Review Article

Assessment of Myocardial Viability: Selection of Patients for Viability Study and Revascularization

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Abstract

The aim of this article is to review the application of current imaging techniques used for the detection of viable myocardium. Each technique is discussed briefly, and the more commonly used techniques are compared. The imaging techniques reviewed herein are dobutamine stress echocardiography, single photon emission tomography, magnetic resonance imaging, positron emission tomography with F-18 fluorodeoxyglucose, and recently introduced tissue Doppler imaging. The estimation of the amount of viable myocardium that could predict a better outcome after revascularization being a challenging issue, the present article also reviews a variety of cut-off points suggested by different investigators as adequate viable myocardium for revascularization and presents a summary of clinical, angiographical, and echocardiographic findings that could assist in selecting patients for viability study.

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Introduction

Viable myocardium can be defined as myocardium that shows severe hypokinesia or akinesia at resting echo which will improve in function after revascularization. Armstrong explained viability as recovery of function (either regional or global) and reduction in symptoms after revascularization.[1] The term “viable” describes myocardial cells that are alive. A precise definition of this term is given by Underwood and colleagues,[2] who carefully defined that this term, whether applied to a myocyte or to a segment of the myocardium, implies nothing with regard to contractile state. Thus, viable myocardium may contract normally or it may be dysfunctional, depending on other circumstances.

The contractile dysfunction of viable myocardium may be seen in two syndromes: myocardial stunning and myocardial hibernation. Myocardial stunning results from a transient coronary occlusion followed by reperfusion and has been defined as reversible myocardial contractile dysfunction in the presence of normal resting myocardial blood flow.[3] Myocardial hibernation refers to chronic ventricular dysfunction associated with severe coronary artery disease with complete or partial recovery of contractile function occurring after revascularization.[4] Vanoverschelde et al.[5] explained that in a subgroup of patients with non-infarcted collateral-dependent myocardium, immature or insufficiently developed collaterals do not provide adequate flow reserve. Despite nearly normal resting flow and oxygen consumption, these collateral-dependent segments exhibit chronically depressed wall motion and demonstrate marked ultrastructural alterations on morphological analysis. The authors proposed that these alterations are in consequence of repeated episodes of ischemia as opposed to chronic hypoperfusion and represent the flow, metabolic, and morphological correlates of myocardial "hibernation".

The term "ischemic cardiomyopathy" is also used by many investigators to describe the condition of the myocardium damaged by severe coronary artery disease (CAD). This

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term has yet to be defined for clinical use. A report of the 1995 World Health Organization/International Society and Federation of Cardiology Task Force defined the term "ischemic cardiomyopathy" as a dilated cardiomyopathy with impaired contractile performance not explained by the extent of CAD or ischemic damage.[6] After this definition, many authors referred this term to the state in which CAD accompanies left ventricular (LV) dysfunction. Bart et al.[7] found the association of the extent of CAD in a large population with both symptomatic and asymptomatic LV dysfunction. A standardized definition of ischemic cardiomyopathy for use in clinical research was developed by Felker et al.[8]

By this definition, the presence of ejection fraction (EF) <40% in patients with a history of myocardial infarction or revascularization, >75% stenosis of the left main or proximal left anterior descending artery, or >75% stenosis of two or more epicardial vessels indicates ischemic cardiomyopathy.

Searching for viability in patients with multi-vessel CAD and LV dysfunction is an important issue because more than 50% of dysfunctional segments are viable.[9] Although patients with reduced LVEF and multi-vessel CAD have shown improved survival after surgical revascularization, [10-15] such patients have increased surgical risk and lower long-term survival rates compared to those with better ventricular function.[11] The main goal of a myocardial viability assessment is to identify patients whose symptom and functional capacity may improve after revascularization.

No prognostic benefit of revascularization was found in patients with poor LV function in one study.[11] Be that as it may, further trials showed that patients with CAD and LVEF<35% benefit from coronary artery bypass grafting (CABG) if adequate viable myocardial tissue was present. In these patients, the amount of viable myocardium necessary to result in clinically significant improvements in the outcome after revascularization is unknown.

Different methods for viability assessments include: 1) dobutamine stress echocardiography (DSE), 2) nuclear imaging by single photon emission computed tomography (SPECT), 3) magnetic resonance imaging (MRI), 4) positron emission tomography (PET) with F-18 fluorodeoxyglucose (^{18}F-FDG), and 5) tissue Doppler imaging (TDI). Furthermore, the definite presence of viable myocardium is confirmed by the recovery of resting function after revascularization. Although sensitivity and specificity of these techniques have been evaluated by different studies, there is no general agreement regarding the adequate number of viable segments to predict a better outcome after CABG. The following section reviews different available techniques for viability study, followed by the presentation of the results of a comparison between the more frequently used modalities. The subsequent section will focus upon the amount of viable myocardium thought to be adequate for patients with CAD and low EF if they are to benefit from revascularization.

Dobutamine Stress Echocardiography

Assessment of contractile reserve

For the first time Pierfird and colleagues[16] described the ability of DSE to detect stunned myocardium and to separate it from irreversibly infarcted myocardium. Among the different proposed imaging techniques, echocardiography enjoys a widespread use and application in any clinical condition. Based on the experimental findings, catecholamine stimulation in ischemic regions can augment myocardial function before ischemia, which occurs as a result of increased myocardial work and blood demand.[17] Early studies supported this concept and showed that there is inotropic reserve in many patients with sustained LV dysfunction by administrating epinephrine.[18,19] Further reports presented low-dose dobutamine to evaluate inotropic response in many patients with acute and chronic ischemia and identify reversible myocardial dysfunction.

Contractility in dysfunctional but viable myocardium increases after the infusion of low-dose dobutamine. There are four defined responses of dysfunctional regions to dobutamine infusion: 1) sustained improvement, 2) improvement at low dose followed by subsequent worsening, 3) progressive worsening of function, and 4) no change. Improvement in segmental wall motion at peak stress by at least one grade (improvement from akinesia to hypokinesia or from hypokinesia to normal motion) compared to the baseline rest study (before dobutamine infusion) is considered the presence of contractile reserve. Although a methodological definition of the presence of contractile reserve and viable myocardium is similar, there is a trend for the use of the term "contractile reserve" instead of viable myocardium in some recent papers. Segments without contractile reserve with inotropes are not always non-viable; they may show viability according to PET or scan or recovery of resting function after revascularization. It has been suggested that contractile reserve is a more appropriate standard than is the recovery of resting function in terms of functional capacity, preventing LV remodeling, and long-term prognosis.[20]

EF response to Dobutamine

A few studies have examined the relation between viability and changes in LVEF.[21,22] Rocchi G et al.[23] demonstrated that an EF improvement ≥10% in low-dose DSE was predictive of >5% increase in EF with radionuclide ventriculography post-operatively in 60% of patients (8±2 months after CABG), whereas an EF improvement <5% at low-dose DSE was predictive of the absence of post-operative functional recovery in 90% of patients. This group concluded that improvement of EF≥10% at low-dose DSE had the highest predictive value (80%) for late functional recovery and EF response to dobutamine infusion was superior to segmental wall motion changes in predicting LVEF recovery after CABG.

Baseline echocardiography

Resting echocardiography provides useful information which may guide viability assessment and assist in viability interpretation. Resting wall motion abnormality is commonly used for viability assessment during the first evaluation of patients. LV end diastolic and systolic volumes in resting echocardiography give additional information to predict global functional recovery.

Left ventricular systolic volume

Regardless of the amount of dysfunctional but viable myocardium, the extent of LV remodeling and enlargement also determines the improvement in function following myocardial revascularization. In the study of Schinkel AF et al.,[24] the likelihood of recovery of global function decreased proportionally with the increase in end systolic volume, and an end systolic volume ≥140 mL was related to a low likelihood of improvement in LVEF post-revascularization. In this study, the value of ≥140 mL had the highest sensitivity/specificity (68% and 65%, respectively) to predict the absence of global recovery.

Left ventricular end diastolic volume

The echocardiographic study of 59 patients[25] before revascularization showed no relationship between resting LV volumes and improvement in global EF (increased EF >5%) after CABG. Although non-significant, approximately 40% of patients with end diastolic volumes <140 ml improved EF by >5%, compared with 70% of patients with volumes of 140-180 ml and 35% of patients with volumes >180 ml. Patients with a very large end diastolic volume (>220 ml) are unlikely to recover significant function.

Nuclear imaging by Single Photon Emission Computed Tomography

This technique evaluates cell membrane integrity and intactness of mitochondria with Thallium-201 (^{201}Tl) or Technetiumm-99 (^{99m}Tc) labeled agents to assess viability. Regional perfusion results in the initial uptake of ^{201}Tl, while sustained uptake depends on cell membrane integrity and myocardial viability.[9] Technetiumm-99 sestamibi assesses perfusion and intact mitochondria under resting conditions and provides information on viability. The addition of nitrate before tracer administration enhances viability detection. There are four markers of viability when utilizing nuclear imaging by SPECT using ^{201}Tl and ^{99m}Tc: 1) normal perfusion, 2) reversible defect, 3) redistribution in fixed defects, and 4) tracer uptake>50% on rest images.

Both ^{201}Tl and ^{99m}Tc regional activities were reported to be similar in segments with reversible as well as irreversible ventricular dysfunction.[26,27] The severity of the defect was the most important variable in predicting improvement in revascularization rather than which tracer was used.[28]

Magnetic Resonance Imaging

Recently used for the detection of viability, MRI has emerged as an important imaging modality for an accurate assessment of regional myocardial function by quantitative wall thickness analysis.[29] Using this variable, segments with an end diastolic wall thickness <5.5 mm never show recovery of function after revascularization. By contrast, segments with a wall thickness ≥5.5 mm do not always show improvement in function after revascularization.[9]

Similar to echocardiography, MRI can use low-dose dobutamine to evaluate contractile reserve. Investigators have explained that an increased systolic wall thickening during dobutamine infusion is an accurate predictor of functional recovery.[30,31] A mean sensitivity of 73% and specificity of 83% were reported for dobutamine MRI (DMRI).[32]

Gotte et al.[33] reported that two-dimensional strain analysis by MRI is more accurate than wall thickness analysis in discriminating dysfunctional from functional myocardium and, therefore, it improves the detection of regional differences in function. Two-dimensional strain analysis provides a strong correlation between regional myocardial function and global ventricular function.

Positron emission tomography with F-18 fluorodeoxyglucose

Cardiac FDG (fluorodeoxyglucose) uptake has traditionally been imaged with PET. In the fasting situation, FDG is taken up mainly by ischemic myocardium, whilst the other areas (scar and normal tissue) do not take FDG.[34] PET imaging has been extensively studied in the diagnosis of CAD, as well as the determination of prognosis and assessment of myocardial viability in patients known to have CAD.[35,36] F-18 fluorodeoxyglucose PET and SPECT assess glucose metabolism,[37,38] but PET is more sensitive and specific than is SPECT for detecting viable myocardium.[39] In recent years, PET has turned into the gold standard for non-invasive assessment of myocardial viability and allows an accurate detection of CAD by the assessment of myocardial perfusion.[5,40] A review of 20 studies[41] showed mean specificity and sensitivity of 58% and 93%, and the mean positive and negative predictive values of 71% and 86% for PET in myocardial viability study, respectively.

Tissue Doppler Imaging

TDI measurements allow the reconstruction of strain and strain rate curves and color-coded images. Echocardiographic strain and strain rate imaging is able to assess myocardial function more reliably.[42] This technique quantifies myocardial function, such as longitudinal myocardial shortening, and differentiates between active and passive movement of myocardial segments. The assessment of myocardial viability is one of the most important clinical indications for echocardiographic strain and strain rate imaging.[43] The augmentation of strain and strain rate with dobutamine is a marker of myocardial viability.[44,45] In the study of Hoffman et al.,[46] thirty-seven patients with CAD but viable myocardial segments (detected by PET) underwent strain rate imaging during a low-dose dobutamine stress test. Viable myocardium showed higher strain rates than did scar tissue after dobutamine infusion. An increase in the longitudinal strain rate of more than -0.23 S^{-1} identified viable tissue with a sensitivity of 83% and a specificity of 84%. The role of strain rate imaging at rest in the detection of ischemia and viability study has recently been under evaluation. A study conducted in our institution by Sadeghian et al. showed that strain and strain rate reduced in akinetic non-viable inferobasal compared to normal segments and the range of strain rate in the studied segments did not overlap with that of normal segments.

Comparison between different methods for viability assessment

Dobutamine Stress Echocardiography and Nuclear Imaging

Many studies have paid attention to a comparison between DSE and nuclear imaging by SPECT.[47-49] A comparison analysis showed higher specificity, but a lower sensitivity of stress echocardiography for the detection of reversible contractile dysfunction.[35] Agreement between the two methods ranges between 60.8% and 72% in these studies.[47,48] Discordance between the two methods was observed more frequently in akinetic segments which were viable by ^{99m}Tc-sestamibi imaging, but did not show contractile reserve by DSE.[47,49]

As already reported by Sadeghian et al., 90% and 59% of akinetic segments were non-viable by DSE and scan (^{99m}Tc), respectively. In addition, the figures were 18% and 16% by the two methods in severely hypokinetic segments.

Panza et al.[49] suggested that the difference in the mechanisms involved in the identification of myocardial viability by the two techniques is responsible for these variations and the cellular processes responsible for a positive inotropic response to adrenergic stimulation require a higher degree of myocyte functional integrity than those responsible for thallium uptake.

A subset of dysfunctional segments; 5.3% and 2% in two studies;[48,49] showed contractile reserve by DSE but did not show technetium uptake. Some investigators[49] have explained this observation by the error inherent in the comparison of the two techniques, including poor anatomic correspondence of LV segmentation in some patients. Armstrong[1] hypothesized thereafter that if infarction involved 15-25% of the thickness of the myocardium and there was hibernation in the remaining thickness, it would show contractile reserve with DSE, but there was less than 50% uptake by scan (considered as non-viable). On the other hand, because the spatial resolution of radionuclide imaging techniques is not sufficient to accurately determine myocardial thickness, non-transmural myocardial infarction cannot be reliably detected on the basis of scintigraphic anatomy. A study[50] reviewed published papers correlating post-revascularization functional recovery following evaluations by myocardial perfusion imaging and stress echocardiography. The mean values of the sensitivity and specificity of the methods are presented in Table1.

Table 1. Accuracy of three most frequently used techniques for myocardial viability study in pooled data reviewed by Bax et al.

	DSE	^{99m}Tc-SPECT	^{201}Tl-SPECT
Sensitivity	81%	81%	86%
Specificity	80%	66%	59%
PPV	77%	71%	69%
NPV	85%	77%	80%

DSE, Dobutamine stress echocardiography; Tc, Technetium; Tl, Thallium; SPECT, Single photon emission tomography; PPV, Positive predictive value; NPV, Negative predictive value

Dobutamine Stress Echocardiography and Positron Emission Tomography with F-18 fluorodeoxyglucose

Comparisons between DSE and PET in the evaluation of viable myocardium in patients undergoing intravenous thrombolysis following acute anterior wall myocardial infarction showed 79% concordance in the affected segments.[51] Early recovery of perfusion in the area at risk was associated with a good functional outcome, whereas a high glucose to perfusion ratio suggested jeopardized myocardium that frequently lost viability. The authors[51] concluded that echocardiography during dobutamine infusion is a promising method to unmask viable myocardium in acute myocardial infarction.

Sawada et al.[52] reported 19% of the segments with FDG uptake did not exhibit contractile reserve, so the number of viable tissue required determining the presence of metabolic activity was likely to be less than that required for the detection of contractile reserve. In line with their study, Baer et al.[53] reported that dobutamine stimulation underestimated the number of segments with preserved FDG uptake. In patients with severe post-ischemic heart failure (mean EF=25%) and New York Heart Association functional class (NYHA)≥III, DSE has higher false negative rate than does PET in identifying the recovery of LV dysfunction.[21]

For DSE, the "specificity" (no evidence of contractile reserve and functional recovery after revascularization) was higher than that for either delayed thallium-201 uptake or F-18 FDG uptake.[37,54] Ghesani et al.[54] believe that this is not surprising because the end point of all of these studies was functional recovery, and low-dose dobutamine echocardiography specifically evaluates functional impro vement. It is yet under question whether other important parameters such as the prevention of ventricular remodeling and the prevention of life-threatening arrhythmias are better predicted by radionuclide or echocardiographic techniques.

between three techniques according to the minimum mass of viable cells required to detect myocardial viability.

In a necrotic area of <31%, DSE was found to be 5.5 times more likely to identify a given segment as viable. In turn, when percentage necrosis was >31%, DSE was 7.7 times more likely to classify the segment as non-viable. For MRI, similar to DSE, in a given segment with a necrotic area of <33%, MRI was found to be 5.2 times more likely to identify such segments as viable. In contrast, when the necrotic percentage of the segment was >33%, the probability of this technique to classify this segment as non-viable was 5.5 higher. Finally, the greatest predictive value for thallium redistribution was reached for a percentage of necrotic tissue of 40%, yielding positive and negative likelihood ratios of 2.2 and 3.6, respectively.

Amount of viable myocardium

Patients without myocardial viability not only do not benefit from CABG but also may have worse prognosis after CABG.[21] Although there is no general agreement on the number of viable segments which result in improvement in LVEF and survival after revascularization, it differs between 3-8 viable segments in different studies with different modalities (Table 2).[56-61]

Table 2. Studies comparing prognosis of patients undergoing coronary artery revascularization with those receiving medical treatment with regard to different number of viable segments according to different techniques

Study	Technique for viability study	Number of viable Segments	Follow-up duration*	End points	Frequency after revascularization	Frequency after MT
Pagano et al.	FDG PET	≥8/16	33±14	EF improvement	14%	43%
Afridi et al.	DSE	≥4/16	18±10	Death	6%	20%
Bax et al.	DSE	≥4/16	18.7±8.1	EF and NYHA FC improvement	17%	40%
Senior et al.	DSE	≥5/12	21±8.0	Death	3	31%
He ZX et al.	^{99m}Tc SPECT	≥3/20	23±14	Death and MI	0	47%
Sadeghian et al.	DSE	≥4/16	8	Death, NYHA FC improvement	9%	11%

* Data are presented as mean ±SD

FDG, Fluorodeoxyglucose; PET, Positron emission tomography; DSE, Dobutamine stress echocardiography; ^{99m}Tc, Technetiumm-99; SPECT, Single photon emission tomography; EF, Ejection fraction; NYHA FC, New York heart association functional class; MT, Medical treatment; MI, Myocardial infarction

Magnetic Resonance Imaging, Dobutamine Stress Echocardiography and Nuclear Imaging

A study by Zamorano et al.[55] compared thallium-201 redistribution imaging, cine DMRI, and DSE for the assessment of myocardial viability in a series of patients with ischemic cardiomyopathy undergoing heart transplantation. The patients were evaluated 3 days before transplantation, and the explanted hearts were analyzed to quantify the amount of living cells per segment thereafter. The results showed that DMRI and DSE identified viable segments similarly, but thallium-201 identified more viable myocardial segments. The authors found differences

Patients with CAD and severe LV systolic dysfunction (LVEF<35%) with ≥4 viable segments by DSE showed improved survival at a mean follow-up time of 18±10 months after revascularization.[59] The authors pointed out that age and LVEF predicted mortality only in patients who were not revascularized. In revascularized patients, the only significant predictor of mortality was the absence of myocardial viability. They found that revascularization did not improve survival in patients without pre-operative myocardial viability (mortality rate of 17%). In addition, their study showed that patients with myocardial viability who underwent medical therapy had a high mortality rate.

Similar to their findings, Bax et al.[60] found that patients with ≥4 viable segments on DSE improved in LVEF (27% to 33%, P<0.01) and NYHA functional class (from 3.2 to 1.6, P<0.01) at three months after revascularization. In patients with <4 viable segments, LVEF and NYHA functional class did not improve. Patients with <4 viable segments had a higher cardiac event rate at long-term (up to two years) follow-up (47% vs. 17%, P<0.05). A cut-off value of 4 viable segments extracted via the receiver operating curve (ROC) analysis in this study, demonstrated an association between a significant improvement in LVEF after revascularization in patients with ≥4 viable segments.

Chiming in with these studies, Senior et al.[61] reported that the presence of ≥5/12 viable segments by DSE is a stronger independent variable to predict reduced mortality (by an average of 95%, with a mortality rate of 3%) and improved LVEF compared to cut-off value of 4/12. In contrast, patients with at least 5 viable segments who were treated medically and patients with fewer than 5 viable segments who underwent revascularization had a much higher mortality rate (31% and 50%, respectively).

To evaluate the predictive value of quantitative PET for symptomatic and functional outcome, Pagano and colleagues[62] studied 30 patients with significant stenosis in three coronary artery and NYHA functional class ≥III. They performed PET and DSE before CABG and resting echocardiography before and six months after surgery. To determine the number of PET and DE viable segments in each patient required to obtain an improvement of >5% points in LVEF, ROC analysis identified 8 segments as the best discriminator for PET (sensitivity=88%, specificity=75%, area under the curve=75%) and 7 segments for DE (sensitivity=47% specificity=91%, area under the curve=0.69). In another study, Pagano et al.[21]

evaluated 35 patients with severe heart failure (NYHA≥III and LVEF <35%) and viability study by FDG-PET who underwent CABG. They emphasized three independent factors for cardiac event-free survival after a mean follow-up time of 33±14 months: 1) presence of ≥8 viable segments, 2) pre-operative LVEF (24% vs. 19%), and 3) patient's age. The presence of at least 8/16 viable segments by PET was the best predictor for more than 5% increase in LVEF 6 months after CABG.[5]

In the study conducted by He ZX et al.,[57] the myocardium was considered viable if there was ≥3 nitrate augmented reversible segments (according to nitrate-augmented Tc-99m sestamibi SPECT). Event-free survival in the patients with myocardial viability was significantly lower in the surgery group compared to the medical group (100% vs. 53%, respectively). In this study, event-free survival was similar between the surgical and medical groups in patients without myocardial viability. The EF of all the patients was <50%, and the mean EF was not different between the two groups.

Clinical end points and myocardial viability

All the currently employed diagnostic techniques for assessing viability are designed as markers of myocardial viability, but none of them is defined as the standard technique.[2] Many studies on viability have focused on different clinical end points. The most commonly used clinical characteristics for this purpose include recovery of resting function and improved EF after revascularization.

In a recent study,[63] the correlations of echocardiography parameters at stress tests (by dobutamine and dipyridamole) before and resting echocardiograms immediately after the intervention and after 3, 6, and 12 months were evaluated. The results showed that during a 1-year follow-up period after CABG, significant improvement in LV systolic function was observed (LVEF increased, wall motion score index reduced), with major changes occurring over the first 6 months. The strongest relationship was found between the change in the wall motion score index at stress tests and the improvement in the wall motion score index observed after 6 months. The authors concluded that the wall motion score index calculated during stress was identified to have the strongest prognostic value. The mean increase of EF was about 5% and 6% after 6 months and one year, respectively.

Of 180 revascularized segments with severe rest LV dysfunction in the study of Afridi et al.,[64] recovery of resting function was seen in [56] (31%) segments late after angioplasty, 80% of which had early recovery. In this study, [34] patients who showed a biphasic response to DSE had the most improvement one and six weeks after percutaneous coronary intervention (PCI). Patients with sustained improvement during DSE had no signification change in wall motion after PCI. In another study,[65] the recovery rates of resting function were 18.2% for severely hypokinetic and 15.6% for akinetic segments respectively at a mean of 8 months' follow-up. Evidence of contractile reserve was demonstrated in 9.4% of the akinetic and 90.9% of the hypokinetic segments.

Zaglavara et al.[20] studied the recovery rate of resting function at 6 weeks, 3 months, and 6 months after surgery and showed that recovery rates at 6 weeks, 3 months, and 6 months post-operatively were 21%, 33%, and 45% for resting function (P<0.01), respectively. The authors reported recovery rates of 52% in hypokinetic and 39% in akinetic segments and a significant increase in EF (10%) 6 months after CABG. They pointed out that recovery in resting function and contractile reserve was time dependent and DSE could predict the myocardium that would demonstrate early recovery in contractile reserve with an excellent accuracy.

Two later studies, however, presented different values of recovery rate for hypokinetic and akinetic regions. There are two possible reasons for this difference: firstly, longer follow-up periods in the study of Zaglavara and coworkers;[20] and secondly, patients in the study of Sadeghian and colleagues were relatively on the longer waiting lists for CABG.[65] It is believed that a delay in revascularization causes myocardial changes to progress to a more advanced stage.[66,67]

Relationship between coronary artery patency and viability

There is a paucity of data concerning the relationship between the coronary blood flow and myocardial viability. Investigators[68] have assessed whether some angiographic variables could be considered as markers of viability after myocardial infarction. They studied 41 patients with previous Q wave infarction and single-vessel CAD by ^{201}Tl SPECT and compared viability with angiographic variables, including the degree of patency and collateralization. They found no association between TIMI grade and reversibility. Collateral circulation to occluded arteries was associated with viability, but its absence did not exclude it. Bourdillon et al.[69] analyzed coronary artery in 64 patients with CAD and reduced LV function to assess whether coronary patency could help in assessing viability in relation to PET. They reported that segments supplied by patent arteries were more likely to be viable by PET than were segments supplied by occluded arteries (P<0.001). Akinetic segments were more likely to be supplied by occluded arteries (56 vs. 23, 72%). Dyskinetic segments were predominantly non-viable by PET (86%) and were usually supplied by occluded arteries (77%).

In the study of Kumbasar and colleagues,[70] forty-seven patients with total occlusion in one coronary artery underwent DSE for viability study; of whom 18 (38.3%) had viable myocardium in the area shed by the totally occluded coronary artery and 29 (61.7%) had non-viable. The incidences of significant coronary collateral circulation to the viable and non-viable areas were 66.7% (12 patients) and 20.7% (6 patients), respectively (P=0.002). In logistic regression analysis between the angiographic data, the only significant coronary collateral circulation (collateral circulation partially fills the epicardial segments of the recipient coronary artery or collateral circulation completely fills the epicardial segments of the recipient coronary artery) was found to be an independent factor for the detection of viable myocardium. The authors concluded that good coronary collaterals had a high sensitivity (75%) and specificity (65.7%) as well as high positive predictive (75%) and negative predictive values (79%).

Some more factors affecting selection of patients for revascularization

With delay in revascularization, myocardial changes may progress to a more advanced stage with a lower likelihood of functional recovery.[66,67] Presence of ischemic mitral valve regurgitation may also influence the patient's outcome after surgery. It is recommended that in the case of significant ischemic mitral regurgitation, concomitant mitral valve repair be considered.

The extent of scar tissue may assist in the prediction of the recovery of global LV function in patients with CAD and severe LV dysfunction.[71] A model developed by PARR-1 study[71] suggested that in patients with extensive scar tissue, bypass surgery could be combined with the resection of non-viable scar tissue.

How to select patients for viability study

It is frequently asked which patients should be considered for viability study. The following clinical, angiographical, and echocardiographic findings can be of great help:

Clinical findings

Presence of chest pain is a marker of jeopardized myocardium, but the absence of chest pain and only dyspnea as the main symptom in the presence of severe LV dysfunction (LVEF<35%) may warrant viability study.[2]

Angiographic findings

Previous studies have demonstrated the effect of poor quality distal run off in the left anterior descending artery and circumflex marginal branch on the operative mortality.[72] It is, therefore, advisable that we recommend viability study for patients with poor run off in these territories in the presence of severe LV systolic dysfunction (LVEF<35%).

Echocardiography findings

As was mentioned previously, some studies have revealed the effect of increased left ventricular end diastolic volume (LVEDV) and left ventricular end systolic volume (LVESV) in pre-operative resting echo on post-operative global recovery of resting function. Also, Pagano et al. showed that in addition to the number of viable segments (≥8/16), mean LVEF had a significant effect on event-free survival after CABG (25% vs. 19%, P=0.02). As a result, it is reasonable to consider viability study for patients with LVEDV>220,[25] LVESV>140,[24] or EF <20%.[21]

With respect to the previous findings by DSE, at least 25-40%[59,62] (Table 2) of viable myocardium is required for patients to benefit from revascularization; consequently, it can be said that patients with LVEF<35% and maximum of 9.5 (60%) dysfunctional segments warrant viability study. The most important question is which proportion of dysfunctional segments should be akinetic in resting echo to show the physician the necessity of viability evaluation. As is shown in Table 3, different published studies have found the incidence of viability in akinetic segments to be between 9.4 and 45%.[73-75] In addition, this figure was reported to be 40-96.6% for hypokinetic segments. Therefore, 55-90.6% of akinetic and 3.4-60% of hypokinetic segments were non-viable, respectively. As a result, it can be hypothesized that if at least 7 akinetic segments are present in patients with EF <35%, viability assessment may be necessary. Larger studies are required to confirm this hypothesis by reviewing and analyzing the results of related studies.

Table 3. Frequency of viable segments in hypokinetic and akinetic segments assessed by DSE in different studies

	Akinetic Ratio (%)	Hypokinetic Ratio (%)	Mean EF (%) mean±SD	Model*
Pagano et al.	67/156 (43)	104/180 (57)	25±7	16
Bax et al.	36/214 (17)	44/108 (41)	28±6	16
Bax et al.	- /629 (37)	- /646 (63)	28±8	16
Zaglavara et al.	38/134 (28)	85/114 (75)	29±8	16
Sadeghian et al.	3/32 (9.4)	40/44 (90.6)	31±3.7	16
Panza et al.	76/170 (45)	97/134/ (72)	32±9	16
Defilippi et al.	27/82 (33)	133/146 (91)	36±9	16
Nagueh et al.	10/40 (25)	24/59 (41)	38±14	-
Pace et al.	64/183 (35)	-	40±11	12

*Each model is named according to the number of segments that myocardium was divided for

Conclusions

If patients with multi-vessel CAD and severe LV systolic dysfunction (EF<35%) meet each of the above-mentioned clinical, angiographical, and echocardiographic criteria, viability study is recommended. We would recommend that DSE be utilized as the first step for viability study, because it is widely available, less invasive, and provides additional information about EF, EDV, ESV, and possible valvular abnormalities.

In our institutional experience, if a patient is suitable for revascularization according to DSE, there is no need for further viability evaluations. The patient is recommended for revascularization if DSE findings meet the following criteria: 1) Presence of ≥4 viable segments[59,60] and 2) >10% increase in EF after low-dose dobutamine infusion compared to baseline.[23]

Nonetheless, if the patient is unsuitable or is a borderline case for revascularization according to DSE (suitable case: presence of the two foregoing findings; borderline case: presence of one of the two aforesaid findings), we recommend the use of SPECT (either ^{201}Tl or ^{99m}Tc mibi) as a more sensitive modality. If the scan demonstrates adequate viable myocardium; i.e. 15%,[57] we recommend revascularization; otherwise, the patient may benefit from medical treatment.

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