stenosis: Is true left atrial pressure needed in this condition? J Am Coll Cardiol 1989; 13: 825–916.

[22] The Committee on M-Mode Standardization of the American Society of Echocardiography. Results of a survey of echocardiographic measurements. Circulation 1978; 58: 1072–83.

[23] Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. Lancet 1986; 8476: 307–10.

[24] Burwash I, Otto C, Pearlmann A. Use of Doppler derived left ventricular time intervals for non-invasive assessment of systolic function. Am J Cardiol 1993; 72: 1331–3.

[25] De Mey C, Belz GG, Nixdorf U *et al.* Relative sensitivity of four non-invasive methods in assessing systolic cardiovascular effects of isoprenaline in healthy volunteers. Clin Pharmacol Ther 1992; 52: 609–19.

[26] Lewis R, Rittgers S, Forester W, Boudoulas H. A critical review of the systolic time intervals. Circulation 1977; 56: 146–58.

[27] Appleton C, Hatle L, Popp R. Relation of transmitral flow velocity patterns to left ventricular diastolic function: new insight from a combined hemodynamic and Doppler echocardiographic study. J Am Coll Cardiol 1988; 12: 426–40.

[28] Katz LN, Feil HS. Clinical observations on the dynamics of ventricular systole. Arch Int Med 1923; 2: 672–92.

[29] Erbel R, Belz GG. Untersuchungen zur Messmethode der systolischen Zeitintervalle. Z Kardiol 1977; 66: 433–5.

[30] Belz GG, Aust PE, Schneider B. Time course of the effects of single intravenous dose of digitoxin and digoxin in normal volunteers J Cardiovasc Pharmacol 1981; 3: 1116–25.

[31] Stern HC, Matthews JH, Belz GG. Influence of dihydralazine induced afterload reduction on systolic time intervals and echocardiography in healthy subjects. Br Heart J 1984; 52: 435–9.

[32] Hanrath P, Mathey DG, Kremer P, Sonntag F, Bleifeld W. Effect of verapamil on left ventricular isovolumic relaxation time and regional left ventricular filling in hypertrophic cardiomyopathy. Am J Cardiol 1980; 45: 1258–64.

[33] Lawson WE. A new use of M-mode echocardiography in detecting left ventricular diastolic dysfunction in coronary artery disease. Am J Cardiol 1986; 58: 210.

[34] García-Fernández MA, Azevedo J, Puerta P *et al.* Regional left ventricular diastolic dysfunction evaluated by tissue Doppler imaging as an earlier sign of myocardial ischemia: Experimental study of induced ischemia and reperfusion in pigs. J Am Coll Cardiol 1996 (Abstract) 1996; Vol 27: 227A.

[18] Gamble WH. A critical appraisal of diastolic time intervals as a measure of relaxation in left ventricular hypertrophy. Circulation 1983; 68: 76–86.