Kardiologia Polska 2016; 74, 9: 1010–1015; DOI: 10.5603/KP.a2016.0040 ISSN 0022–9032

ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Transthoracic ultrasonic tissue indices identify patients with severe left anterior descending artery stenosis. Correlation with fractional flow reserve. Pilot study

Piotr Dobrowolski[1], Mirosław Kowalski[1], Justyna Rybicka[1], Agnieszka Lech[1], Paweł Tyczyński[2], Adam Witkowski[2], Piotr Hoffman[1]

[1]Department of Congenital Heart Diseases, Institute of Cardiology, Warsaw, Poland

[2]Department of Interventional Cardiology and Angiology, Institute of Cardiology, Warsaw, Poland

Abstract

Background and aim: The aim of this study was to evaluate the potential clinical application of ultrasonic tissue indices, with a focus on systolic strain (SS) and systolic strain rate (SSR) parameters derived from transthoracic echocardiography, in the assessment of left anterior descending artery (LAD) stenosis.

Methods: The data of 30 patients with significant LAD stenosis were analysed. All patients underwent transthoracic echocardiography to obtain systolic myocardial velocity (Sm), longitudinal SS, and SSR from basal, mid, and apical segments of anterior and inferior walls in two-chamber apical view. Severity of LAD obstruction was measured by means of fractional flow reserve (FFR) during coronary catheterisation.

Results: Systolic velocities, strain, and strain rate measured in basal, middle, and apical segments of the anterior left ventricular (LV) wall were lower when compared to those obtained from the corresponding, i.e. unaffected, inferior LV wall. There was a significant correlation between FFR and the value of SS, SSR characterising the apical LV segment of the anterior wall ($r = –0.583$, $p = 0.01$; $r = –0.598$, $p = 0.01$, respectively). Moreover, we found significant correlation between FFR and Sm in the mid-segment of the LV anterior wall ($r = 0.611$, $p = 0.009$).

Conclusions: We conclude that SS and SSR obtained from the apical segment of the anterior LV wall may be related to the severity of LAD stenosis.

Key words: echocardiography, systolic strain, systolic strain rate, left anterior descending artery stenosis, coronary disease, fractional flow reserve

Kardiol Pol 2016; 74, 9: 1010–1015

INTRODUCTION

In patients with coronary artery disease, evaluation of the functional significance of intermediate artery lesions remains a challenge. On the basis of pressure-derived analysis of stenosis during maximal coronary dilation, the concept of myocardial fractional flow reserve (FFR) has been developed as an invasively determined index of the functional severity of coronary stenosis [1, 2]. This index is widely accepted as the gold standard for the assessment of intermediate coronary artery narrowing [2, 3]. The noninvasive measurement of left anterior descending artery (LAD) stenosis by transthoracic echocardiography is feasible but it has some limitations [4]. Direct visualisation of coronary artery with the measurement of flow velocity remains difficult for everyone. Another approach could be dobutamine stress echocardiography applied both on

Address for correspondence:
Piotr Dobrowolski, MD, PhD, Department of Congenital Heart Diseases, Institute of Cardiology, ul. Alpejska 42, 04–628 Warszawa, Poland, tel: +48 22 34 34 263, e-mail: p.dobrowolski@ikard.pl

Received: 09.12.2015 **Accepted:** 09.03.2016 **Available as AoP:** 01.04.2016

the basis of traditional qualification and quantitative assessment [5]. In the latter, deformation indices have been extensively used (strain, strain rate). So far, there have not been many studies on the relationship between selected tissue indices obtained from the anterior left ventricular (LV) wall and FFR results. Therefore, the aim of this study was to investigate potential clinical application of systolic strain (SS) and systolic strain rate (SSR) parameters, as well as other ultrasonic indices derived from rest transthoracic echocardiography, in the assessment of LAD stenosis in comparison to FFR results.

METHODS

Study population

A total of 30 patients with suspicion of significant, isolated (> 70% luminal narrowing) LAD stenosis by quantitative coronary angiography and computed tomography angiography underwent transthoracic echocardiography and FFR study. Exclusion criteria were history of myocardial infarction, unstable angina, congestive heart failure, persistent atrial or ventricular arrhythmia, uncontrolled hypertension, atrioventricular block, atrial fibrillation, more than mild valvular heart disease, or LV ejection fraction (LVEF) less than 35% and obstructive pulmonary disease. All patients were in stable sinus rhythm and had normal resting LV function. The study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki. It was approved by the local Research Ethics Committee. Written informed consent was also obtained from each patient.

Standard echocardiography

All patients underwent a complete transthoracic echocardiographic study with the use of GE Medical System Vivid 7 (GE Healthcare) and with a 2.5-MHz transducer. M-mode, two-dimensional, tissue Doppler echocardiography were obtained by imaging in parasternal long and short axes and in apical four-, three-, and two-chamber views. The left ventricle was divided according to the 16-segment model of the American Society of Echocardiography [6]. The values of all echocardiographic parameters were obtained as the average of three consecutive cardiac cycles. LV end-systolic and LV end-diastolic diameters, as well as interventricular septal diastolic diameter and posterior LV wall diastolic diameter, were measured using the M-mode technique. LV systolic function was evaluated by LVEF, mitral lateral annular systolic velocity wave (S'LV), and LV outflow tract velocity-time integral. LVEF was calculated using the biplane Simpson formula. S'LV was measured using Doppler tissue imaging placed sample volume in the basal segment of the LV lateral wall in a four-chamber view. All parameters were recorded in accordance with current guidelines [7].

Strain and strain rate imaging

After performing conventional echocardiography, strain rate images were obtained with commercially available echocardiography equipment GE Medical System Vivid 7 (GE Healthcare). Apical four-, three-, and two-chamber colour Doppler tissue imaging were taken at a high frame rate (150–200 fps) and analysed using Echo Pac 3.0 (GE Medical System). The region of interest was placed at basal, mid, and apical segments of LV anterior and inferior walls. To determine longitudinal strain and strain rates, data were averaged from three consecutive cardiac beats at each site. An offset to measure strain and strain rate was set at 9–11 mm. Manual tracking throughout the cardiac cycle was used for all the patients. Aortic valve closure was preserved as a marker for end systole. SS was defined as the magnitude of the deformation measured from end diastole to end systole. SSR described the maximum rate of deformation during systole.

Fractional flow reserve assessment

Fractional flow reserve was calculated as the ratio of mean distal coronary pressure to the mean aortic pressure at rest and during maximal hyperaemia. FFR measurement was performed with a 0.014-inch pressure wire (RADI Medical systems, Uppsala, Sweden, or PressureWire® Aeris, St. Jude Medical) advanced via a 6 Fr guiding catheter distal to the target coronary lesion. To achieve the maximal hyperaemia, continuous adenosine infusion (140 μg/min/kg) via a forearm vein was administered up to 3 min. FFR value ≤ 0.8 was considered functionally significant.

Statistical analysis

Collected data are presented as mean ± standard deviation, and frequency is presented as percentage. Student's t-test was used to compare the mean differences between basal, mid, and apical segments of inferior wall variables and anterior LV wall strain, strain rate, and velocities. Pearson's correlation was used to investigate the correlation of variables. Parameters identified as statistically significant based on univariate analysis ($p < 0.05$) were included in the multivariable linear regression model to determine the combined effect of several variables on the prevalence of the characteristics. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using the commercially available computer software PASW Statistics 18 (SPSS, Chicago, IL).

RESULTS

The data sets of 30 patients were obtained and analysed. The mean age of the study subjects was 62.6 ± 7.5 years (range 60.1–65.1 years; 21 males and 9 females). Mean heart rate was 65 ± 11 bpm. LVEF was above 50% in all cases, and mean LVEF amounted to 54.5 ± 8.0%. The baseline echocardiographic characteristics of the patients are shown

Table 1. Echocardiographic characteristic of study subjects

Variables	
LVEDd [mm]	48.9 ± 5.1
LVESd [mm]	33.3 ± 6.8
IVSd [mm]	11.7 ± 1.6
PWd [mm]	11.5 ± 1.5
S'LV [cm/s]	7.5 ± 2.0
GLS [%]	–16.6 ± 3.4
LVOT VTI [cm]	21.5 ± 3.5

LVEDd — left ventricular end-diastolic diameter; LVESd — left ventricular end-systolic diameter; IVSd — intraventricular septum diastolic diameter; PWd — posterior wall diastolic diameter; S'LV — mitral lateral annular systolic velocity wave; GLS — global longitudinal strain; LVOT VTI — left ventricular outflow tract velocity-time integral

in Table 1. Mean FFR value was 0.78 ± 0.13. In 15 (50%) patients FFR was less than 0.8.

Systolic velocity, SS, and SSR measured in basal, mid, and apical segments of the anterior LV wall were lower when compared to those obtained from the corresponding, i.e. unaffected, inferior LV wall in all patients (Table 2).

There was a significant correlation between FFR and the value of SS and SSR obtained only from the apical segment of the anterior LV wall (r = –0.583, p = 0.01; r = –0.598, p = 0.01, respectively). Moreover, we found a significant correlation between FFR and systolic myocardial velocity (Sm) in the mid segment of the anterior LV wall (r = 0.611, p = 0.009).

To evaluate independent factors related to FFR value, a linear regression model was performed. The factor independently associated with FFR was only SSR measured in the apical segment of the anterior wall (Table 3).

DISCUSSION

In some patients the appropriate assessment of the severity of coronary artery stenosis continues to be a challenge for cardiologists. The quantification of coronary artery lesion does not describe the amount of ischaemia in the relevant territory. A number of methods can give an insight into regional myocardial performance. One of these is echocardiography, which is widely available and cheap but yet subjective [8].

Table 2. Differences in systolic myocardial velocities (Sm), systolic strain (SS), and systolic strain rate (SSR) parameters measured on anterior and inferior wall

Variables	Anterior wall	Inferior wall	P
Sm — basal segment [cm/s]	4.2 ± 1.2	6.2 ± 1.4	< 0.0001
Sm — middle segment [cm/s]	2.9 ± 1.1	4.1 ± 1.4	< 0.0001
Sm — apical segment [cm/s]	1.9 ± 1.4	2.3 ± 1.3	< 0.0001
SSR — basal segment [s^{-1}]	–0.9 ± 0.4	–1.2 ± 0.4	< 0.0001
SSR — middle segment [s^{-1}]	–0.7 ± 0.4	–1.1 ± 0.3	< 0.0001
SSR — apical segment [s^{-1}]	–0.8 ± 0.4	–1.2 ± 0.5	< 0.0001
SS — basal segment [%]	-13.9 ± 7.7	–20.5 ± 5.1	< 0.0001
SS — middle segment [%]	–16.8 ± 3.3	–19.3 ± 5.5	< 0.0001
SS — apical segment [%]	–16.6 ± 3.9	–19.5 ± 6.4	< 0.0001

Table 3. Univariate and multivariate linear regression model for factors associated with fractional flow reserve value

Variables	Univariate model		Multivariate model	
	β	P	β	P
Age	–0.377	0.08		
Gender	0.141	**0.001**		
Basal ANT SSR	0.211	0.41		
Mid ANT SSR	–0.303	0.20		
Apical ANT SSR	–0.598	**0.01**	–0.598	**0.01**
Basal ANT SS	0.384	**0.001**		
Mid ANT SS	–0.073	0.78		
Apical ANT SS	–0.583	0.01		

ANT — anterior wall; SSR — systolic strain rate; SS — systolic strain

Ultrasonic strain and strain rate can help to overcome the subjectivity of the method [9, 10]. In the recent years, these techniques have been extensively used to differentiate clinically significant coronary stenosis [11–13]. Ultrasonic strain and strain rate are, in theory, independent of the overall heart motion and can be reliably used to measure regional myocardial deformation and deformation rate [10, 14]. It is known that Sm, SS, and SSR are different in particular walls of LV. In the HUNT study, which investigated the distribution of longitudinal strain and strain rate in a healthy population of 1296 subjects, the authors did not find statistically important differences between basal, mid, and apical segments of anterior and inferior wall [15]. In the presented study, we evaluated patients with LAD stenosis confirmed in computed tomography or coronary catheterisation. We found that Sm, SS, and SSR measured in basal, mid, and apical segments of the anterior LV wall were lower when compared to those obtained from the corresponding, i.e. unaffected, inferior LV wall. Ojaghi-Haghighi et al. [16] evaluated 14 patients with severe LAD stenosis, who underwent successful selective percutaneous coronary intervention (PCI). In this study the referenced myocardial deformation indices (SS and SSR) were recorded before and after PCI, both at rest and during stress echo test. The authors showed differences in SS and SSR in resting condition and during stress test echocardiography before and after PCI of LAD [16]. Edvardsen et al. [17] evaluated whether strain rate imaging could detect acute myocardial ischaemia, and compared the method with tissue Doppler imaging during acute coronary ischaemia. They examined patients undergoing angioplasty of the LAD, and they assessed LV longitudinal wall motion by tissue velocities and strain obtained from the apical four-chamber view. They concluded that the strain rate imaging detected longitudinal dyskinesia during occlusion of the LAD more frequently than the tissue Doppler velocity. Weidemann et al. [18] evaluated patients with acute ST elevation myocardial infarction and found that before and after PCI both strain and strain rate were markedly reduced in the ischaemic segments as compared with the non-ischaemic remote regions [18].

Fractional flow reserve is defined as the ratio of maximum blood flow in a stenotic coronary artery in reference to normal maximum flow in the same vessel [19]. In contrast to other invasive indices, FFR has a direct clinical relevance for determining critical coronary stenosis, which causes myocardial ischaemia [20]. Compared to other invasive indices, FFR is not dependent on changes in heart rate, blood pressure, or contractility. An approved correlation between FFR and tissue echocardiographic parameters would make transthoracic echo scan a clinically useful tool for diagnosis of the severity of coronary artery disease. Dagdelean et al. [21] enrolled in their study 17 patients, and FFR was studied in 22 vessels, in which 10 lesions were found to be critically important. There were no differences in Sm, SSR, and SS values between critical or noncritical FFR groups in resting condition. Baseline Sm value and change between baseline and peak Sm and SS during stress echocardiography were significantly lower in the noncritical FFR group ($p < 0.01$, $p < 0.001$, $p < 0.001$, respectively). The authors found mild correlation between FFR and SSR ($r = 0.47$, $p = 0.044$) and good correlation with SS ($r = 0.66$, $p = 0.002$). The authors concluded that quantification of regional myocardial deformation by using stress echocardiography rather than the motion would be more appropriate in detecting the ischaemic dysfunctional segment supplied by the vessel with critical stenosis. Strain measurement during the dobutamine infusion could then provide information on the FFR results of the culprit vessel.

To the best of our knowledge, there are no studies to investigate the direct correlation between FFR measurement and strain and strain rate parameters obtained from the territory of the LV segment supplied by the relevant vessel in resting echocardiography. In the presented study statistically significant differences were observed in systolic velocities, strain, and strain rate between the anterior and inferior wall. We also found a correlation between FFR results and SS and SSR obtained from the apical segment of the LV anterior wall ($r = -0.583$, $p = 0.01$; $r = -0.598$, $p = 0.01$, respectively). We managed to document that tissue velocity, SS, and SSR might be promising for the differentiation between the ischaemic myocardial segment and the non-ischaemic during resting echocardiography as compared to the severity of the supplying artery, i.e. LAD.

CONCLUSIONS

Systolic strain rate measured in the apical segment of the anterior wall may be related to the severity of LAD stenosis in resting echocardiography. These data might be implemented in a clinical setting. It should be underlined that the described method is completely non-invasive. This study may help to predict the functional improvement of the myocardial wall before revascularisation.

Future studies including a larger study population and more selective cases will be needed to show the accuracy of SSR imaging results in resting condition when compared with FFR values.

Conflict of interest: *none declared*

References

1. Pijls NH, Van Gelder B, Van der Voort P et al. Fractional flow reserve. A useful index to evaluate the influence of an epicardial coronary stenosis on myocardial blood flow. Circulation, 1995; 92: 3183–3193.
2. Windecker S, Kolh P, Alfonso F et al. 2014 ESC/EACTS Guidelines on myocardial revascularization. Kardiol Pol, 2014; 72: 1253–1379. doi: 10.5603/KP.2014.0224.
3. Bech GJ, De Bruyne B, Pijls NH et al. Fractional flow reserve to determine the appropriateness of angioplasty in moderate coronary stenosis: a randomized trial. Circulation, 2001; 103: 2928–2934.

4. Colonna P, D'Agostino C, Del Salvatore B et al. New echocardiographic technologies in the study of acute myocardial infarction. Ital Heart J, 2004; 5 (Suppl. 6): 25S–40S.
5. Franke A, Hoffmann R, Kuhl HP et al. Non-contrast second harmonic imaging improves interobserver agreement and accuracy of dobutamine stress echocardiography in patients with impaired image quality. Heart, 2000; 83: 133–140.
6. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J Am Soc Echocardiogr, 2005; 18: 1440–1463. doi: 10.1016/j.echo.2005.10.005.
7. Lang RM, Bierig M, Devereux RB et al. Recommendations for chamber quantification. Eur J Echocardiogr, 2006; 7: 79–108. doi: 10.1016/j.euje.2005.12.014.
8. 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: 666–669.
9. Kowalski M, Kukulski T, Jamal F et al. Can natural strain and strain rate quantify regional myocardial deformation? A study in healthy subjects. Ultrasound Med Biol, 2001; 27: 1087–1097. doi: 10.1016/S0301-5629(01)00388-X.
10. 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: 1158–1164. doi: 10.1161/01.CIR.102.10.1158.
11. 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: 1059–1065. doi: 10.1161/hc3501.093818.
12. Voigt JU, Exner B, Schmiedehausen K et al. Strain-rate imaging during dobutamine stress echocardiography provides objective evidence of inducible ischemia. Circulation, 2003; 107: 2120–2126. doi: 10.1161/01.CIR.0000065249.69988.AA.
13. Weidemann F, Jung P, Hoyer C et al. Assessment of the contractile reserve in patients with intermediate coronary lesions: a strain rate imaging study validated by invasive myocardial fractional flow reserve. Eur Heart J, 2007; 28: 1425–1432. doi: 10.1093/eurheartj/ehm082.
14. Abraham TP, Belohlavek M, Thomson HL et al. Time to onset of regional relaxation: feasibility, variability and utility of a novel index of regional myocardial function by strain rate imaging. J Am Coll Cardiol, 2002; 39: 1531–1537.
15. Dalen H, Thorstensen A, Aase SA et al. Segmental and global longitudinal strain and strain rate based on echocardiography of 1266 healthy individuals: the HUNT study in Norway. Eur J Echocardiogr, 2010; 11: 176–183. doi: 10.1093/ejechocard/jep194.
16. Ojaghi-Haghighi Z, Abtahi F, Fazlolah S et al. Coronary flow reserve, strain and strain rate imaging during pharmacological stress before and after percutaneous coronary intervention: comparison and correlation. Echocardiography, 2011; 28: 570–574. doi: 10.1111/j.1540-8175.2011.01366.x.
17. Edvardsen T, Skulstad H, Aakhus S et al. Regional myocardial systolic function during acute myocardial ischemia assessed by strain Doppler echocardiography. J Am Coll Cardiol, 2001; 37: 726–730.
18. Weidemann F, Wacker C, Rauch A et al. Sequential changes of myocardial function during acute myocardial infarction, in the early and chronic phase after coronary intervention described by ultrasonic strain rate imaging. J Am Soc Echocardiogr, 2006; 19: 839–847. doi: 10.1016/j.echo.2006.01.024.
19. Pijls NH, van Son JA, Kirkeeide RL et al. Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. Circulation, 1993; 87: 1354–1367.
20. Pijls NH, De Bruyne B, Peels K et al. Measurement of fractional flow reserve to assess the functional severity of coronary-artery stenoses. N Engl J Med, 1996; 334: 1703–1708. doi: 10.1056/NEJM199606273342604.
21. Dagdelen S, Yuce M, Emiroglu Y et al. Correlation between the tissue Doppler, strain rate, strain imaging during the dobutamine infusion and coronary fractional flow reserve during catheterization: a comparative study. Int J Cardiol, 2005; 102: 127–136. doi: 10.1016/j.ijcard.2004.05.012.

Cite this article as: Dobrowolski P, Kowalski M, Rybicka J et al. Transthoracic ultrasonic tissue indices identify patients with severe left anterior descending artery stenosis. Correlation with fractional flow reserve. Pilot study. Kardiol Pol, 2016; 74: 1010–1015. doi: 10.5603/KP.a2016.0040.

Zastosowanie tkankowej echokardiografii przezklatkowej do identyfikacji pacjentów z ciasnym zwężeniem gałęzi przedniej zstępującej. Korelacja parametrów odkształcenia podłużnego z wynikami cząstkowej oceny przepływu wieńcowego. Badanie pilotażowe

Piotr Dobrowolski[1], Mirosław Kowalski[1], Justyna Rybicka[1], Agnieszka Lech[1], Paweł Tyczyński[2], Adam Witkowski[2], Piotr Hoffman[1]

[1]Department of Congenital Heart Diseases, Instytut Kardiologii, Warszawa

[2]Department of Interventional Cardiology and Angiology, Instytut Kardiologii, Warszawa

Streszczenie

Wstęp i cel: Celem niniejszej pracy była ocena przydatności klinicznej parametrów maksymalnego odkształcenia podłużnego (SS) i tempa odkształcenia podłużnego (SSR) uzyskanych w przezklatkowym badaniu echokardiograficznym w określeniu stopnia zwężenia gałęzi przedniej zstępującej lewej tętnicy wieńcowej.

Metody: Analizie poddano 30 pacjentów z istotnym zwężeniem gałęzi przedniej zstępującej. U wszystkich wykonano przezklatkowe badanie echokardiograficzne, na podstawie którego oceniono prędkość skurczową (Sm), podłużne SS i SSR z segmentu podstawnego, środkowego i koniuszkowego ściany przedniej i dolnej. Stopień zwężenia gałęzi przedniej zstępującej był oceniany za pomocą pomiaru cząstkowej rezerwy przepływu (FFR).

Wyniki: Wszystkie wartości prędkości miokardialnych, SS i SSR oceniane z podstawnego, środkowego i koniuszkowego segmentu ściany przedniej były niższe w porównaniu z odpowiednimi wartościami uzyskanymi z segmentów nieobjętych niedokrwieniem ściany dolnej. Uzyskano istotne statystycznie korelacje wartości FFR z wartościami SS, SSR dla segmentu koniuszkowego ściany przedniej (odpowiednio: r = –0,583; p = 0,01; r = –0,598; p = 0,01). Ponadto stwierdzono korelację między FFR i wartością Sm dla segmentu środkowego ściany przedniej (r = 0,611; p = 0,009).

Wnioski: Spoczynkowe wartości SS i SSR uzyskane z koniuszkowego segmentu ściany przedniej mogą odzwierciedlać istotność zwężenia gałęzi przedniej zstępującej lewej tętnicy wieńcowej.

Słowa kluczowe: echokardiografia, skurczowe odkształcenie podłużne (*strain*), tempo odkształcenia podłużnego, zwężenie gałęzi przedniej zstępującej, choroba wieńcowa, cząstkowa rezerwa przepływu

Kardiol Pol 2016; 74, 9: 1010–1015

Adres do korespondencji:
dr n. med. Piotr Dobrowolski, Department of Congenital Heart Diseases, Instytut Kardiologii, ul. Alpejska 42, 04–628 Warszawa, tel: +48 22 34 34 263, e-mail: p.dobrowolski@ikard.pl

Praca wpłynęła: 09.12.2015 r. **Zaakceptowana do druku:** 09.03.2016 r. **Data publikacji AoP:** 01.04.2016 r.