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Case Report

Dobutamine Stress Echo For Myocardial Viability Assessment

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The prevalence of left ventricular (LV) dysfunction and resultant heart failure is increasing in developing countries. Two thirds of cases of left ventricular dysfunction are the result of coronary artery disease (CAD). Although there have been significant advances in medical therapy for LV dysfunction and resulting symptoms of heart failure, the prognosis from heart failure remains extremely poor. Many of these patients had previous myocardial infarctions, the extent of remaining viable tissue is of clinical interest, and also related to prognosis. Thus assessing myocardial viability is very important in patient with left verntricuar dysfunction to choose the right management. Dobutamine stress echo is one of the most common tool that used to asses myocardial viability.
A 67 years old patient with chronic heart failure because of old anterior and inferior MCI with low ejection fraction. It is very important to assess the viability in patients with advanced heart failure to know the future management because it is related to patient's morbidity and mortality. With little viable myocard in this patient, the best management for this patient is conservative therapy with medical therapy. Dobutamine stress echocardiography therefore, may well provide complementary information in the assessment of myocardial viability. Future modalities are now being studied to give more objective measurement of myocardial viability with higher sensitivity and specificity.

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Laporan Kasus

Penilaian Viabilitas Miokardium Dengan Dobutamine Stress Echo

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Prevalensi dari disfungsi ventrikel kiri dan kejadian gagal jantung meningkat dalam negara berkembang. Dua pertiga dari kasus disfungsi ventrikel diakibatan oleh penyakit arteri koroner. Walaupun dengan adanya kemajuan terapi medis yang signifikan untuk disfungsi ventrikel kiri dan gejala gagal jantung, prognosis gagal jantung tetap buruk. Banyak dari pasien- pasien ini pernah mengalami infark miokard sebelumnya, adanya jaringan yang masih viable menjadi pusat perhatian karena terkait dengan prognosis. Dengan demikian penilaian viabilitas miokard sangat penting pada pasien dengan disfungsi ventrikel untuk memilih terapi yang tepat. Dobutamine stress echo adalah salah satu modalitas yang dapat digunakan untuk menilai viabilitas miokard.

Seorang pasien usia 67 tahun dengan gagal jantung kronik yang diakibatkan oleh infark miokard anterior dan inferior dengan fraksi ejeksi yang rendah. Sangat penting untuk melakuan penilaian terhadap viabilitas miokard pada pasien dengan gagal jantung lanjut untuk mengetahui managemen selanjutnya karena terkait dengan morbiditas dan mortalitas. Dengan hanya sedikit miokard yang masih viable maka terapi yang terbaik pada pasien ini adalah dengan terapi konservatif berupa terapi medis. Dengan demikian dobutamine stress echo dapat memberian informasi tambahan untuk managemen lanjutan dari pasien. Saat ini sedang dikembangkan modalitas untuk memberikan penilaian objektif tentang viabilitas miokard dengan sensitifitas dan spesifisitas yang lebih baik.

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Kata kunci: Dobutamine stress echocardiography, viabilitas

The prevalence of left ventricular (LV) dysfunction and resultant heart failure is increasing in developing countries. Two thirds of cases of left ventricular dysfunction are the result of coronary artery disease (CAD). [1] Not only are these patients at high risk for subsequent cardiac death, severe morbidities, and recurrent hospitalizations for congestive heart failure, they also frequently have severe limitations in their lifestyles and well-being. Although there have been significant advances in medical therapy for LV dysfunction and resulting symptoms of heart failure, the prognosis from heart failure remains extremely poor. Many of these patients had previous myocardial infarctions, the extent of remaining viable tissue is of clinical interest, and also related to prognosis.[1]

The need for making the diagnosis of resting ischemia, hibernation, or stunning stems from their role in exacerbating LV dysfunction, heart failure symptoms sudden death, hemodynamic deterioration and from the need to decide between revascularization and medical therapy. Several clinical studies have

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shown that myocardial dysfunction in patients with CAD may be reversible.[2] After an initial ischemic injury, various processes can occur that lead to LV dysfunction, including LV remodeling, impairment of energetics, myocyte dysfunction, and cell death via necrosis and/or apoptosis. Other than cell death, these processes are, to an extent, reversible, and LV function often can be improved, resulting in better patient outcome. Although medical therapy can be extremely beneficial, revascularization in the appropriate patient often is the best therapy. Left ventricular dysfunction, in some cases, is the result of ''stunned myocardium," which is defined as myocardium that has become dysfunctional because of a transient coronary occlusion, has been salvaged by coronary reperfusion, yet exhibits prolonged but transient postischemic dysfunction, lasting hours to weeks. Thus, in myocardial stunning, blood flow has been restored but contraction has not returned to baseline thus there is a flow-contraction mismatch. Left ventricular dysfunction, in other cases, is the result of hibernating myocardium. This term is refer to persistent LV dysfunction in the presence of severe CAD that is reversible after revascularization. The pathophysiology underlying these phenomena is thought to reflect the down-regulation of function in the presence of reduced blood flow and oxygen supply.[3] By this definition, hibernating myocardium is a flow-contraction match. Regardless of the mechanism, it is important to identify hibernating myocardium because ventricular function will generally improve after revascularization or other therapies.

Objective

The aim of this presentation is to present a case of advanced heart failure and the role of dobutamine stress echo in assessing myocardial viability.

Case Illustration

Mr. GP, 67 years old is a patient of National Cardiac and Vascular Center of Harapan Kita. He was diagnosed having chronic heart failure because of old anterior inferior MCI with low ejection fraction. He complains of having dyspnea on effort with moderate activities like walking 100 m or climbing up the stairs. From the physical examination we cannot hear any murmurs or gallop. The electrocardiographic in out patient clinic reveals as sinus rhytm, with QRS rate 99x/ minute, QRS axis -30 degree, normal P wave, PR interval 0,18", no ST changes, T inverted in lead I and aVL with Q pathologic in lead II, III, aVF, V1-V6 (**Figure 1**).

Chest x-ray shows CTR 60%, with dilated and calcified aortic segment, normal pulmonic segment,

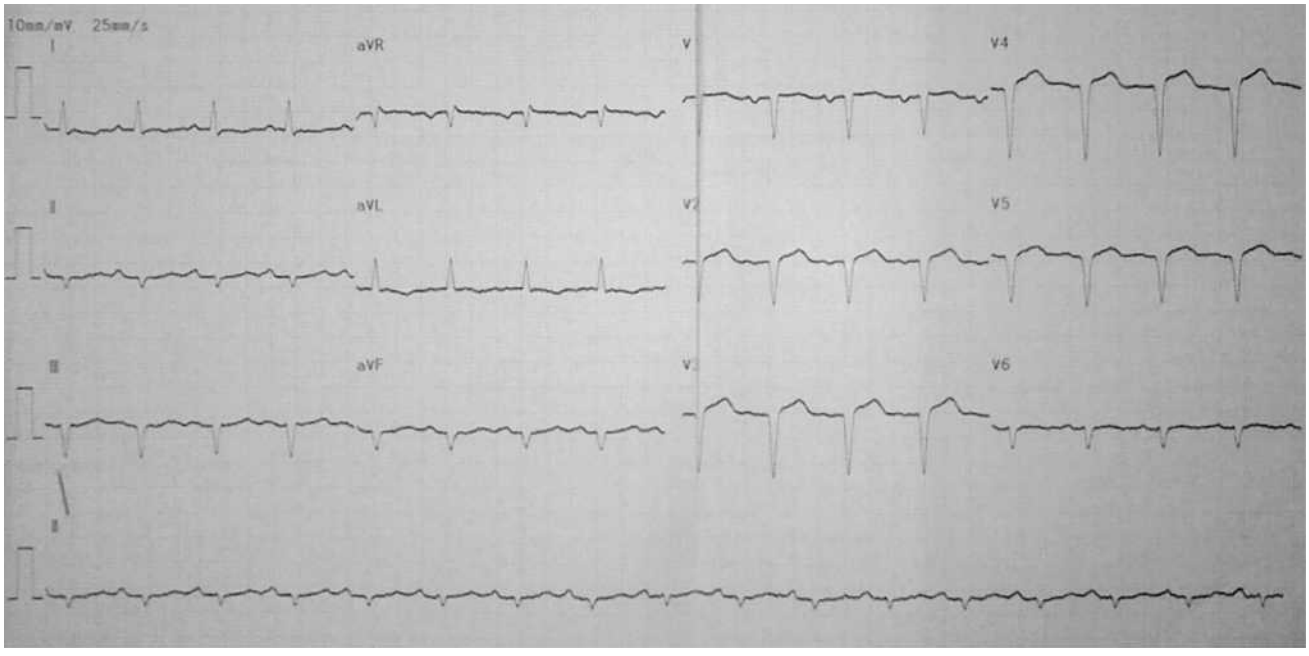

Figure 1. 12-lead electrocardiogram

flattening cardiac waist, apex lateral downward. Then he underwent cardiac catheterisarion in Decemer 2009 and showed CAD 3VD : LM normal, LAD 95% stenotic after D1, 80-90% stenotic from mid to distal, LCX tandem stenotic 80% before OM1 and 80% stenotic at distal part, RCA proximal total occlution. The echocardiography shows EDD 58 ESD 52, reduced LV systolic function EF 25%, akinetic apicoseptal, apical, midseptal and hypokinetic other segment, diastolic dysfunction restrictive, TR mild, PH mild, reduced RV contractility TAPSE 1,3 cm with SEC (+) in LV. He is considered to undergo revascularisation by CABG. Before having CABG, he underwent viability study by using Dobutamine stress echo and TC-99 Sestamibi myocardial perfusion scanning in February 2010. Dobutamine stress echo showed viable myocardium of basal segments of left ventricle, the rest of the LV were non viable (**Figure 2**).

In this patient tissue perfusion imaging was done to assess the viability of the left ventricle. Strain and strain rate value was measured. From the assessment we got the value of strain are 4% in apicolateral and apicoseptal, -4% in midseptal and basal septal, -2% in midlateral, and -11% in basal lateral. With these result we concluded that there is dyskinetic in apical segment of the left ventricle (**Figure 3**).

Perfusion scanning showed fixed defect in anterior apical and apex (non viable), partial reversible defect in septum and inferior (viable) with stress LVEF 17% and rest LVEF 25% (**Figure 4**). With these results then the patient is managed with medical therapy only (conservative).

Literature Review And Discussion

Myocardial viability

Assessment of myocardial viability is of critical importance for the management of patients with chronic coronary artery disease and reduced left ventricular function. Asynergic but viable myocardium has been assumed to improve its systolic function after revascularization, whereas nonviable segments do not. Thus, patients with a large portion of dysfunctional but viable myocardium are believed to benefit from revascularization.[4] In addition, revascularization of viable myocardium may be beneficial by preventing remodeling and electrical instability. **Figure 5** showed the death rates for patients with and without myocardial viability treated by revascularization or medical therapy.

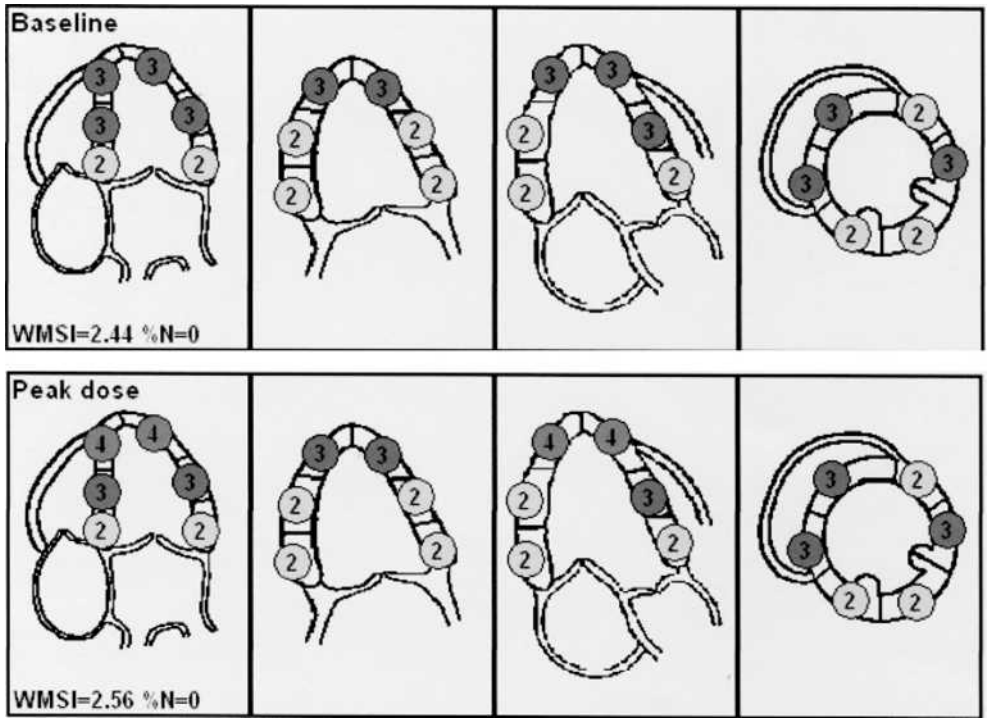

Figure 2. DSE result

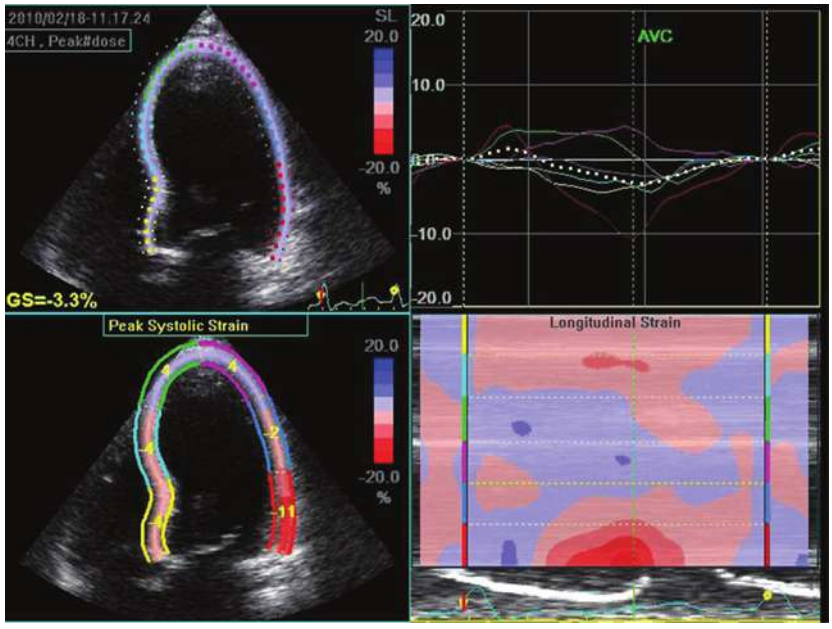

Figure 3. Myocardial viability assessment using strain

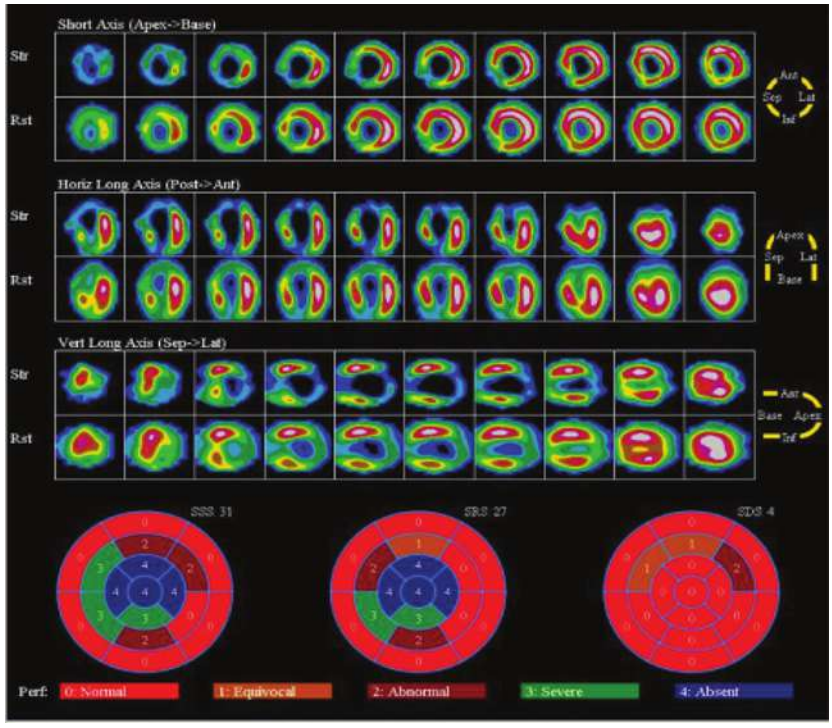

Figure 4. The result of TC-99 Sestamibi myocardial perfusion scanning

Since many studies have established a relation between LV function and cardiovascular prognosis, it is reasonable to speculate that improved LV function following revascularization would be associated with a favorable effect on outcome. The superiority of revascularization compared to medical management in patients with coronary disease and LV dysfunction is compatible with this hypothesis.[6] The recoverable myocardium after revascularization has been called "hibernating".[7]

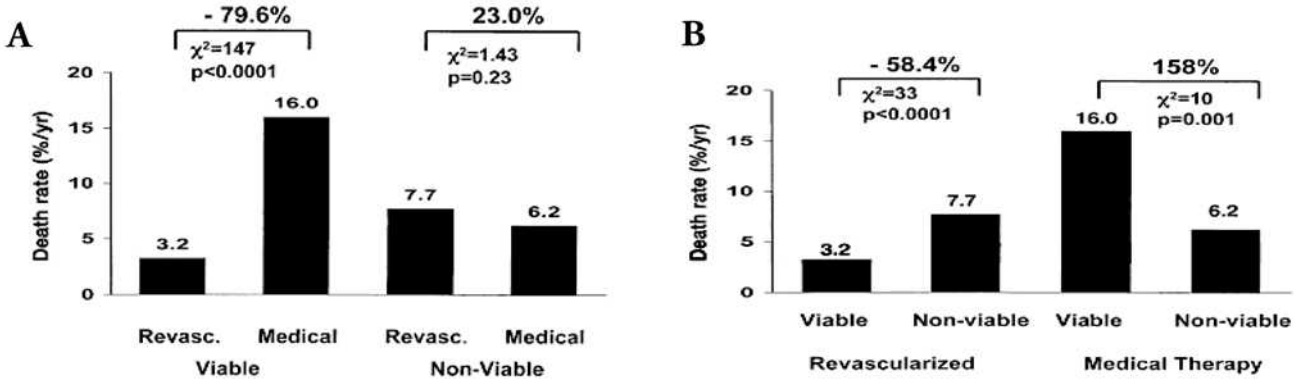

Figure 5.(A) Death rates for patients with and without myocardial viability treated by revascularization or medical therapy. There is 79.6% reduction in mortality for patients with viability treated by revascularization (p <0.0001). In patients without myocardial viability, there was no significant difference in mortality with revascularization versus medical therapy. **(B)** Same data as **(A)** with comparisons based on treatment strategy in patients with and without viability. Annual mortality was lower in revascularized patients when viability was present versus absent (3.2% vs. 7.7%, p <0.0001). Annual mortality was significantly higher in medically treated patients when viability was present versus absent (16% vs. 6.2%, p <0.001).[5]

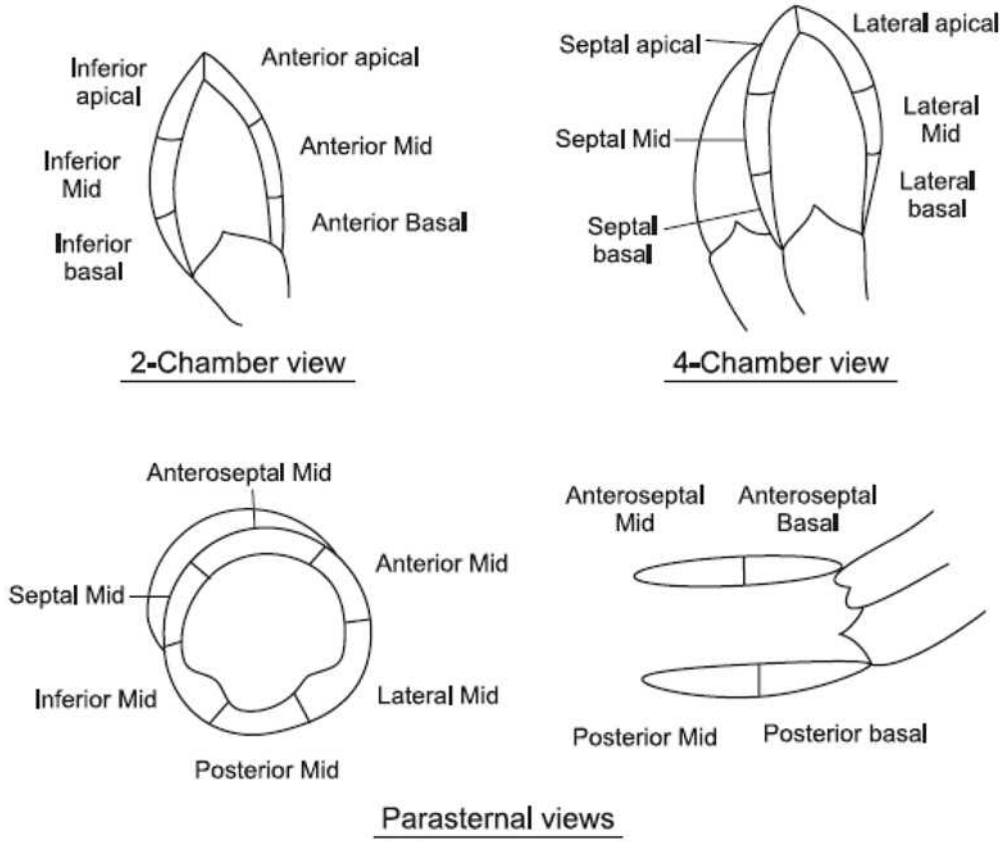

Figure 6. The anatomical segments in the 16 segmental model.8

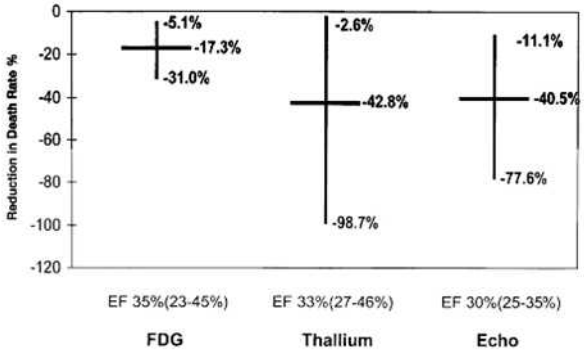

Figure 7. Decrease in mortality with revascularization of viable myocardium for each testing technique shown as mean value with 95% confidence limits. Note wide confidence limits, especially for thallium and echocardiography. No measurable differences in test performance were observed. EF =ejection fraction; FDG=F-18 fluorodeoxyglucose.7

This patient is diagnosed with chronic heart failure because of old anterior and inferior MCI with low ejection fraction. Assessment of myocardial viability is very important in this patient before he undergo revascularization either by CABG. This viability assessment is important to know the next management for this patient if CABG is still a good choice or conservative treatment with medical therapy is better than CABG. The decision can be made by assessing the number of viable segment in this patient.

Dobutamine stress echo(DSE)

Several noninvasive approaches have been developed for the identification of myocardial viability in regions with contractile dysfunction due to coronary artery disease. The three most frequently proposed methods are based on the identification of very different physiologic markers: PET imaging assesses myocardial metabolic activity, typically using F-18 gluorodeoxyglucose as a marker of glucose utilization and N-13 ammonia for assessment of perfusion; Tl-SPECT assesses myocardial perfusion and membrane integrity; and dobutamine stress echocardiography (DSE) assesses myocardial contractile reserve (**Figure** 7).[5]

There are several specific indications for stress echocardiography as noted in the 2007 ASE stress echocardiography guidelines. One of it is risk stratification for patients with known or suspected coronary artery disease. The presence and extent of ischemic, as well as dysfunctional but viable myocardium, can be evaluated.[8] Dobutamine echocardiography has emerged as the noninvasive clinical tool for the detection of hibernating myocardium. Dobutamine echocardiography examines the "inotropic reserve" of dysfunctional but viable myocardium by the administration of inotropic agents such as dobutamine, dopamine and isoproterenol. Dobutamine is generally safe and well tolerated by patients, including elderly adults and those also receiving atropine . However, both cardiac and noncardiac side effects can occur. Serious complications, such as ventricular fibrillation or myocardial infarction, occur in about 1 in 2000 studies.[8] The 2002 ACC/AHA guidelines identified absolute and relative cardiovascular contraindications to stress testing. Absolute contraindications include the following: acute myocardial infarction (within two days), unstable angina pectoris, uncontrolled arrhythmias causing symptoms of hemodynamic compromise, symptomatic severe valvular stenosis, uncontrolled symptomatic heart failure, active endocarditis or acute myocarditis or pericarditis, acute aortic dissection, acute pulmonary or systemic embolism, acute noncardiac disorders that may affect exercise performance or may be aggravated by exercise.[9] Viable myocardium shows improved regional contractile function (inotropic reserve), as assessed by simultaneous transthoracic echocardiography, in response to these agents. The prevalence of contractile reserve in patients with CHD and LV dysfunction is independent of the angiographic extent and severity of coronary disease and the improvement in contractility in hypoperfused viable myocardium does not require an increase in regional myocardial perfusion.[5]

The improvement in regional or global LV function is a significant goal in such patients, the ability to accurately assess regional myocardial viability in a dysfunctional territory prior to revascularization becomes an important component of the decision making process.

Dobutamine stress echocardiography protocole include stopping beta-blockers, calcium antagonists and nitrates in patients at least 2 days before DSE.After baseline echocardiography, dobutamine infusion was administered using a mechanical pump. Dobutamine was delivered intravenously beginning at 5 mikrogram/kg/min for three minutes, Some protocole starts at 2,5 mikrogram/kg/min increasing by 5 mikrogram/kg/min increments every three minutes until it reached 20 mikrogram/kg/ min for an additional three minutes. Blood pressure was measured periodically, and the 12-lead ECG was continuously monitored throughout

the study and during the recovery phase. Grounds for termination of the infusion were a severe hypotensive or hypertensive response, significant arrhythmias, prolonged angina, significant electrocardiographic changes, appearance of new wall motion abnormalities in at least two segments, achievement of 85% of the maximum age-predicted heart rate, or completion of the protocol. Echocardiographic images were analyzed off-line and a 16-segment model was used, as suggested by the American Society of Echocardiography.[10] The anatomical segments of the 16-segmental model are shown in Figure 6. Segmental wall motion at rest was scored on a four-point scale: (1) normal or mildly hypokinetic; (2) severely hypokinetic (decreased endocardial excursion and systolic wall thickening); (3) akinetic (absence of endocardial excursion and systolic wall thickening); and (4) dyskinetic or aneurysmal (paradoxical outward movement in systole).[11]

Demonstration of wall thickening in a previously akinetic segment or normalization of thickening in a previously hypokinetic segment were considered as criteria of myocardial viability. A dysfunctional left ventricular segment was considered to have contractile reserve if infusion of dobutmine at 10 or 15 Ìg/kg/min resulted in an improvement in contractile function of at least one grade.

There are four different patterns were observed in the segments that were dysfunctional at baseline: (1) Biphasic response: improvement of wall motion during low dose (either at 5 or 10 mg) followed by worsening of wall motion during high dose dobutamine; (2) Sustained improvement: improvement at low or high dose dobutamine without deterioration of wall motion; (3) Worsening: deterioration of wall motion during either low or high dose dobutamine; (4) No change: absence of improvement or worsening during the entire test.[8]

The predictive value to dobutamine echocardiography appears to be greatest when there is a biphasic response: improvement at low dose and worsening at high dose. The initial improvement in wall motion reflects recruitment of contractile reserve during low-dose dibutamine . In comparison, higher doses lead to subendocardial ischemia and worsening of the wall motion abnormality. Thus, testing at various doses appears to be needed for the optimal assessment of myocardial hibernation by this technique.

Dobutamine stress echocardiography showed a high sensitivity and specificity to predict improvement of regional LV function. The number of viable segments on DSE was linearly related to the magnitude of improvement of LVEF. The analysis showed that the cutoff value of four dysfunctional but viable segments (25% of the LV) yielded the highest sensitivity/specificity to predict improvement of global LV function: 86% versus 90%. Patients with >4 viable segments showed improvement in heart failure symptoms and had a significantly lower event rate during 2-year follow-up (as compared with patients with, 4 viable segments on DSE).These findings imply that a substantial amount of viable myocardium needs to be present to establish improvement of global LV function after revascularization. Moreover, the magnitude of improvement of LVEF was linearly related to the number of viable segments on DSE. The presence of viable myocardium was linked not only to improvement of function, but also to improvement of heart failure symptoms. It has been demonstrated that the presence of substantial viability on DSE is associated with improvement in LVEF and heart failure symptoms after revascularization, and is accompanied by a favorable prognosis. Hence, viability testing by DSE may guide therapeutic management in patients with severely ischemic LV dysfunction.[12]

Patients who demonstrate myocardial viability with dobutamine echocardiography have a better outcome with revascularization than with medical therapy. In a study which evaluated 318 patients with coronary disease and a left ventricular ejection fraction ≤35 percent, those with myocardial viability (as determined by dobutamine echocardiography) had a lower mortality at 18 months when treated with CABG compared to those with viability who were treated medically or those without viability who underwent CABG (6 versus 20 and 17 percent, respectively).[13] This patient has underwent dobutamine stress echo to asses the viability of the left ventricle and the test showed there is only viable myocardium in basal segment and the rest is non viable.

DSE Vs other modalities

Combining DSE with either PET or Tl-SPECT allowed for stratification of asynergic segments into three subsets: (1) Segments found to be viable by both DSE and either of the scintigraphic techniques had the highest percentage of viable myocytes on histopathologic examination; (2) segments found to be nonviable by both DSE and a scintigraphic technique had the lowest percentage of viable myocytes; (3)

segments that were viable by scintigraphy and had no contractile response with dobutamine had a percentage of viable cells intermediate.[12]

Thus, discrepancies among these methods appear to be primarily caused by the fact that dobutamine-induced improvement of mechanical function depends on a greater percentage of viable myocytes than that required for demonstration of perfusion, cell integrity or metabolism by Tl-SPECT and PET. Dobutamine has been reported to be more specific for predicting functional recovery, while nuclear methods can detect smaller amounts of viable myocytes in asynergic myocardial regions. More importantly, that the combined use of echocardiography and nuclear methods may enhance our understanding about the degree of viability in a given segment and may offer information above and beyond simplistic classification as either viable or nonviable.[14]

It appears that a given segment has to contain at least approximately 50% viable myocytes to allow demonstration of contractile reserve, as evidenced by a positive dobutamine response. Comparison of the results presented here with previously reported clinical data make it likely that a similar percentage of viable myocytes may be required to allow functional recovery after revascularization and that functional recovery may be more accurately predicted by methods directly evaluating contractile reserve, such as DSE.[14]

However, scintigraphic methods that assess perfusion and/or metabolism appear also to identify segments with less than 50% or even less than 25% viable myocytes. Although revascularization of these segments may not contribute to a significant improvement of left ventricular systolic function, it may well provide clinical benefits by attenuating ventricular dilatation and remodeling, by reducing the risk of ventricular arrhythmias and by reducing the risk of subsequent fatal ischemic events. Dobutamine echocardiography and scintigraphic methods, therefore, may well provide complementary information in the assessment of myocardial viability. Current nuclear techniques appear to be highly sensitive for the detection of myocardial viability in asynergic myocardium, and negative tests make it highly unlikely that a significant number of viable myocytes are present in a given segment. Conversely, DSE appears to be particularly useful for identifying segments with a greater number of viable myocytes and may, thus, have particular value for predicting recovery of systolic function after revascularization.[14]

The TC-99 Sestamibi myocardial perfusion scanning was done February 2010. Perfusion scanning showed fixed defect in anterior apical and apex (non viable), partial reversible defect in septum and inferior (viable) with stress LVEF 17% and rest LVEF 25%. Both the dobutamine stress echo and perfusion scanning showed the viable segment is less than 4 segment so the best management for this patient is conservative therapy with medical management. Viability assessment with dobutamine stress echocardiography and Thalium scanning is concordace to the literature. Perfusion scanning showed more viable segment in left ventricle compare to dobutamine stress echo. This is because perfusion scanning is more sensitive but less spesific than dobutamine stress echo. With this result then revascularisation either by CABG or PCI is not indicated and will increase the morbidity and mortality in this patient as showed by previous study.

Recent and future developments

Doppler tissue imaging

Dobutamine stress two-dimensional echocardiography is an established method for the evaluation of patients with coronary artery disease. Although the present modality is clinically useful, a major limitation is the difficulty in deriving quantitative measures of regional wall motion and therefore the interpretation is mainly dependent on the ability of the operator. Recent advances in echocardiography have made it possible to measure directly the velocities of regional myocardium by use of Doppler tissue imaging (DTI), tissue velocity imaging and spekcle tracking. For the diagnosis of viable myocardium, Nishino, *et al.*[15] firstly applied this technique to dobutamine stress echocardiography and demonstrated the usefulness of color DTI M-mode for the prediction of reversible dysfunction early after reperfusion in patients with acute myocardial infarction. Jun et al demonstrated that infarct segments with reversible dysfunction showed larger % S and smaller % PEP / ET than those without recovery, and % S ≥ 150% or % PEP / ET ≤ 100% may be useful criteria for the diagnosis of viable myocardium.[16]

Other modalities that can be use to assess myocardial viability is using tissue velocity and specle tracking. With these modalities we can count srain and strain rate deformation parameters to assess myocardial viability. Over the past 10 years, Color Doppler Myocardial

Imaging (CDMI) and more recently 2D-speckle tracking have evolved as new clinical and research tools to quantify regional myocardial function. This approach seems to offer substantial advantages over standard gray scale echocardiography. In this patient the value of strain concluded that there is dyskinetic in apical segment of left ventricle. The viability assessment using tissue doppler imaging, strain and strain rate value are now being study in large trial to prove that this modalities are usefull. Up till now there are no value of stain and strain rate that can be used to determine weather the segment is viable or non viable.

Myocardial contrast perfusion imaging

The onset of ischemic wall-motion abnormalities is preceded by development of regional disparities in coronary perfusion that can be assessed by contrast agents. Thus, use of contrast agents to assess myocardial perfusion during vasodilator stress may improve the sensitivity of stress echocardiography. Both real-time (low energy) and triggered (high energy) imaging techniques have been shown to be useful for detection of coronary stenosis. The timing of contrast replenishment of a vascular bed has been found to be a useful indicator of the degree of coronary stenosis. Myocardial contrast perfusion imaging may have greater sensitivity than wall-motion analysis. However, the specificity of contrast perfusion imaging may be lower than for wall-motion analysis.

The viability assessment using tissue doppler imaging, strain and strain rate echo, and myocardial contrast perfussion imaging are now being study in large trial to prove that this modalities are usefull . Preliminary study showed very promising fact that this modalities can be use to assess viability to reduce the limitation with the clasic dobutamine stress echocardiography.[17]

Summary

We have reported a case related to advanced heart failure because of old anterior and inferior MCI with low ejection fraction. It is very important to assess the viability in patients with advanced heart failure to know the future management because it is related to patient's morbidity and mortality. Viability testing using dobutamine stress echo showed that there is only little segments in the left ventricle that is still viable so the best management in this patient is conservative with medical therapy. Dobutamine stress echocardiography is one of the methods that can provide complementary information in the assessment of myocardial viability. Future modalities are now being studied to give more objective measurement of myocardial viability with higher sensitivity and specificity.

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