European Heart Journal (2004) **25**, 1517–1525

Clinical research

Comparison of deformation imaging and velocity imaging for detecting regional inducible ischaemia during dobutamine stress echocardiography

Jens-Uwe Voigt[a,*], Uwe Nixdorff[a], Ruxandra Bogdan[a], Bert Exner[a], Kristin Schmiedehausen[b], Günther Platsch[b], Torsten Kuwert[b], Werner G. Daniel[a], Frank A. Flachskampf[a]

[a] *Medizinische Klinik II, Friedrich-Alexander-Universität Erlangen-Nürnberg, Ulmenweg 18, 91054 Erlangen, Germany*
[b] *Nuklearmedizinische Klinik, Friedrich-Alexander-Universität Erlangen-Nürnberg, Erlangen, Germany*

Received 10 December 2003; revised 3 April 2004; accepted 13 May 2004
Available online 23 July 2004

See page 1477 for the editorial comment on this article[†]

KEYWORDS
Tissue Doppler;
Strain rate imaging;
Ischaemia;
Dobutamine stress echocardiography;
Coronary disease

Aims To determine whether Doppler based myocardial tissue velocity imaging (TVI) or strain rate imaging (SRI) is more accurate in detecting stress-induced ischaemia during dobutamine stress echocardiography (DSE).

Methods and results Regional myocardial velocity, displacement, strain rate and strain patterns during DSE were investigated in 44 routine patients with known or suspected coronary artery disease. Simultaneous perfusion scintigraphy defined regional ischaemia. Curves and curved-M-mode patterns were analysed and receiver-operating-characteristics of TVI and SRI parameters were compared by their area under the curve (AUC) in the receiver-operating-characteristics.

In non-ischaemic segments, peak systolic velocity and strain rate increased significantly. Unlike SRI, TVI parameters had higher values in basal than in apical segments. In 47 segments of 19 segments DSE-induced ischaemia, which was proven by scintigraphy. In ischaemia, velocity and strain rate increased less. Post-systolic shortening (PSS) was always seen in SRI but not regularly in TVI.

Peak systolic velocity and systolic displacement were the best TVI-parameters of stress-induced ischaemia (AUC 0.68 and 0.77, respectively.), in SRI it was the ratio of PSS and maximal segmental deformation (AUC $= 0.95$, $p < 0.0001$).

Conclusion Compared to TVI, SRI parameters showed no major apico-basal gradient and had significantly higher diagnostic accuracy, comparable to conventional reading. SRI thus appears superior to TVI for regional ischaemia detection during DSE and may be preferred to support conventional DSE reading.

* Corresponding author. Tel.: +49-9131-85-35301; fax: +49-9131-85-35303.
E-mail address: jens.uwe.voigt@gmx.net (J.-U. Voigt).

† doi:10.1016/j.ehj.2004.07.006

0195-668X/$ - see front matter
doi:10.1016/j.ehj.2004.05.014

Introduction

Dobutamine stress echocardiography (DSE) is well established for detecting inducible ischaemia. Ischaemia is defined by a regional reduction or deterioration of myocardial thickening or inward motion of the endocardial border.[1–3] Reading DSE is subjective and strongly dependent on experience, making more objective markers desirable.[4–6]

Tissue velocity imaging (TVI) parameters like velocity (*V*) or its temporal integral displacement (*D*) have been suggested for the quantitative assessment of regional myocardial function.[7–9] Since velocities are measured relative to the transducer, however, values depend on the site of measurement and are influenced by overall heart motion (e.g., due to breathing). In addition, interactions between myocardial regions make data difficult to interpret. Therefore, most TVI stress echo studies excluded patients with wall motion abnormalities at rest although those patients are common in the clinical routine and their stress echoes are particularly difficult to read visually.[8,9]

Strain rate imaging (SRI)[10] measures myocardial deformation (strain, ε) and deformation rate (strain rate, SR) by Doppler velocity gradient calculation. SRI parameters are relatively homogeneous throughout the myocardium[11] and are less influenced by cardiac motion. SRI accurately depicts regional myocardial function at rest and during acute and chronic ischaemia,[11–13] including dobutamine-induced ischaemia in animal models and man.[14–19] A recent report showed the superiority of SRI over TVI for the detection of viability by low-dose-DSE.[20]

Thus, this study sought to compare the accuracy of TVI and SRI parameters for the detection of stress-induced ischaemia in the clinical setting of DSE in routine patients.

Methods

Study population

As reported previously,[18] we studied 44 consecutive patients referred for DSE to detect the regional presence or absence of inducible ischaemia (Table 1). 15 patients had regional wall motion abnormalities at rest due to prior infarction. Medication was not discontinued. Patients not in sinus rhythm, with bundle branch block or more than mild valvular heart disease were excluded. All participants gave written informed consent prior to the examinations.

Dobutamine challenge

Patients underwent a standard DSE protocol[2] with incremental dobutamine infusion rates of 10, 20, 30 and 40 μg/(kg min) for 3 min each and up to 2 mg of atropine if necessary. Criteria for terminating the test were achieving target heart rate of (220-age) × 0.85 beats/min, development or deterioration of wall motion abnormalities, angina, ischaemic ECG changes, systolic blood pressure increase above 240 mmHg or decrease below 100 mmHg as well as severe arrhythmias.

Echocardiographic image acquisition

Patients were scanned in a left supine position from an apical window using a Vivid Five ultrasound scanner (GE Vingmed, Horton, Norway). At baseline, at each step of the DSE and during recovery, three heart cycles of the apical four-, three- and two-chamber view were captured in conventional 2D and colour tissue Doppler mode and stored digitally. A narrow image sector allowed colour tissue Doppler frame rates between 133 and 147 frames/s (temporal resolution 7.5—6.8 ms).

Tissue Doppler data processing

Our way of processing tissue Doppler data has previously been described.[11,13] In brief, we used dedicated research software (TVI 6.0, GE Vingmed, Horton, Norway and TVA, JU Voigt, University Erlangen, Germany). Strain rate was calculated with a sample volume distance of 8 mm. An 18 segment model of the left ventricle was used, i.e., each wall was sub-divided in an apical, mid and basal segment. Strain rate curves were obtained from the centre of the segment and velocity curves were obtained from the basal end. Wall motion was manually tracked to keep mid-wall position. Three heart cycles were temporally averaged to improve the signal to noise ratio of the curves. Displacement and strain curves were calculated by integrating velocity and strain rate data, respectively, and were baseline-corrected. TVI and SRI curved M-modes were obtained from all

Table 1 Characteristics of patients with and without ischaemic response during dobutamine stress

	Non-ischaemic		Ischaemic		*p*-value
No. of patients	25	(57%)	19	(43%)	
Age (years)	62 ± 10		63 ± 9		0.7338
β-Blocker	18	(72%)	13	(68%)	0.7041
Nitrate	3	(12%)	8	(42%)	0.1297
Hypertension	19	(76%)	15	(79%)	0.8287
Diabetes	7	(28%)	7	(37%)	0.9999
Smoking	8	(32%)	9	(47%)	0.9207
Ejection fraction (%)	64 ± 6		61 ± 4		0.0604
Baseline WMA (pat.)	6	(14%)	9	(20%)	0.7368
Ischaemic segments	0		47	(7.2%)	
Ischaemic segments/patient	0		2.5 ± 2.1		
Baseline BP (mmHg)	132/77		134/73		0.6249/0.2442
Peak stress BP (mmHg)	146/79		158/73		0.2020/0.1688

WMA, wall motion abnormalities; BP, blood pressure.

walls. Timing of aortic and mitral valve opening (AVO, MVO) and closure (AVC, MVC) was derived from the echo recordings.[13]

Measurements

We measured velocity peaks at systole ($V_{peak\,sys}$), post-systole (V_{ps}) and early diastole (V_e), the maximum displacement during the entire heart cycle (D_{max}), during ejection time (D_{et}), and post-systole (D_{ps}). Similarly, the SRI parameters peak systolic strain rate ($SR_{peak\,sys}$), maximum strain (ε_{max}), strain during ejection time (ε_{et}) and post-systolic strain (ε_{ps}) were measured. Post-systole was defined as time between AVC and regional onset of motion or deformation due to early filling. Values are expressed in [cm/s] (velocity), [mm] (displacement), [s^{-1}] (strain rate) and [%] (strain). Since acquired from apical views, data reflect longitudinal left ventricular function. TVI parameters are positive if the region of interest moves towards the transducer (for longitudinal velocities usually systole) and negative if it moves away from it. SRI parameters are negative in shortening and positive in lengthening myocardium. To account for systolic function changes and to normalise for overall curve amplitude, ratios (D_{ps}/D_{max}) and ($\varepsilon_{ps}/\varepsilon_{max}$) were calculated. Results are given in percent of D_{max} or ε_{max}, respectively. TVI and SRI data were analysed separately and blinded to other patient data.

Visual assessment

Conventional 2D recordings were read by an experienced reader blinded to all patient data using a quad screen with synchronised display of baseline, low dose, peak and recovery stage. Ischaemia was defined as regional reduction or deterioration of radial myocardial thickening in at least one segment.

Scintigraphic image acquisition and data processing

During DSE, the radioactive tracer (Tc-99m-MIBI, Cardiolite®, Bristol-Meyers-Squibb, Germany) was injected at peak stress and dobutamine was continued for two more minutes. Scintigraphic images were acquired within 1 h. Baseline perfusion scintigraphy was performed prior to the stress test or the day after. Single photon emission computed tomography (SPECT) was performed and corrected myocardial tracer uptake at baseline and peak stress was quantified (Multi-SPECT 3/ECT-Tool Box, Siemens, Germany). Corresponding to echocardiography, 18 myocardial segments were defined and assigned as non-ischaemic, ischaemic or scarred by an experienced blinded reader.

Coronary angiography

Coronary angiograms were obtained within 4 ± 21 days from the stress echo study and stenosed vessels were quantified (QCA Quantcor, Siemens, Germany). A diameter stenosis of more than 50% was considered inducive of stress ischaemia. To account for variable coronary anatomy, a blinded reader experienced in both coronary angiography and echocardiography assigned myocardial segments to the presumed perfusion territories of stenosed vessels considering the left coronary to generally supply anterior, antero-septal and mid and apical septal segments, the circumflex to supply the lateral wall and the right coronary the basal septal as well as the basal and mid-inferior segments. The remaining segments were assigned depending on the relative size of the three coronaries and their branches.

Statistics

In this study, scintigraphy was the gold standard for defining ischaemia. Segments with scintigraphic evidence of scar or echocardiographic wall motion abnormalities at baseline were excluded from the analysis.

If not stated otherwise, all data analysis and comparisons between imaging modalities were performed on a segmental level. To account for the apico-basal gradient in TVI parameters, data were grouped separately for the basal, mid and apical level. Data from ischaemic and non-ischaemic segments were averaged per patient (SRI) or per patient and level (TVI) before statistical analysis to minimise the influence of segment interaction. Continuous parameters are expressed as means ± SD. Grouped data were tested for normal (Gaussian) distribution, equality of standard deviation (Bartlett, Kolmogorov and Smirnov) and compared using a two-tailed *t*-test. For more than two groups, analysis of variance (ANOVA) was used considering segment and patient interaction terms (SAS 8.2, SAS Institute, Cary, NC, USA). *p*-values below 0.05 were considered statistically significant.

Diagnostic accuracies of TVI and SRI parameters were determined as areas under the curves (AUC) of receiver-operating-characteristics (ROC). To account for possible segment interaction, AUCs were compared using a two-tailed test for clustered data based on a bivariate normal distribution model ("cluster.for" and "clusterbi.for", Department of Biostatistics and Epidemiology, Cleveland Clinic Foundation, Cleveland, OH, USA). Sensitivities and specificities compared to scintigraphy were calculated for 2D echo readings, TVI and SRI parameters.

Results

No adverse events occurred during DSE. DSE was terminated due to signs of ischaemia in 10 cases and in 34 patients after achieving target heart. 792 myocardial segments on at least four stress levels each were analysed (3786 segmental analyses). 80 segments (10.1%) were excluded because of scintigraphic evidence of scar, echocardiographic wall motion abnormalities or abnormal strain rate patterns at rest. On scintigraphy, 19 of 44 patients (43%) had an ischaemic response in altogether 47 segments (7.2%). 33 of the segments were located apically, 12 mid-wall and two basally. Because of this distribution, results of ischaemic basal segments were not deemed meaningful and therefore not considered for conclusions. All analysed segments with inducible ischaemia on scintigraphy had significant stenosis (mean 80 ± 18%) in the supplying coronary artery. No analysed segment without scintigraphic ischaemia was supplied by a stenosed vessel. Patients with and without ischaemic response did not significantly differ with respect to age, medication, risk factors, baseline ejection fraction and average blood pressure and heart rate at baseline and peak stress (Table 1).

Feasibility

Conventional visual wall motion assessment was possible in 97% of the segments. Quantitative analysis of velocity and displacement was possible in 92% of the segments. Due to noise and artefacts, strain and strain rate curves

could be assessed in only 85%. Qualitative visual assessment of SRI curved M-modes, however, was achieved in 95% of the segments. Inter- and intra-observer variability of myocardial Doppler data and time interval measurements in our lab ranges from 5% to 10% and 10—15 ms, respectively.[11,13]

Results

Conventional 2D reading

Compared to the scintigraphic gold standard, 78% of the readable ischaemic segments were detected by conventional reading. With this, DSE sensitivity and specificity per patient was 81% and 82%, respectively, vs. scintigraphy.

Quantitative assessment of velocity and displacement

Data are provided in Table 2 and illustrated in Fig. 1. Baseline parameters of ischaemic and non-ischaemic segments were not significantly different. All tissue Doppler parameters differed significantly between basal, mid and apical segments both at baseline and during stress. Furthermore, ANOVA revealed significant differences between patients. With dobutamine stress, the amplitude of $V_{peak\,sys}$, V_e, D_{max} and D_{ps} increased. Relative changes were highest at the apex. D_{et} decreased slightly but significantly.

In ischaemic segments, TVI parameters changed significantly with dobutamine stress if compared to baseline (Figs. 2(a) and (b)). However, no statistically significant difference was found between ischaemic and non-ischaemic segments at peak stress.

Positive post-systolic displacement occurred in a relevant number of segments at baseline and became more frequent with stress in both ischaemic (42% vs. 63%) and non-ischaemic (30% vs. 61%) segments.

Quantitative assessment of strain and strain rate

Data have been previously published in Ref. [18]. Baseline parameters of ischaemic and non-ischaemic segments were not significantly different. Values of basal, mid and apical segments did not differ. During DSE, $SR_{peak\,sys}$ increased clearly in non-ischaemic segments. (-1.6 ± 0.6 vs. -3.4 ± 1.4 s^{-1}, $p < 0.01$). Individual ε_{max} and ε_{et} showed a bi-phasic response in most non-ischaemic segments which resulted in minor differences between

Table 2 Representative segmental TVI parameters in non-ischaemic ($n_{ni} = 665$, in all 44 patients) and ischaemic ($n_i = 47$, in 19 of 44 patients) response to peak dobutamine stress, separated for the apical, mid, and basal level

	Baseline			Peak stress				
	Non-ischaemic	Ischaemic	p^a	Non- ischaemic	p^b	Ischaemic	p^a	p^b
HR (1/min)	68 ± 12	67 ± 13	0.9202	133 ± 19	0.0001	136 ± 14	0.5559	0.0001
$V_{peak\,sys}$ (cm/s)								
Apical	1.6 ± 1.1	1.3 ± 0.8	0.4314	3.4 ± 3.0	0.0001	1.8 ± 2.6	0.409	0.6551
Mid	3.1 ± 1.0	3.0 ± 1.0	0.7941	5.3 ± 3.5	0.0001	4.5 ± 2.2	0.7666	0.1793
Basal	4.3 ± 1.2	4.5 ± 0.0	0.6167	7.4 ± 3.2	0.0001	8.1 ± 0.0	0.5935	n.a.
V_e (cm/s)								
Apical	−2.0 ± 1.0	−1.2 ± 0.7	0.0198	−3.7 ± 2.6	0.0001	−3.0 ± 2.1	0.2355	0.0339
Mid	−3.4 ± 1.3	−3.3 ± 1.4	0.1327	−5.4 ± 2.5	0.0001	−4.2 ± 4.6	0.3029	0.614
Basal	−4.6 ± 1.8	−2.0 ± 0.0	0.4077	−6.8 ± 2.3	0.0001	−3.8 ± 0.0	0.7237	n.a.
D_{et} (mm)								
Apical	2.0 ± 1.3	1.6 ± 0.8	0.0632	1.9 ± 2.2	0.6359	1.4 ± 1.4	0.0626	0.9132
Mid	4.7 ± 1.5	4.0 ± 1.7	0.2207	3.5 ± 2.2	0.0007	1.4 ± 2.3	0.4066	0.0511
Basal	7.2 ± 1.7	7.3 ± 0.0	0.9506	5.2 ± 2.4	0.0001	6.0 ± 0.0	0.3389	n.a.
PSD (% of seg.)								
Apical	43	48		59		54		
Mid	26	25		62		78		
Basal	22	50		61		100		
D_{ps} (mm)[c]								
Apical	0.3 ± 0.4	0.2 ± 0.2	0.5853	0.9 ± 0.6	0.0028	1.2 ± 0.8	0.7068	0.1342
Mid	0.3 ± 0.5	0.5 ± 0.4	0.3471	1.1 ± 0.8	0.0001	1.1 ± 1.0	0.3695	0.0066
Basal	0.3 ± 0.3	0.1 ± 0.0	0.7208	1.0 ± 0.6	0.0001	0.6 ± 0.0	0.5594	n.a.

For corresponding SRI data, see Ref. [18]

[a]Significance compared to non-ischaemic stress response. NB: Differences between individual patients were significant in all parameters at almost all levels. None of the velocity parameters differed significantly between ischaemic and non-ischaemic segments within a given patient.

[b]Significance compared to baseline. Only two basal segments in only one patient became ischaemic during peak dobutamine stress. Thus, no *p*-value is given.

[c]Segments with post-systolic displacement only.

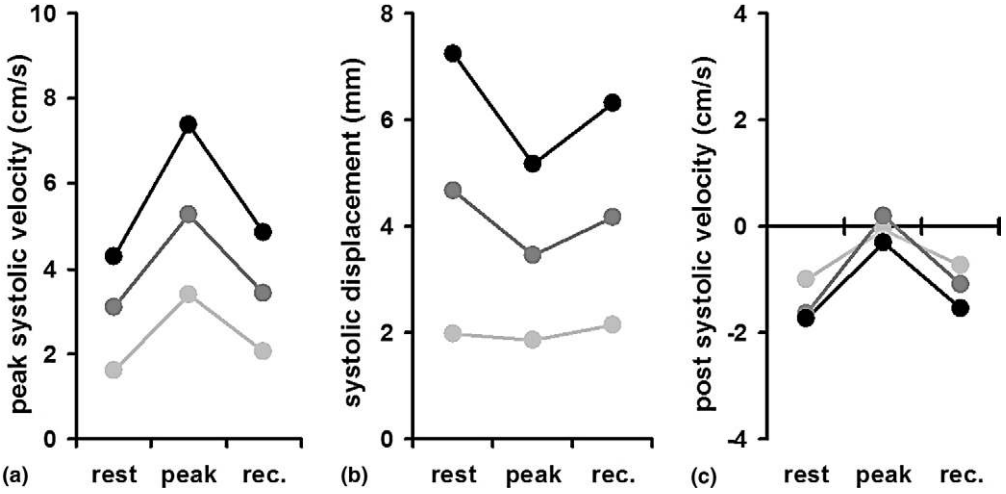

Fig. 1 Mean (a) peak systolic velocity, (b) systolic displacement, (c) post systolic velocity during dobutamine stress of non-ischaemic segments. Note different values in apical (light grey), mid (dark grey) and basal segments (black).

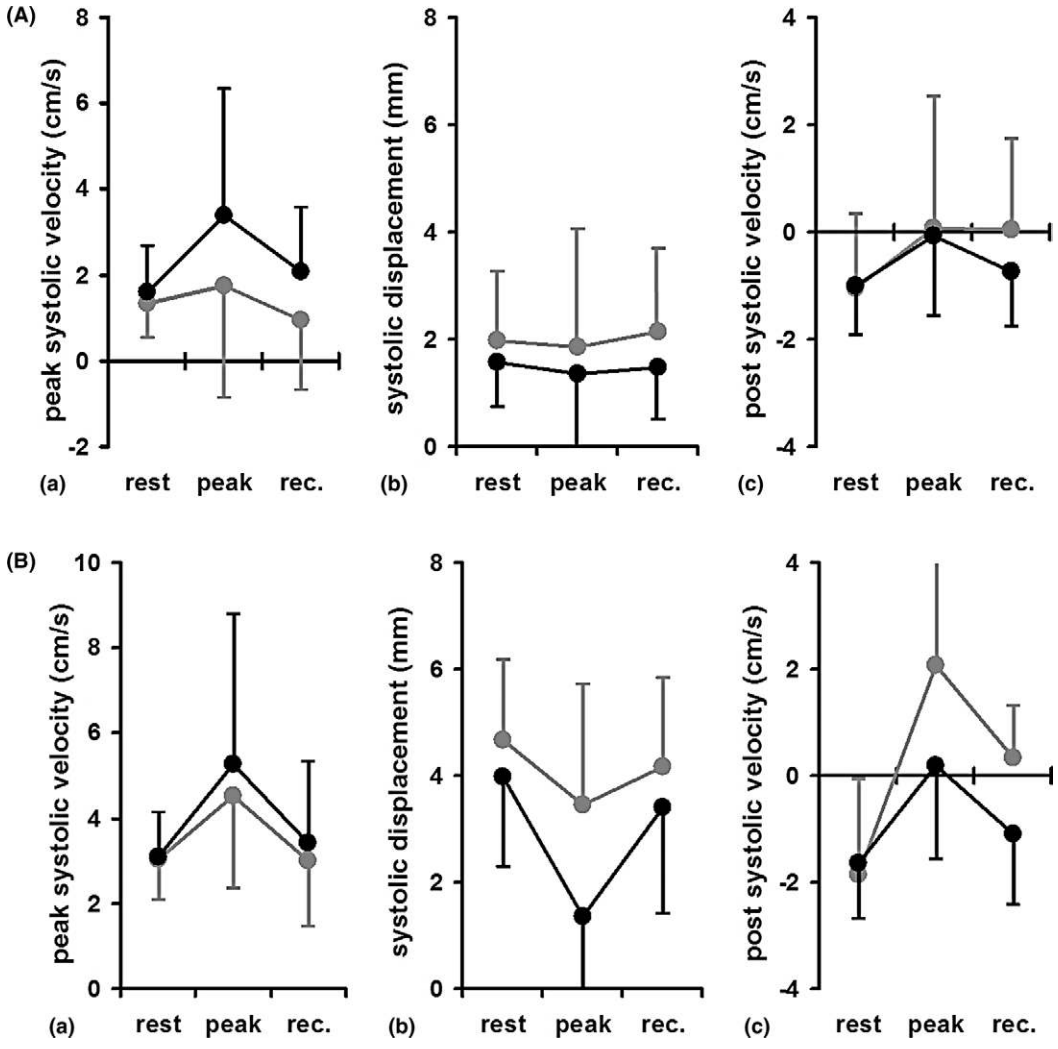

Fig. 2 Behaviour of non-ischaemic (black) and ischaemic (grey) apical (A) and mid (B) segments during dobutamine stress. (a)—(c) Same parameters as in Fig. 1.

baseline and peak stress values (ε_{max}: $-20 \pm 6\%$ vs. $-23 \pm 9\%$, $p < 0.01$, ε_{et}: $-17 \pm 6\%$ vs. $-16 \pm 9\%$, $p < 0.05$).

In ischaemic segments at peak stress, ε_{et} and increase in $SR_{peak\,sys}$ were clearly reduced, while ε_{max} remained almost constant (ε_{et}: $-16 \pm 7\%$ vs. $-10 \pm 8\%$, $p < 0.01$, $SR_{peak\,sys}$ -1.6 ± 0.8 vs. -2.0 ± 1.1 s^{-1}, $p < 0.01$, ε_{max}: $-19 \pm 8\%$ vs. $-20 \pm 10\%$, $p =$ n.s.).

In two-fifths of all segments at baseline as well as non-ischaemic segments at peak stress post-systolic shortening of minor amplitude was found. In contrast, all ischaemic segments developed marked PSS at peak stress which was of significantly higher amplitude than PSS in non-ischaemic segments (ε_{ps} $0.4 \pm 4.1\%$ vs. $-6.7 \pm 4.5\%$, $p < 0.01$). An $\varepsilon_{ps}/\varepsilon_{max}$ cut-off of 35% identified patients with ischaemia with a sensitivity of 82% and a specificity of 85%.

ROC analysis

Results of the ROC analysis are provided in Table 3 and illustrated in Fig. 3. Most TVI parameters had a low, but statistically significant discriminating power for the detection of regional stress-induced ischaemia. D_{et} performed best in mid segments (area under the curve, AUC $= 0.77$) and $V_{peak\,sys}$ offered the most constant performance in all three levels. TVI parameters of basal segments had an only weak discriminating power for detecting ischaemia in other segments of the respective wall (Table 3).

SRI parameters had high and significant discriminatory power in both the pooled segment data and at single levels. The AUC of $\varepsilon_{ps}/\varepsilon_{max}$ and $-$ with one exception $-$ $SR_{peak\,sys}$ were in all cases significantly higher than the AUC of the best TVI parameter (AUC $\varepsilon_{ps}/\varepsilon_{max} = 0.95$ vs. AUC $D_{et} = 0.77$, $p < 0.0001$).

Discussion

Main findings

This study compared the segmental response of different TVI and SRI parameters in ischaemic and non-ischaemic myocardium of 44 consecutive patients undergoing DSE. TVI parameter had only weak discriminatory power to detect regional ischaemia. In contrast, SRI parameters were closely related to regional ischaemia. The ratio $\varepsilon_{ps}/\varepsilon_{max}$ proved to be the best quantitative marker with a sensitivity and specificity comparable to an experienced observer (Figs. 4 and 5, Tables 3 and 4).

Objectifying regional function

In the setting of clinical stress echo studies, a long learning curve[6] and a marked inter-observer variability[4,5] make a tool desirable that is able to objectively detect stress-induced ischaemia. Ideally, such a tool would be uniformly applicable to all myocardial segments and allow a clear decision whether ischaemia is present or not. Moreover, results should be independent from baseline wall motion abnormalities. In contrast to other studies we therefore did not exclude patients with baseline wall motion abnormalities.

Defining regional ischaemia by TVI

Systolic TVI parameters showed significant differences between the basal, mid and apical segments both at baseline and during dobutamine stress (Fig. 5). This is in concordance with previous studies.[8,9] The three levels were therefore analysed separately. $V_{peak\,sys}$ showed the most constant, albeit only moderate, power to distin-

Table 3 Areas under the ROC curve for representative TVI and SRI parameters at apical, mid and basal level as well as for all left ventricular segments testing the detection of ischaemia during peak dobutamine stress

	Apical	Mid	Basal	Basal[c]	All
$V_{peak\,sys}$	0.63 ± 0.06	0.62 ± 0.06	0.63 ± 0.10	0.60 ± 0.06	0.68 ± 0.05
	0.0012[a]	0.0014[a]	0.0062[a]	0.0046[a]	0.0001[a]
D_{et}	0.52 ± 0.06	0.77 ± 0.05	0.43 ± 0.05	0.54 ± 0.06	0.72 ± 0.05
	0.3183[a]	0.0001[a]	0.0369[a]	0.1380[a]	0.0001[a]
D_{ps}/D_{max}	0.50 ± 0.07	0.65 ± 0.06	0.61 ± 0.05	0.61 ± 0.05	0.54 ± 0.07
	0.4849[a]	0.0001[a]	0.0012[a]	0.0015[a]	0.1546[a]
$SR_{peak\,sys}$	0.83 ± 0.05	0.73 ± 0.06	0.75 ± 0.05		0.80 ± 0.06
	0.0001[a]	0.0001[a]	0.0001[a]		0.0001[a]
	0.0001[b]	0.0602[b]	0.0001[b]		0.0001[b]
$\varepsilon_{ps}/\varepsilon_{max}$	0.94 ± 0.02	0.93 ± 0.02	0.77 ± 0.04		0.95 ± 0.01
	0.0001[a]	0.0001[a]	0.0001[a]		0.0001[a]
	0.0001[b]	0.0001[b]	0.0001[b]		0.0001[b]

Other TVI parameters (V_e, D_{max}, D_{ps}) behaved similarly. For detailed SRI data, see Ref. [18]

[a]Significance against null-hypothesis, i.e., AUC $= 0.5$.

[b]Significance against best TVI parameter of the same column.

[c]Sub-analysis of the diagnostic value of TVI parameters of basal segments for detecting ischaemia in any of the three segments of the respective wall. Basal segments with wall motion abnormalities at baseline were excluded.

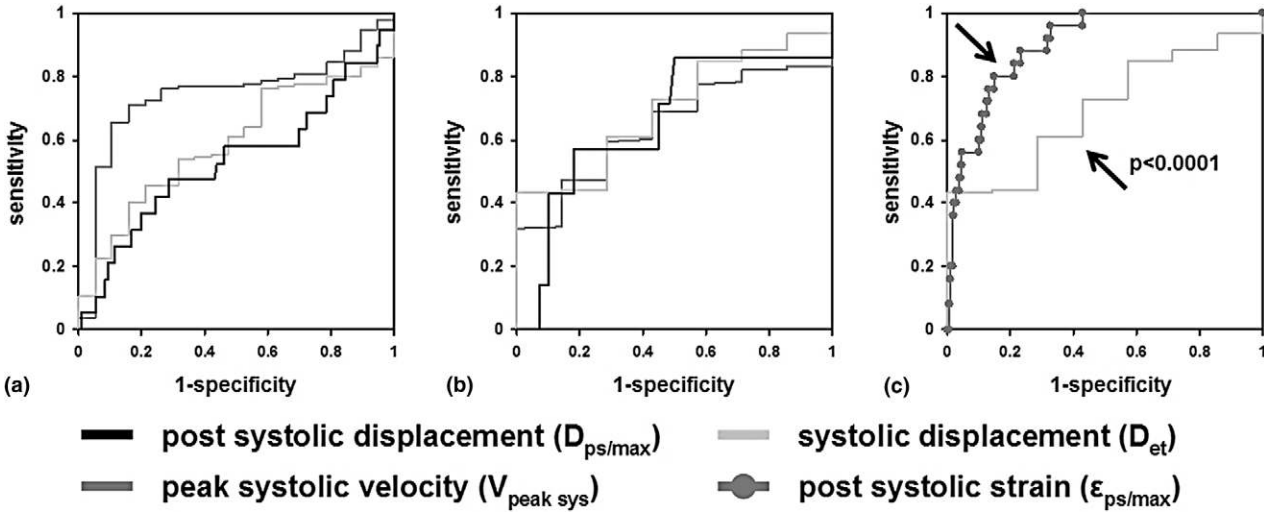

Fig. 3 Receiver-operating characteristics (ROC) of segmental TVI parameters. (a) Apical segments, (b) mid segments, (c) comparison of best TVI ($D_{et,\,mid}$) and best SRI parameter ($\varepsilon_{ps}/\varepsilon_{max}$). NB: AUCs differ to Table 3 due to correction for possible segment interaction in the statistical analysis.

guish between normally perfused and ischaemic segments at all three levels. None of the TVI parameters differed statistically significant between ischaemic and non-ischaemic segments at peak stress. This is in contrast to other studies[8,9] but may be due to the fact that our baseline values of non-ischaemic segments were already influenced by adjacent regions with wall motion abnormalities and/or peak stress values of normal segments were also reduced due to ischaemia in adjacent or remote regions of the ventricle.

The concept of detecting ischaemia anywhere in a given left ventricular wall by considering only TVI parameters of basal segments was also tested in our study. ROC analysis revealed no advantage over other approaches (Table 3, Figs. 4 and 5).

Defining regional ischaemia by SRI

In contrast to TVI, systolic SRI values were comparable in apical, mid-wall and basal segments. The observed $SR_{peak\,sys}$ increase in non-ischaemic segments with dobutamine is in agreement with previous studies.[14,15] Both ε_{et} and the increase in $SR_{peak\,sys}$ were significantly reduced in ischaemic segments, confirming earlier studies,[12,14,15] while ε_{max} remained almost constant due to the increasing or newly occurring PSS. At peak stress, PSS was found in 100% of the ischaemic segments. If related to the overall amplitude of the strain curve, PSS detects regional ischaemia significantly better than TVI parameters and with a clinically relevant accuracy (AUC = 0.95, $p < 0.0001$ vs. best TVI parameter, see Ref.[18] for further details).

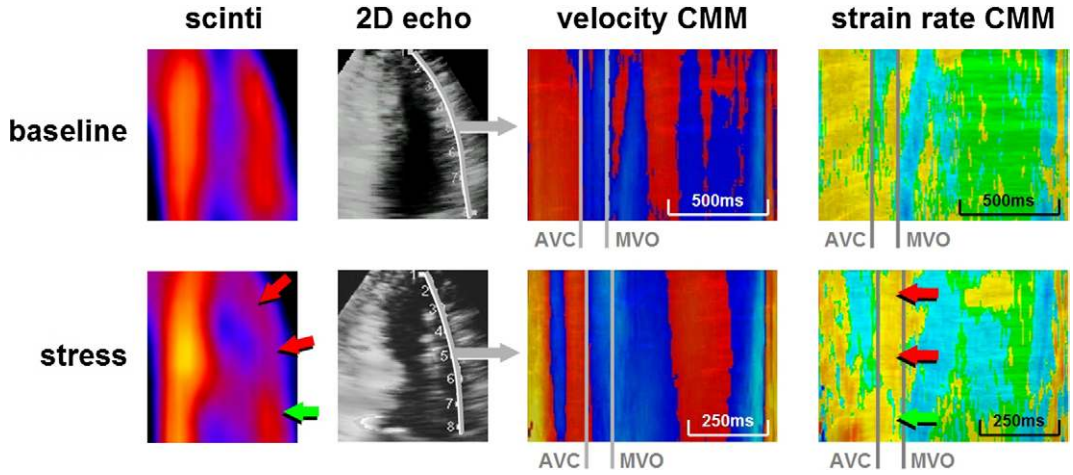

Fig. 4 Example of a patient with apical and mid-antero-septal wall ischaemia (red arrows) and normal response (green arrows) in the basal segment during dobutamine stress. Note that the curved M-mode (CMM) of the anteroseptal wall shows no difference in timing and amplitude of velocities. Strain rate CMM reveals a marked post-systolic shortening in the ischaemic region (red arrows) allowing a distinction from non-ischaemic myocardium (green arrow). AVC, aortic valve closure; MVO, mitral valve opening.

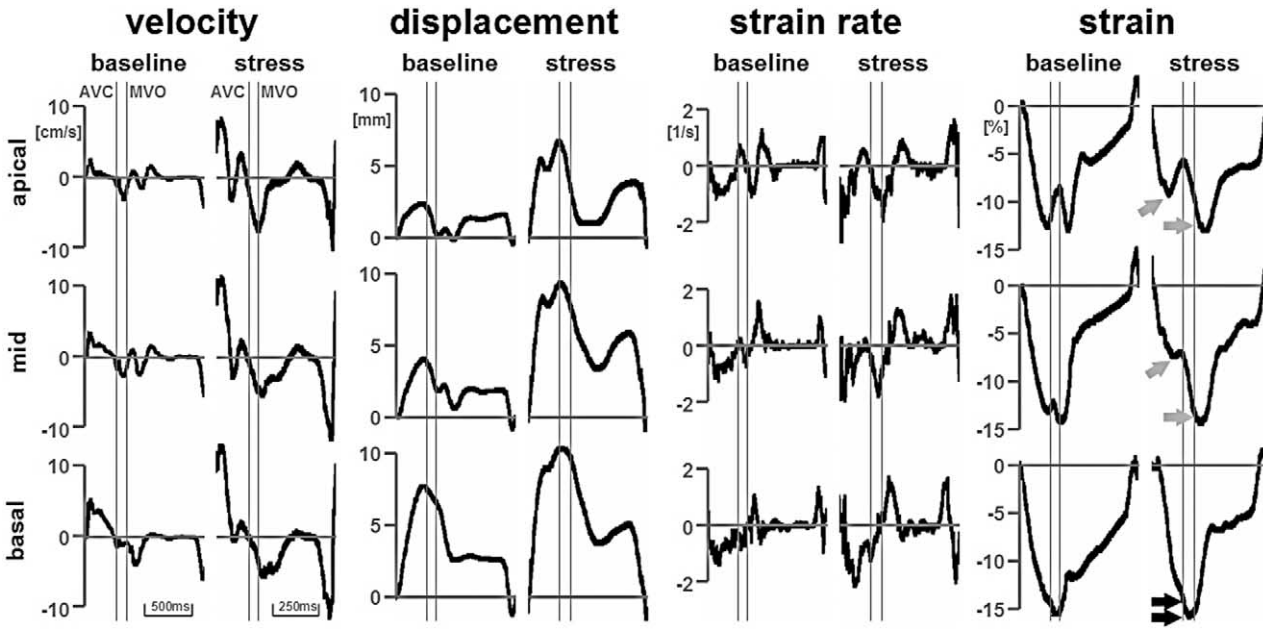

Fig. 5 Same patient as in Fig. 4. Curves of the apical, mid and basal segment of the anteroseptal wall compare velocity, displacement, strain rate and strain data from one heart cycle (RR interval) at baseline and during dobutamine stress. Note the apico-basal gradient in curve amplitude for TVI parameters while SRI parameters are similar in all segments. Note that only the strain and, less pronounced, strain rate curves reveal apical and mid-wall ischaemia by showing reduced systolic strain (first grey arrow) and marked post-systolic shortening (second grey arrow). The non ischaemic basal segment shows normal systolic and negligible post systolic shortening (black arrows). AVC, aortic valve closure; MVO, mitral valve opening.

Table 4 Sensitivities and specificities of different DSE analysis methods

Method	Parameter	Cut-off	Sensitivity (%)	Specificity (%)
Visual	Wall motion	New/increasing WMA	81	82
TVI	$V_{peak\,sys}$	$<$6.3/4.6/2.0 cm/s	74	63
SRI	$\varepsilon_{ps/max}$	$>$35%	82	85

WMA, wall motion abnormality; $V_{peak\,sys}$, peak systolic velocity; $\varepsilon_{ps/max}$, post-systolic shortening. Velocity cut-offs are given separately for basal, mid and apical level.

Clinical implications

Conventional DSE is based on visual assessment of regional myocardial function and is thus subjective. Both TVI and SRI are feasible during DSE. According to other studies,[8,9] velocity imaging may be used as a valid approach in patients with normal resting function. In a realistic clinical setting including patients with wall motion abnormalities at baseline, however, only SRI offered quantitative and objective parameters of clinical relevance which are at least equivalent to the eye of an experienced observer. Similar values of SRI parameters at the apical, mid-wall and basal level of the ventricle allowed the simple approach of using only one cut-off-value which is an advantage over TVI. PSS developing with dobutamine stress is strongly suggestive of stress-induced ischaemia (Figs. 4 and 5). PSS can be easily observed or excluded in 95% of the segments by SRI curved M-modes, despite artefacts which prevent a quantitative assessment of the data. While SRI was superior to TVI in identifying regional ischaemia, its diagnostic accuracy was similar to visual reading by an expert. Hence, SRI may be used as an additional tool to objectify DSE reading in difficult circumstances and to shorten the learning curves of novices.

Our study revealed a lower diagnostic accuracy of velocity parameters than other studies. In our opinion, this is explained by the inclusion of patients with wall motion abnormalities at baseline. These affect measurements in other segments of the same wall or in remote regions of the ventricle by tethering both at baseline and during dobutamine stress. Since such patients inevitably belong to the clinical routine of a stress echo lab, we feel that our approach offers a realistic estimate of the potential of the different techniques.

Limitations

This study sub-stratified myocardial segments into three levels: apical, mid and basal. Separate cut-off-values for each LV segment[8] or more sophisticated models which include more than one segment, age, gender and other

factors[9] may improve results that can be obtained by TVI. Such criteria for ischaemia, however, result in considerable complexity. Moreover, previous studies did not consider baseline wall motion abnormalities or counted the patient as positive for CAD if they were present.

Further studies are needed to investigate the applicability of SRI to patients with conduction disturbances or arrhythmias. In addition, SRI characteristics of scar, partial scar and dysfunctional but viable myocardium during DSE have to be addressed in man.[17]

While visual DSE reading was possible in 97% of the segments, quantitative analysis of TVI and SRI data was limited to 92% and 85%, respectively, by noise and artefacts. However, for the assessment of stress-induced ischaemia, visual analysis of SRI curved M-modes allows a recognition or exclusion of PSS in 95%.

Time demand for analysing TVI and, in particular, SRI data was high for this investigative study. Once markers of inducible ischaemia are well-defined, however, assessment of DSE studies may be performed within minutes.

Conclusion

In this study, TVI did not allow sufficiently reliable segmental recognition of stress-induced ischaemia, while SRI was able to objectively differentiate ischaemic and non-ischaemic myocardium. In particular, PSS measured by SRI identifies stress-induced ischaemia with high sensitivity and, if amplitude of PSS ($\varepsilon_{ps}/\varepsilon_{max}$) was taken into account, with good specificity, which was superior to all TVI parameters and more objective — although not more accurate — than conventional visual DSE assessment.

Acknowledgements

This work was in part supported by a grant from the "Staedler Stiftung", Nürnberg. Dr. Bogdan received a research grant from the German Society of Cardiology and an educational fellowship of the European Society of Cardiology. We thank Dipl.-Math. T. Reinecke and R. Minkenberg for their statistical counselling.

References

1. Mairesse GH, Marwick TH, Vanoverschelde JL et al. How accurate is dobutamine stress electrocardiography for detection of coronary artery disease? *J Am Coll Cardiol* 1994;**24**:920—7.
2. Pellikka PA, Roger VL, Oh JK, Miller FA et al. Stress echocardiography. Part II. Dobutamine stress echocardiography: techniques, implementation, clinical applications, and correlations. *Mayo Clin Proc* 1995;**70**:16—27.
3. Geleijnse ML, Fioretti PM, Roelandt JR. Methodology, feasibility, safety and diagnostic accuracy of dobutamine stress echocardiography. *J Am Coll Cardiol* 1997;**30**:595—606.
4. Hoffmann R, Lethen H, Marwick T et al. Analysis of interinstitutional observer agreement in interpretation of dobutamine stress echocardiograms. *J Am Coll Cardiol* 1996;**27**:330—6.
5. Hoffmann R, Marwick TH, Poldermans D et al. Refinements in stress echocardiographic techniques improve inter-institutional agreement in interpretation of dobutamine stress echocardiograms. *Eur Heart J* 2002;**23**:821—9.
6. Picano E, Lattanzi F, Orlandini A et al. Stress echocardiography and the human factor: the importance of being expert. *J Am Coll Cardiol* 1991;**17**:666—9.
7. Sutherland GR, Stewart MJ, Groundstroem KW et al. Color Doppler myocardial imaging: a new technique for the assessment of myocardial function. *J Am Soc Echocardiogr* 1994;**7**:441—58.
8. Cain P, Short L, Baglin T et al. Development of a fully quantitative approach to the interpretation of stress echocardiography using radial and longitudinal myocardial velocities. *J Am Soc Echocardiogr* 2002;**15**:759—67.
9. Mädler CF, Payne N, Wilkenshoff U et al., for the MYDISE Study Investigators. Non-invasive diagnosis of coronary artery disease by quantitative stress echocardiography: optimal diagnostic models using off-line tissue Doppler in the MYDISE study. *Eur Heart J*2003;**24**:1584—94.
10. Heimdal A, Støylen A, Torp H et al. Real-time strain rate imaging of the left ventricle by ultrasound. *J Am Soc Echocardiogr* 1998;**11**:1013—9.
11. Voigt JU, Arnold MF, Karlsson M et al. Assessment of regional longitudinal myocardial strain rate derived from Doppler myocardial imaging indices in normal and infarcted myocardium. *J Am Soc Echocardiogr* 2000;**13**:588—98.
12. Urheim S, Edvardsen T, Torp H et al. Myocardial strain by Doppler echocardiography: validation of a new method to quantify regional myocardial function. *Circulation* 2000;**102**:1158—64.
13. Voigt JU, Lindenmeier G, Exner B et al. Incidence and characteristics of segmental post-systolic longitudinal shortening in normal, acutely ischaemic and scarred myocardium. *J Am Soc Echocardiogr* 2003;**16**:415—23.
14. Jamal F, Strotmann J, Weidemann F et al. Noninvasive quantification of the contractile reserve of stunned myocardium by ultrasonic strain rate and strain. *Circulation* 2001;**104**:1059—65.
15. Weidemann F, Jamal F, Sutherland GR et al. Myocardial function defined by strain rate and strain during alterations in inotropic states and heart rate. *Am J Physiol Heart Circ Physiol* 2002;**283**:H792—9.
16. Pislaru C, Belohlavek M, Bae R et al. Regional asynchrony during acute myocardial ischaemia quantified by ultrasound SRI. *J Am Coll Cardiol* 2001;**37**:1141—8.
17. Weidemann F, Dommke C, Bijnens B et al. Defining the transmurality of a chronic myocardial infarction by ultrasonic strain-rate imaging implications for identifying intramural viability — an experimental study. *Circulation* 2003;**107**:883—8.
18. Voigt JU, Exner B, Schmiedehausen K et al. Strain-rate imaging during dobutamine stress echocardiography provides objective evidence of inducible ischemia. *Circulation* 2003;**107**:2120—6.
19. Kowalski M, Herbots L, Weidemann F et al. The potential value of ultrasonic deformation measurement in differentiating regional ischaemic substrates during dobutamine stress echocardiography. *Eur J Echocardiogr* 2003;**4**:23—8.
20. Hoffmann R, Ertune E, Nowak B et al. Strain rate measurements by Doppler echocardiography allows improved assessment of myocardial viability in patients with depressed left ventricular function. *J Am Coll Cardiol* 2002;**39**:443—9.