Echocardiographic Assessment of Revascularization Completeness Impact on Diastolic Dysfunction in Ischemic Heart Disease

Tomislav Šipić, Krešimir Štambuk, Aleksandar Trbović, Ksenija Kapov-Sviličić, Janko Szavits-Nossan and Robert Bernat

Clinic for Cardiovascular diseases »Magdalena«, Department of Cardiology, Krapinske toplice, Croatia

A B S T R A C T

Diastolic dysfunction indicates a functional abnormality of diastolic relaxation, filling, or distensibility of the left ventricle (LV), regardless of whether the LVEF is normal or abnormal. Diastolic dysfunction is practically always progressive and connected with higher morbidity and mortality rates, and, if not treated may lead to a diastolic heart failure. The golden standard for evaluation of diastolic function is echocardiography. One of the most important causes of diastolic dysfunction is ischemic heart disease. The revascularization of chronic myocardial ischemia can be partial (incomplete) or complete. Previous data have shown that the completeness of revascularization could have influence on clinical outcomes. The aim of this study was to asses, by means of echocardiography, the impact of completeness of revascularization on diastolic dysfunction in ischemic heart disease. This study included 65 consecutive patients with previously recognized diastolic dysfunction that met criteria for PCI revascularization. Two groups of patients were identified; one with complete revascularization achieved and another one with incomplete one. There were no statistical differences between two groups considering gender, age, arterial hypertension, hyperlipoproteinaemia, previous CABG and left ventricle systolic function. In the incomplete revascularization group, the proportion of patients that had diabetes mellitus, previous myocardial infarction and previous PCI procedure were statistically higher ($p<0.05$). The diastolic function recovery was statistically significant in both groups ($p<0.001$), and there was no statistically significant difference in recovery between the two groups. Lack of recovery was registered in 18.2% patients with incomplete revascularization achieved, and 15.6% in the complete group, which was not significant, but shows a trend. The causes of somewhat worse recovery in the incomplete revascularization group could be attributed to the higher proportion of diabetics, to the somewhat older population and ultimately to the incomplete revascularization. The E/A ratio on diastolic transmitral flow as well as the E/E lat ratio on tissue doppler were found as the best echocardiographic parameters in diastolic function evaluation. In follow up recovery after complete or incomplete revascularization the tissue doppler (E/E lat) was recognized as the best parameter. In conclusion, we found that echocardiographic assessment of diastolic function recovery was a safe method, and our results showed that even in incomplete revascularization group of patients the recovery of diastolic function could be as good as in the complete one, if the indication for revascularization was correct.

***Key words**: diastolic dysfunction, myocardial ischemia, completeness of revascularization, PCI revascularization, echocardiographic parameters of diastolic dysfunction*

Introduction

Ischemic heart disease is the leading cause of the left ventricular systolic dysfunction in developed countries[1]. Generally, systolic dysfunction is well documented and described, while the diastolic dysfunction is much less recognized[1,2]. Because of the fact that diastolic dysfunction practically always precedes systolic, it came to a point of interest. The golden standard for evaluation of diastolic function (and systolic, as well) is echocardiography[3]. There are four grades of diastolic dysfunction described by echo: impaired relaxation (grade I), pseudonormalization (grade II) and reversible (grade III) and irreversible (grade IV) restrictive patterns (Figure 1)[4].

Received for publication November 11, 2013

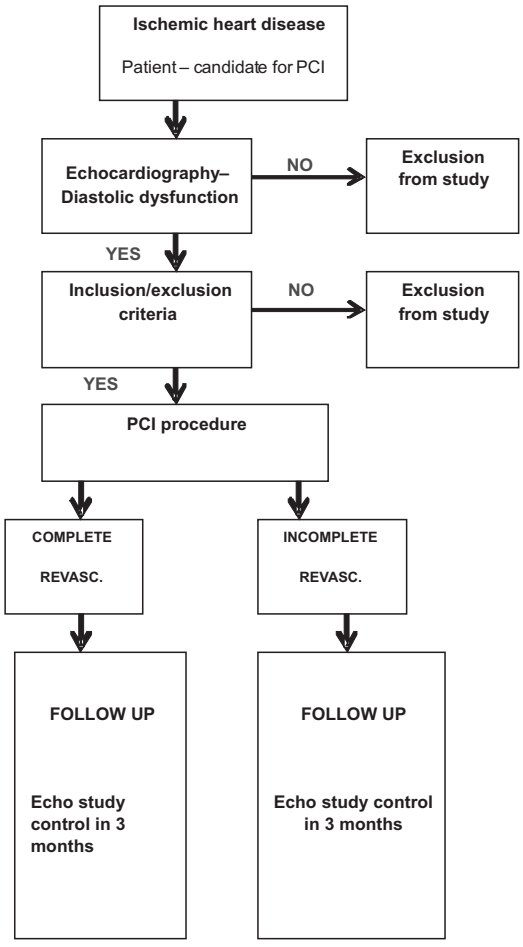

Fig. 1. Study algorithm. PCI – percutaneous coronary intervention.

Besides echocardiography, evaluation of diastolic function can be investigated directly by invasive methods[5] and by analyzing some laboratory parameters taken from blood samples (such as BNP)[6–8]. The most important causes of diastolic dysfunction are ischemic heart disease, hypertension, valvular diseases, pericardial disease (constrictive pericarditis) and cardiomyopathies (hypertrophic and infiltrative). Other important causes include chronic renal insufficiency, diabetes mellitus and aging[9].

Diastolic dysfunction indicates a functional abnormality of diastolic relaxation, filling, or distensibility of the left ventricle (LV), regardless of whether the LVEF is normal or abnormal and whether the patient is symptomatic or not. Thus, diastolic dysfunction refers to abnormal mechanical properties of the ventricle[10]. Diastolic dysfunction is practically always progressive and connected with higher morbidity and mortality rates[11,12], and, if not treated, although asymptomatic, may lead to a diastolic heart failure (DHF). DHF denotes the signs and symptoms of clinical HF in a patient with a normal LVEF and LV diastolic dysfunction[13,14].

Myocardial ischemia is well-known cause of diastolic dysfunction. Treatment of myocardial ischemia with any kind of myocardial revascularization (PCI or CABG) could be complete or incomplete, and there are some data that completeness of revascularization has influence on clinical outcomes[15]. In the case of incomplete revascularization, the recovery of diastolic function could also be partial, because of the residual ischemia, with negative implication for patient prognosis[16].

The aim of this study was to investigate the role of the echocardiography in assessment of recovery of diastolic function after percutaneous revascularization. The leading interest was to assess how the completeness of revascularization refers to diastolic function recovery.

Patients and Methods

Between December 2011 and January 2013 more than 1000 patients were treated in our hospital with PCI for coronary artery disease. In our study, we included 65 patients with previously recognized diastolic dysfunction that met criteria for PCI coronary revascularization. Inclusion criteria were: angiographically verified coronary vessel disease (one or more vessels) feasible for PCI procedure with previously recognized diastolic dysfunction, preserved systolic ejection fraction (50% or more), no significant valvular disease, aged between 30 and 75 years, and PCI procedure done on at least one artery. All patients were clinically stable. Exclusion criteria were pregnancy, active malignant disease, significant anemia (Hgb <110 for women, <120 for men), chronic renal disease (creatinine >150 μmol/L), prepocedural troponin I >0.5 ng/mL and postprocedural troponin I >2 ng/mL, bradycardia and tachycardia (<50/min and >80/min) and other causes of diastolic dysfunction (hypertensive heart disease – iv septum, or free wall >13 mm, constrictive pericarditis, or cardiomiopathy – restrictive, hyper-

TABLE 1
PATIENT CHARACTERISTICS

Characteristics	Incompl. revasc.	Complet. revasc.	Statistics
Number	33	32	NS
Female	8.24%	11.34%	NS
Male	25.76%	21.66%	
Age years (average)	64.5	62.6	NS
RR	81.8%	75.0%	NS
DM	51.5%	25.0%	p<0.05
HLP	90.9%	78.1%	NS
Prev MI	63.6%	37.5%	p<0.05
Prev PCI	66.7%	40.6%	p<0.05
Prev CABG	9.1%	0.0%	NS
EFLV	59.6%	61.0%	NS

RR – arterial hypertension; DM – diabetes mellitus; HLP – hyperlipoproteinaemia; MI – myocardial infarction; PCI – percutaneous coronary intervention; CABG – coronary artery bypass grafting; EFLV – ejection fraction left ventricle

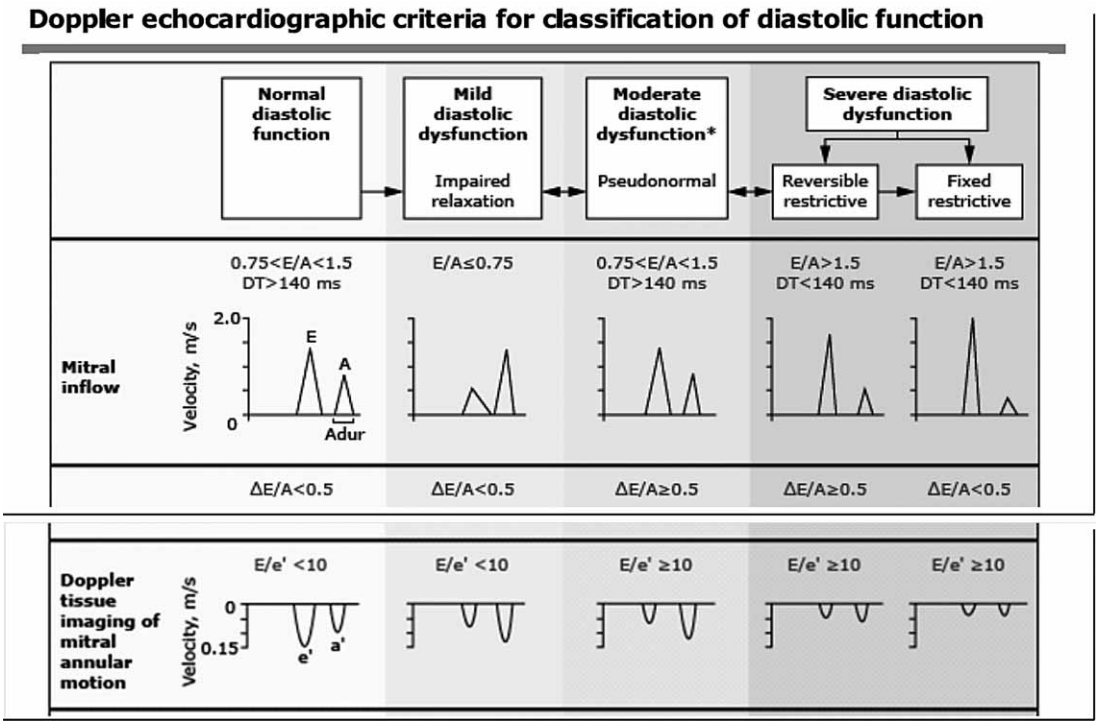

Fig. 2. Doppler echocardiographic criteria for diastolic dysfunction. Redfield MM, Jacobsen SJ, Burnett JC Jr, et al. Burden of systolic and diastolic dysfunction in the community: Appreciating the scope of the heart failure, JAMA, (2003) 289.

tensive or infiltrative). Study algorithm is presented in Figure 1.

Two groups of patients were identified (Table 1). One group is characterized by achieving complete revascularization (32 patients) and the other one by incomplete revascularization (33 patients). Completeness of revascularization was analyzed by our expert team. The characteristics of these two groups were as follows: for complete vs incomplete revascularization average age was 62.6 *vs*. 64.5 years, hypertension 75 *vs*. 81.8%, diabetes mellitus 25 *vs*. 51.5%, hyperlipoproteinaemia 78.1 *vs*. 90.9%, prior MI 37.5 *vs*. 63.6%, prior PCI 40.6 *vs*. 66.7%, and prior CABG 9.1 *vs*. 0%. Systolic function was as follows: for complete revascularization 61 *vs*. 59.6% in incomplete group. Diastolic function was evaluated with echocardiographic study and tissue doppler analysis as well. All patients had an echocardiography study before PCI procedure and the control echo study performed up to three months later. All echo studies contained assessment of diastolic mitral inflow (E/A and deceleration time), doppler tissue imaging of mitral annular motion (E/E lat. and E/E sept.) and pulmonary venous flow. For the grading determination we used only E/A and tissue doppler parameter E/E lat., because of the inconsistency of other parameters. Depending on the grade of diastolic dysfunction, patients were classified in different groups before and after the procedure, depending on the result and the level of the recovery.

After the procedure, routine blood tests were performed including cardiac troponin I and creatinine, and all patients that had elevated troponin I (>2ng/mL) were treated as acute complication (acute myocardial infarction) and been excluded from this study (2 patients). Neither of patients had an acute renal insufficiency.

Statistical methods

Discrete variables were expressed as whole numbers or percentage compared using chi-square test. P value of less than 0.05 was considered statistically significant.

Results

Echocardiographic evaluation of diastolic function in coronary patients before and after PCI procedure was performed in all 65 patients. The indication for revascularization was made by our expert team. All of them met inclusion criteria for the study and have had with follow up completed.

The primary success rate (PCI procedure) was 100%, 2 patients were excluded because of troponin I raise out of range (2.2 ng/mL and 3.1 ng/mL). Neither of patients had an acute renal insufficiency.

Using the echocardiographic findings (E/A and E/E lat, respectively) statistically significant improvement in diastolic function was observed in both groups. In complete revascularization group the complete recovery of diastolic function was present in 71.9% of all patients and the partial recovery in 12.5%, what makes 84.4% in total. In incomplete group the results were 72.7% for complete recovery and 9.1% for partial recovery what makes 81.8% in total, respectively. The lack of recovery

TABLE 2
GRADE OF DIASTOLIC DYSFUNCTION BEFORE AND AFTER PCI FOR COMPLETE REVASCULARIZATION

Revascularization				Time	
				Before	After
Complete	DD	Complete recovery	Count	0	23
			% within Time	0.0%	71.9%
		I. grade DD	Count	19	7
			% within Time	59.4%	21.9%
		II. grade DD	Count	11	2
			% within Time	34.4%	6.3%
		III. grade DD	Count	2	0
			% within Time	6.3%	0.0%

DD – diastolic dysfunction

TABLE 3
GRADE OF DIASTOLIC DYSFUNCTION BEFORE AND AFTER PCI FOR INCOMPLETE REVASCULARIZATION

Revascularization				Time	
				Before	After
Inkomplete	DD	Complete recovery	Count	0	24
			% within Time	0.0%	72.7%
		I. Grade DD	Count	23	6
			% within Time	69.7%	18.2%
		II. Grade DD	Count	9	3
			% within Time	27.3%	9.1%
		III. Grade DD	Count	1	0
			% within Time	3.0%	0.0%

DD – diastolic dysfunction

was observed in 18.2% of patients in incomplete group (6 of 33 patients), and 15.6% in complete revascularization group (5 of 32 patients). There is no statistical difference between two groups, but the trend is recognized in the complete revascularization group toward better diastolic function recovery. Grade of diastolic dysfunction before and after PCI for complete and incomplete revascularization are shown in Table 3 and 4. Change of grade of diastolic dysfunction after complete and incomplete revascularization are shown in Figures 3 and 4.

Discussion and Conclusion

It has been shown, that diastolic dysfunction is almost always progressive and associated with higher morbidity and mortality rates. If not treated, it may lead to diastolic heart failure. The coronary heart disease is one of the most important causes of diastolic dysfunction and almost all coronary patients have a certain degree of diastolic dysfunction, regardless of concomitant systolic dysfunction. Considering its epidemiologic character in recent times, the recognition and treatment of diastolic dysfunction represents a challenge.

Coronary artery disease is treated with an intention to achieve as complete revascularization as possible, especially functionally and, if it is possible, anatomically as well. The studies that investigate the connection between coronary artery disease and the diastolic dysfunction are very rare, and the study that compares the influence of completeness of revascularization on diastolic dysfunction recovery is not to be found in recent published papers. Echocardiography is an noninvasive and well established method that represents a golden standard in diastolic function analysis. There is no data suggesting which echocardiographic parameter is the most sensitive for evaluation of diastolic function recovery after revascularization.

The primary goal of our study was to exclude other causes of diastolic dysfunction as much as possible with an idea to emphasize the relationship between coronary heart disease and diastolic dysfunction. All patients had one or more vessel disease and were scheduled for PCI procedure, that has been done consequently. Two patient groups were followed; one with the complete revascularization achieved and another one with incomplete one. The indication for revascularization and the estimation

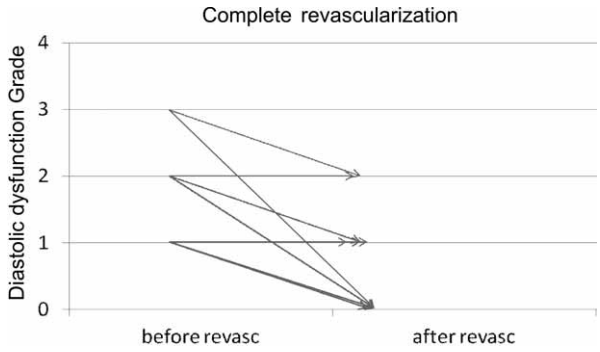

Fig. 3. Change of grade of diastolic dysfunction after complete PCI revascularization.

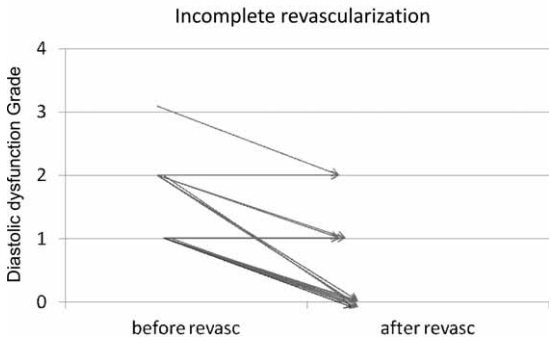

Fig. 4. Change of grade of diastolic dysfunction after incomplete PCI revascularization.

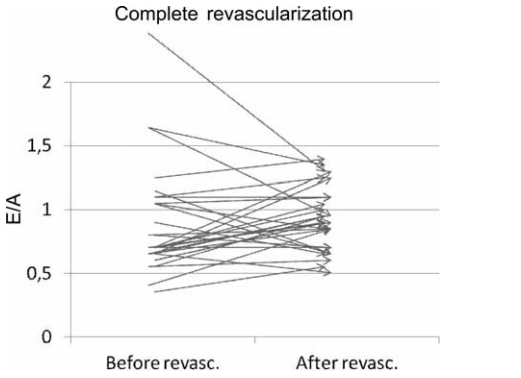

Fig. 5. a) Change of the E/A ratio for the all patients in the complete revascularization group.

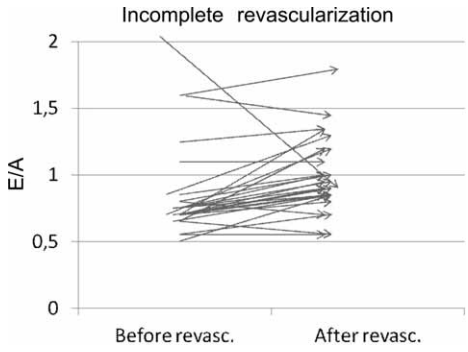

Fig. 5. b) Change of the E/A ratio for the all patients in the incomplete revascularization group.

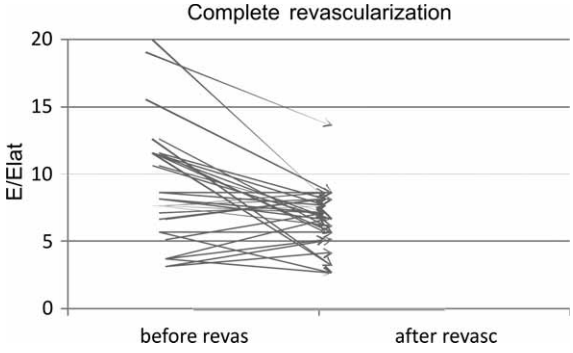

Fig. 6. a) Change of the E/E lat ratio for the all patients in the complete revascularization group. The improvement of diastolic function was followed with decrease of E/E lat ratio under the threshold of 10.

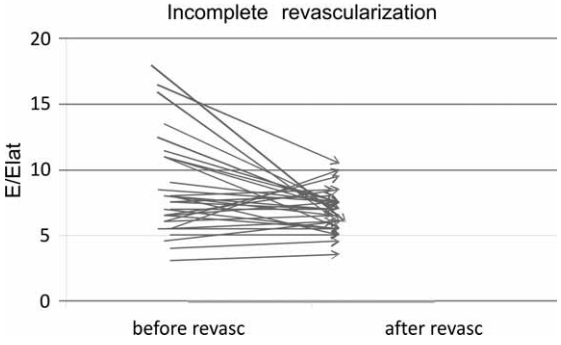

Fig. 6. b) Change of the E/E lat ratio for the all patients in the incomplete revascularization group. The improvement of diastolic function was followed with decrease of E/E lat ratio under the threshold of 10.

of revascularization completeness was assessed by our expert team.

Two patient groups had similar characteristics; there was no statistical difference in terms of age, gender, arterial hypertension, and hyperlipoproteinaemia, but in the incomplete revascularized group there were more patients with diabetes, previous myocardial infarction and previous PCI procedures, and this was statistically important ($p<0.05$). Irrespective of that fact, especially more infarction and previous PCIs, the systolic function in two group was comparable, 61% for complete group and 59.6% for incomplete group, respectively (ns).

Analyzing our results it is quite obvious that diastolic function recovery was achieved in both groups, regardless of revascularization completeness, and it was statistically important ($p<0.001$). In complete revascularization group the complete or partial diastolic recovery was achieved in 84.4% and in incomplete one 81.8% (ns). The complete lack of recovery was present in 18.2% patients in incomplete group and 15.6% in complete group, re-

spectively. The difference was not statistically significant, but the trend toward better diastolic recovery was observed in complete revascularization group.

According to our echocardiographic criteria, that include E/A and E/E lat ratios, the majority of patients were classified in the first or second diastolic dysfunction group, only 2 patients (6.1%) in complete group and only 1 (3.1%) in incomplete one were classified as diastolic dysfunction grade III. There was no patient classified as diastolic dysfunction grade IV. In generally, our cohort had mostly mild diastolic disorder.

Whereas the medium age was 64.5 *vs*. 62.6 years (ns), the diastolic function was influenced by natural changes that comes to the light after age of 55, as well. In addition, there is a statistical difference in incomplete group regarding diabetics (51.5 *vs*. 25%, $p<0.05$). The importance of statistically higher number of previous MIs and PCIs in incomplete group ($p<0.05$), is mostly abolished regarding ejection fractions that are practically the same (61% in compl. *vs*. 59.6% in incompl. group, ns).

In our view, the main reason for lack of difference in diastolic dysfunction recovery regardless of the completeness of revascularization depends on the right indication.

In the complete revascularization group, all diseased vessels were treated and solved, and in incomplete group some of the vessels were not treated. But regarding the results, it is obvious that even in the incomplete revascularization group the »most important vessels« were treated properly and revascularized. Only the minor vessels were not treated – vessels that are diffusely diseased, have small diameter, or lead to the infarcted areas. Thus, so called »functional« revascularization has been accomplished in most patients. Partially, the trend for the lack of recovery in incomplete group could relate to higher number of diabetics and higher age average and to the fact that some vessels were not revascularized.

Although combination of ratios E/A and E/E lat are very useful for the grading of diastolic dysfunction in the revascularized patients, we found E/E lat ratio as the most sensitive for the evaluation of recovery of diastolic function. Figures 5a and 5b show change of the E/A ratio for the all patients in the complete revascularization group. Although the majority of patients had improvement of diastolic function, E/A ratio could be increased and decreased irrespectively of the diastolic function recovery. Changing of the E/E lat ratio for the all patients in complete and incomplete revascularization group are graphically shown in Figures 6a and 6b. The improvement of diastolic function was followed by a decrease of E/E lat ratio under the threshold of 10.

In summary, the aim is to achieve completeness of revascularization, albeit in functional manner, and in anatomical if possible. That is the logical answer to our question. Ischemia has to be looked for and evaluated, because only the viable myocardium is to be revascularized. So if it is not possible to achieve the complete anatomical revascularization, the result of incomplete revascularization could be as good as for the complete one if the main arteries are revascularized. This primarily depends on the right indication as is has been shown in this study.

REFERENCES

1. REDFIELD MM, JACOBSEN SJ, BURNETT JC JR, MAHONEY DW, BAILEY KR, RODEHEFFER RJ, JAMA, 289 (2003) 194. — 2. LAM CS, LYASS A, KRAIGHER-KRAINER E, MASSARO JM, LEE DS, HO JE, LEVY D, REDFIELD MM, PIESKE BM, BENJAMIN EJ, VASAN RS, Circulation, 124 (2011) 24. DOI: 10.1161/circulationaha.110.979203. — 3. OTTO CM, Textbook of Clinical Echocardiography (Saunders, 2013). — 4. NAGUEH SF, APPLETON CP, GILLEBERT TC, J Am Soc Echocardiogr, 22 (2009) 107. DOI: 10.1016/j.echo.2008.11.023. — 5. GRANT AD, NEGISHI K, NEGISHI T, COLLIER P, THOMAS D, MARWICK TH, POPOVIC ZB, Circ Heart Fail, 3 (2010) 617. — 6. NIKISHIMI T, Circ J, 76 (2012) 2540. — 7. GREWAL J, McKELVIE R, LINN E, TAIT P, CARLSON J, GIANNI M, JARNERT C, PERSSON H, Eur J Heart Fail, 10 (2009) 252. DOI: 10.1016/j.ejheart.2008.01.017. — 8. RICHARDS M, NICHOLLS MG, ESPINER EA, J Am Coll Cardiol, (2006) 47. — 9. GATES PE, TANAKA H, GRAVES J, SEALS DR, Eur Heart J, 24 (2003) 221. — 10. ZILE MR, BRUTSAERT DL, Circulation, 105 (2002) 1387. — 11. HALLEY CM, HOUGHTALING PL, KHALIL MK, Arch Intern Med, 171 (2011) 1082. DOI: 10.1001/archinternmed.2011.244. — 12. PIRTA IL, Arch Intern Med, 171 (2011) 1088. DOI: 10.1001/archinternmed.2011.245. — 13. KASS DA, BRONZWAER J, PAULUS W, Circ Res, 94 (2004) 1533. — 14. VASAN RS, LEVY D, Circulation, 101 (2000) 2118. — 15. CARLUCCIO E, BIAGIOLI P, ALUNI G, Eur Heart J, 30 (2009) 1501. DOI: 10.1093/eurheartj/ehp125. — 16. VANHECKE TE, KIM R, RAHEEM SZ, McCULLOUGH PA, Curr Cardiol Rep, 12 (2010) 216. DOI: 10.1007/s11886-010-0101-1.

T. Šipić

Clinic for Cardiovascular Diseases »Magdalena«, Department of Cardiology, Ljudevita Gaja 2, 49217 Krapinske toplice, Croatia
e-mail: tomislav.sipic@magdalena.hr

ULTRAZVUČNA PROCJENA UTJECAJA KOMPLETNOSTI REVASKULARIZACIJE NA DIJASTOLIČKU FUNKCIJU KOD ISHEMIJSKE BOLESTI SRCA

S A Ž E T A K

Dijastolička disfunkcija je funkcionalni poremećaj relaksacije srčanog mišića, dijastoličkog punjenja te raztezljivosti srčanog mišića koji se javlja neovisno o sistoličkoj funkciji. Dijastolička disfunkcija gotovo uvijek prethodi sistoličkoj, a ukoliko je neliječena u pravilu progredira, te je povezana s povećanim morbiditetom I mortalitetom. Zlatni standard za evaluaciju dijastoličke funkcije je ultrazvuk srca. Mnogo je čimbenika koji dovode do nastanka dijastoličke disfunkcije srčanog mišića, a jedan od najčešćih je ishemijska bolest srca. Revaskularizacija kronično ishemičnog miokarda može biti kompletna ili parcijalna (inkompletna). Postoje podaci koji govore da bi o kompletnosti revaskularizacije ishemičnog miokarda mogao ovisiti daljnji klinički tijek. Cilj ovog istraživanja je evaluacija uloge ultrazvuka srca u procjeni oporavka dijastoličke funkcije kronično ishemičnog miokarda ovisno o kompletnosti revaskularizacije. U istraživanje je uključeno 65 bolesnika s prethodno ultrazvučno dokazanom dijastoličkom disfunkcijom srčanog mišića, a prethodno su zadovoljili kriterije uključivanja/isključivanja. Kod svih je učinjena PCI procedura, a s obzirom na kompletnost postignute revaskularizacije podijeljeni su u dvije skupine – jednu s postignutom kompletnom i drugu s postignutom inkompletnom revaskularizacijom. Uspoređujući skupine, nije bilo statistički značajne razlike s obzirom na dob i spol bolesnika, učestalost hipertenzije, hiperlipoproteinemije, prethodno učinjene operacije aortokoronarnog premoštenja te sistoličke funkcije miokarda. U skupini inkompletne revaskularizacije bilo je statistički značajno više bolesnika koji su prethodno preboljeli infarkt miokarda, te imali prethodno učinjene PCI procedure. Ultrazvučno dokazan oporavak dijastoličke funkcije je bio statistički značajan u obje promatrane skupine ($p<0,001$). Nije registrirano statistički značajne razlike u oporavku dijastoličke funkcije između bolesnika kod kojih je postignuta kompletna ili inkompletna revaskularizacija miokarda. Izostanak oporavka je bio registriran u 18,2% bolesnika s postignutom inkompletnom revaskularizacijom, a u onih s postignutom kompletnom revaskularizacijom iznosio je 15,6%, što nije statistički značajno, ali ipak pokazuje trend. Razlozi nešto manjeg oporavka dijastoličke funkcije u skupini inkompletno revaskulariziranih pripisujemo većem postotku dijabetičara, ipak nešto starijoj životnoj dobi te svakako nepotpunoj revaskularizaciji. Kao najbolji ultrazvučni parametri procjene dijastoličke funkcije pokazali su se omjer E/A na dijastoličkom transmitralnom protoku kao i E/E lat na tkivnom dopleru. Za praćenje samog oporavka dijastoličke funkcije nakon kompletne kao i inkompletne revaskularizacije tkivni dopler (E/E lat) se pokazao najboljim parametrom. Zaključno možemo reći da se ultrazvučna procjena oporavka dijastoličke funkcije pokazala kao pouzdana metoda, a naši rezultati su pokazali da se kod inkompletne revaskularizacije može postići gotovo jednako učinkovit oporavak dijastoličke funkcije ukoliko se postavi dobra indikacija za revaskularizacijom.