SEGMENTAL COLOR DOPPLER MYOCARDIAL IMAGING DERIVED PRE-EJECTION VELOCITIES ARE NOT CLINICALLY USEFUL IN THE ASSESSMENT OF POST-INFARCTION SCAR TRANSMURALITY

Tomas Skala^{a*}, Martin Hutyra^a, David Horak^b, Milos Taborsky^a

^a 1st Department of Internal Medicine (Cardiology), University Hospital Olomouc, I. P. Pavlova 6, 775 20 Olomouc, Czech Republic

^b Department of Radiodiagnostics, University Hospital Olomouc
E-mail: tomasskala@gmail.com

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Introduction. The presence of a velocity in isovolumic contraction phase (Vivc) evaluated using tissue Pulse wave Doppler myocardial imaging (PWDMI) correlates with a transmural extent of scar after myocardial infarction. The possible clinical usefulness of Vivc evaluated using color Doppler myocardial imaging (CDMI) in detection of a scar after myocardial infarction extent in patients with coronary heart disease (CHD) and low LV systolic function remains to be clarified.

Patients and methods. 57 patients with CHD (average LVEF 33.5±5%), examined echocardiographically (17-segment LV model, 689 segments evaluated) and by cardiac magnetic resonance. All segments were scanned for Vivc presence using CDMI. Vivc presence/absence was correlated with signs of a scar after MI in all segments and in akinetic segments separately.

Results. We found significantly larger values of wall thickness (8.2±2.2 vs. 7.1±1.9, p<0.0001), significantly lower values of average late enhancement (LE) extent (1.32±1.78 vs. 1.66±1.98, p=0.041) and LE/wall thickness ratio (20.1±29.8 vs. 29.6±36.7, p=0.008) in segments with present Vivc. Vivc presence in a segment with an abnormal wall motion had a sensitivity of 72.9% and a specificity of 35.7% in recognizing a segment without a transmural scar (LE/wall thickness ratio ≤75%).

Vivc absence in a segment with an abnormal wall motion had a sensitivity of 72.7% and a specificity of 41.2% in recognizing a segment with a transmural scar (LE/wall thickness ratio ≥75%).

Conclusions. Isovolumic velocities evaluation assessed using color Doppler myocardial imaging is not applicable in a real-world clinical setting. The presence or absence of a velocity pattern during LV isovolumic contraction is not useful in the assessment of a post-infarction scar transmurality.

INTRODUCTION

An accurate detection of viable myocardium is of great importance in patients with coronary heart disease (CHD) and impaired systolic function of left ventricle (LV) (ref.¹). The presence of a pre-ejection velocity (Vivc – velocity in isovolumic contraction phase) evaluated using tissue Pulse wave Doppler myocardial imaging

(PWDMI) correlates with a transmural extent of scar after myocardial infarction (MI) in experimental studies² and recently in a clinical study³. The possible clinical usefulness of Vivc evaluated using color Doppler myocardial imaging (CDMI) in detection of extent of a scar after myocardial infarction in patients with CHD and low LV systolic function remains to be clarified.

ABBREVIATIONS

CDMI	– Color Doppler myocardial imaging
CHD	– Coronary heart disease
EF	– Ejection fraction
IT	– Inversion time
LE	– Late enhancement
LV	– Left ventricle
MI	– Myocardial infarction
MR	– Cardiac magnetic resonance
PW	– Pulse Doppler wave
PWDMI	– Tissue Pulse wave Doppler myocardial imaging
TDE	– Tissue Doppler echocardiography
Vivc	– Pre-ejection velocity

PATIENTS AND METHODS

Patient group

57 patients of average age 69.3±15.9 years (50 men, 7 women) were included in the study. The baseline clinical characteristics are listed in Table 1. All patients had chronic ischemic heart disease with a depressed LV ejection fraction (EF) (average LVEF 33.5±5%). They all had stable LV dysfunction. Patients with a history of MI in the last 6 months were excluded. Those with an acute coronary syndrome or any sign of an acute myocardial ischemia as well as patients with a significant valvular disease were not included. All patients had a coronarogra-

phy and were then examined echocardiographically and by cardiac magnetic resonance (MR). All patients had sinus rhythm during all examinations.

Echocardiography

Echocardiography was performed on a GE Ultrasound Vivid 7 (GE Healthcare; Chalfont St. Giles, UK). A resting echocardiography examination with 1-lead ECG registration was performed in the standard way using 2, 3 and 4-chamber views according to a 17-segments LV model⁴. Individual walls were imaged separately to get a higher frame rate and optimized parallel beam alignment with longitudinal wall motion. The echocardiography machine was set-up to obtain an optimal tissue signal under standard clinical conditions (frame rate above 160 fps, gain 2 dB, scale 1,00 kHz, frequency 2,5 MHz, average smoothing 30 ms). All data were obtained during a calm end-expirium. Color-Doppler sequences superposed on 2D-image (3 cardiac cycles were recorded for every sequence) were saved in the archival program EchoPac 7 Option (version BT 06) and subsequently evaluated offline blindly without knowledge of the clinical status and results of other examinations. A region of interest was set to the middle of an analyzed segment. The pre-ejection phase was defined as an interval between the beginning of QRS complex and onset of flow in aorta evaluated using pulse Doppler wave (PW) signal at LV outflow tract. All segments were scanned for the presence or absence of Vivic.

Feasibility and reproducibility

Apical segments were excluded (57 of 969 segments). Only segments with a very good image quality were included in the analysis. Segments with poor image quality were not scanned for the presence of Vivic and thus excluded from analysis. A sum of 689 LV segments (76% of all possible LV segments) was included in the statistical analysis. To study the intra- and inter-observer variability, the presence or absence of Vivic was assessed in 87 segments with a very good image quality from 6 patients during one day and subsequently again after one week by two observers with experience with tissue Doppler echocardiography (TDE). Each observer placed a new sample volume in the studied segment. Examinations by two observers were performed 5 min apart. Inter-observer agreement in detection of a present Vivic was 100% (30/30) for basal segments, 100% (29/29) for middle segments and 89% (25/28) for the apical segments. Intra- and inter-observer variability of evaluation of Vivic presence were 8.9 ± 6.1 and 9.7 ± 7.6 in average, 6.7 ± 5.2 and 8.1 ± 7.0 separately for basal segments, 8.2 ± 5.8 and 8.4 ± 7.0 for middle segments and 11.8 ± 7.3 and 12.3 ± 8.7 for apical segments. An evident increase in variability of examinations from basal to apical segments can be explained by an unsatisfying incident angle and diminishing systolic velocities from base to apex. Apical segments were thus not included into statistical analysis.

Table 1. Patient group characteristics.

Men / Women	50/7
Average age	66.4±15.9
MI in history	44 (77%)
Angina pectoris (CCS)	1.6±0.6
LVEF	33.5±5%
Heart failure symptoms	
NYHA I	11 (19%)
NYHA II	26 (46%)
NYHA III	20 (35%)
NYHA IV	0 (%)
Type 2 diabetes mellitus	24 (42%)
Arterial hypertension	41 (72%)
Stroke in history	11 (19%)
Smoking in history	22 (39%)
Coronarography: 2-vessel disease	21 (37%)
Coronarography: 3-vessel disease	36 (63%)
Number of CABG	3.2±1.02
Medical therapy:	
ACEI/ARB	48 (84%)
BB	53 (93%)
CaB	13 (23%)

Table 2. Vivic presence.

LE/wall thickness <75%		95% CI (confidence interval)
Sensitivity	72.9 %	69.6 % - 76.2 %
Specificity	35.7 %	32.2 % - 39.3 %
Accuracy	60.2 %	56.6 % - 63.9 %
PPV	68.7 %	65.2 % - 72.1 %
NPV	40.6 %	36.9 % - 44.2 %

A segment with an abnormal wall motion. Vivic present. Usefulness of Vivic presence in detecting a viable segment (LE/wall thickness ≤75%).

Table 3. Vivic absence.

LE/wall thickness >75%		95% CI (confidence interval)
Sensitivity	72.7 %	69.4 % - 76.0 %
Specificity	41.2 %	37.5 % - 44.9 %
Accuracy	66.5 %	62.9 % - 70.0 %
PPV	83.4 %	80.6 % - 86.2 %
NPV	27.1 %	23.7 % - 30.4 %

A segment with an abnormal wall motion. Vivic absent. Usefulness of Vivic absence in detecting a nonviable segment (LE/wall thickness ≥75%).

Vs – peak systolic velocity. Ve – early diastolic velocity. Va – late diastolic velocity. MVO – mitral valve opening. MVC – mitral valve closure. AVO – aortic valve opening. AVC – aortic valve closure.

The cardiac MR was performed on the Siemens Magnetom Avanto (Siemens, Erlangen, Germany), Q engine (33 mT/m), Tim 76x18, installed in 2005, equipped with the Syngo 2004A software and complete cardio-MR equipment (Advanced Cardiac Package, post-processing software Argus). A standard protocol of myocardial viability evaluation included a functional cinematic examination focused on LV using TrueFisp2D-CINE sequence (evaluation of end-diastolic myocardial thickness and LVEF) and late enhancement (LE) with high space resolution sequences CE-IR-MRI. Both types of LV myocardium display were performed at consonant planes (series of layers at short-axis plane, 4-chamber and 2-chamber projection and apical long axis). For LE depiction a paramagnetic extra-cellular contrast agent based on gadolinium was applied in a unified dose of 20 ml (0.5 molar contrast agent) or 10 ml (1 molar contrast agent) respectively. Scanning was started 10 minutes after contrast agent application. Standardly a modern sequence PSIR-TrueFisp2D (PSIR = Phase Sensitive Inversion Recovery) was used. A manual adjustment of inversion time (TI) for viable myocardium signal zero setting was not necessary. Automatically reconstructed images of this sequence were used for the myocardial viability assessment. LV segmentation was

Statistical analysis

Statistical analysis was performed on the statistical software SPSS 15. Values of $p \leq 0,05$ were evaluated as statistically significant. The chi square test and Mann-Whitney test were used for the statistical analysis: the results of Vvc presence measured echocardiographically were compared to magnetic resonance (LE extent/wall thickness ratio parameter) as a reference method.

- 1) Presence or absence of Vvc in all segments was compared with wall thickness, average LE extent and LE/wall thickness ratio to evaluate correlation of Vvc with the signs of a scar after MI.
- 2) Of all 689 segments 148 were evaluated as akinetic. Vvc presence/absence was evaluated in these akinetic segments. A specificity, sensitivity, positive and

negative predictive value of Vivic presence or absence respectively in accuracy of detection of a scar after MI were calculated for LE extent/wall thickness ratio in individual LV segments on MR below and above 75%. This cut-off value was based on previous studies⁵ chosen to assess the usefulness of Vivic presence/absence in exclusion/confirmation of a transmural scar in each individual segment.

RESULTS

- 1) Nonparametric Mann-Whitney test showed significantly larger values of wall thickness (8.2 ± 2.2 vs. 7.1 ± 1.9 , $p < 0.0001$) (Fig. 2) and significantly lower values of an average LE extent (1.32 ± 1.78 vs. 1.66 ± 1.98 , $p = 0.041$) (Fig. 3) and LE/wall thickness ratio (20.1 ± 29.8 vs. 29.6 ± 36.7 , $p = 0.008$) (Fig. 4) in segments with present Vivic.
- 2) Vivic presence in a segment with an abnormal wall motion had a sensitivity of 72.9% and a specificity of 35.7% in recognizing a segment without a transmural scar (LE/wall thickness ratio $\leq 75\%$). The accuracy of Vivic presence in detection of a segment without a transmural scar was 60.2% (Table 2). Vivic absence in a segment with an abnormal wall motion had a sensitivity of 72.7% and a specificity of 41.2% in recognizing a segment with a transmural scar (LE/wall thickness ratio $\geq 75\%$). The accuracy of Vivic absence in detection of a segment with a transmural scar was 66.5% (Table 3).

DISCUSSION

In an experimental model of MI a presence of Vivic was linked with the presence of a non-transmural necrosis. An absence of Vivic, on the other hand, pointed to a transmural scar. The pathophysiologic basis for this is the ability of a viable myocardial segment to perform a minimal contraction power during the isovolumic contraction phase, in which the intraventricular pressure rises, but is still low compared to the ejection phase, in which the contraction force of the particular segment is not sufficient enough and it appears as dysfunctional. Nonviable segments are not able to generate contraction even in the pre-ejection phase^{2,6}. Pathophysiologically the presence of pre-ejection velocities in the isovolumic contraction phase should reflect the presence of a viable myocardium in the particular segment and vice-versa; the absence of pre-ejection velocities should mean that there is not a remarkable amount of viable myocardium in the particular segment. These velocities are detectable on TDE as a shortly lasting positive wave before a subsequent positive wave representing systolic myocardial motion (Fig. 1).

According to a recent clinical study, the evaluation of pre-ejection velocities should be useful as a marker of myocardial viability also under clinical conditions³. Penicka et al.³ evaluated the presence of Vivic using PDWMI. The

Fig. 2. Correlation of Vivic presence/absence with wall thickness.

(thick line inside of the box = median, bottom of the box = 1st quartile, upper edge of the box = 3rd quartile, horizontal line above the box = minimal and maximal proximal value, circle = distant value, star = extreme)

Fig. 3. Correlation of Vivic presence/absence with LE/wall thickness ratio.

(thick line inside of the box = median, bottom of the box = 1st quartile, upper edge of the box = 3rd quartile, horizontal line above the box = minimal and maximal proximal value, circle = distant value, star = extreme)

possible clinical usefulness of Vivic evaluated using CDMI in the detection of the extent of a scar after myocardial infarction in patients with CHD and low LV systolic function remains to be clarified.

MRI was used as a reference method to assess the extent of post-infarction scar presence and transmural. Late enhancement evaluation corresponds well with the

Fig. 4. Correlation of Vivic presence/absence with average LE.

(thick line inside of the box = median, bottom of the box = 1st quartile, upper edge of the box = 3rd quartile, horizontal line above the box = minimal and maximal proximal value, circle = distant value, star = extreme)

presence and extent of a scar after MI according to several studies. In myocardial segments with LE/wall thickness ratio on MR $\geq 75\%$ a transmural scar is known to be present and a contractile recovery is unlikely⁷.

We have found a significant correlation of Vivic with the signs of a scar after MI (wall thickness, average LE extent, LE/wall thickness ratio) generally in all evaluated segments. This finding supports the above mentioned pathophysiological relation of Vivic presence/absence and post-infarction scar presence and transmurality.

The question is in which segments it is useful to evaluate Vivic presence? There is no need to assess myocardial viability in segments with normal wall motion, because these segments are by definition viable. Hence for further analysis we included only the segments evaluated as akinetic on echocardiography. These segments could have a transmural scar or they could be hibernated due to a prolonged ischemia with a nontransmural scar or a no scar at all. The clinical question is whether Vivic presence or absence can help us to distinguish these clinical units in individual segments.

The Vivic presence in akinetic segments had in our study a sensitivity of 72.9% and a specificity of 35.7% in recognizing a segment without a transmural scar (LE/wall thickness ratio $\leq 75\%$). The accuracy of Vivic presence in detection of a segment without a transmural scar was 60.2%.

On the other hand Vivic absence in a segment with an abnormal wall motion had a sensitivity of 72.7% and a specificity of 41.2% in recognizing a segment with a transmural scar (LE/wall thickness ratio $\geq 75\%$). The accuracy of Vivic absence in detection of a segment with a transmural scar was 66.5%.

Regarding these results we can not reliably presume a transmural (LE extent $\geq 75\%$) scar just from the absence of Vivic in a given segment. We also can not presume a non-transmural (LE extent $\leq 75\%$) scar just from the presence of Vivic. Hence viability of myocardium in the particular segment can not be confirmed or disapproved merely from an absence or presence of Vivic evaluated using CDMI. In our patient group, the assessment of presence or absence of Vivic does not represent a clinically useful marker of viability in the particular segment.

The difference of these results from those earlier published could be explainable with limitations of this parameter when evaluated using CDMI. There are several limitations present using CDMI for evaluation of Vivic. CDMI data must be collected at frame rates in excess of 100/s. These are not obtainable if a standard wide sector imaging contralateral walls is used. Optimally to capture such short lived events such as Vivic even higher frame rates (in excess of 400 frames/s) should be used. This is hardly achieved using CDMI and these parameters surely are not part of a standard echocardiographic machine setting in daily praxis. Prior studies used pulsed tissue Doppler which has a higher temporal resolution than color tissue Doppler imaging³. Capturing of such brief events as Vivic could also be effected by sampling rate. An average smoothing of 30 ms was employed in this study. This could have limited determination of peak Vivic. Smoothing leads to a possibility of omission of Vivic but on the other hand smaller value of average smoothing results in the presence of a lot of artifacts making proper evaluation of Vivic presence difficult. Another limitation of Vivic detection using CDMI may be influence of deformation of apical and mid segments. This deformation could lead to a velocity trace of basal segments of the same wall and thus possibly render evaluation of velocities in basal segments impossible. The above stated limitations of usefulness of CDMI in myocardial velocities evaluation seem to be the reason why this methodology is according to these results not clinically applicable. Another distortion of the predictive value of Vivic presence can be caused by the presence or absence of resting myocardial ischemia in the particular segment interfering with the regional tissue velocities. A poor echocardiography image quality in some patients is also a limiting factor. Assessment of tissue velocities is also difficult in apical segments considering an unsatisfactory incidence angle and low tissue velocity values when minimal Vivic can be overlooked and thus falsely evaluated as not present.

CONCLUSION

Isovolumic velocities evaluation assessed using color Doppler myocardial imaging is not applicable in a real-world clinical setting. The presence or absence of a velocity pattern during LV isovolumic contraction is not useful in the assessment of a post-infarction scar transmurality.

REFERENCES

1. Allman KC, Shaw LJ, Hachamovitch R, Udelson JE. Myocardial viability testing and impact of revascularization on prognosis in patients with coronary artery disease and left ventricular dysfunction: a meta-analysis. *J Am Coll Cardiol* 2002; 39:1151–58.
2. Pislaru C, Bruce CJ, Belohlavek M, Seward JB, Greenleaf JF. Intracardiac measurement of pre-ejection myocardial velocities estimates the transmural extent of viable myocardium early after reperfusion in acute myocardial infarction. *J Am Coll Cardiol* 2001; 38:1748–56.
3. Penicka M, Tousek P, De Bruyne B, Wijns W, Lang O, Madaric J, Vanderheyden M, Tintera J, Maly M, Widimsky P, Bartunek J. Myocardial positive pre-ejection velocity accurately detects presence of viable myocardium, predicts recovery of left ventricular function and bears a prognostic value after surgical revascularization. *Eur Heart J* 2007; 28(11):1366–73.
4. Cerqueira MD, Weissman NJ, Dilsizian V, Jacobs AK, Kaul S, Laskey WK, Pennell DJ, Rumberger JA, Ryan T, Verani MS. Standardized myocardial segmentation and nomenclature for tomographic imaging of the heart. A statement for healthcare professionals from the Cardiac Imaging Committee of the Council on Clinical Cardiology of the American Heart Association. *Circulation* 2002; 105:539–542.
5. Schuijf J, Kaandorp T, Lamb H, Geest R, Viergever E, Wall E, De Roos A, Bax J. Quantification of myocardial infarct size and transmural by contrast-enhanced magnetic resonance imaging in men. *Am J Cardiol*. 2004;Aug 1;94(3):284–8.
6. Edvardsen T, Urheim S, Skulstad H. Quantification of Left Ventricular Systolic Function by Tissue Doppler Echocardiography. Added Value of Measuring Pre- and Postejction Velocities in Ischemic Myocardium. *Circulation* 2002; 105(17):2071–77.
7. Kuhl HP, Beek AM, van der Weerd AP, Hofman MBM, Visser CA, Lammertsma AA, Heussen N, Visser FC, van Rossum AC. Myocardial viability in chronic ischemic heart disease: Comparison of contrast-enhanced magnetic resonance imaging with 18F-fluorodeoxyglucose positron emission tomography. *J Am Coll Cardiol* 2003; 41(8):1341–1348.