IJC Heart & Vasculature 5 (2014) 51–56

Contents lists available at ScienceDirect

IJC Heart & Vasculature

journal homepage: http://www.journals.elsevier.com/ijc-heart-and-vasculature

Non-invasive imaging in detecting myocardial viability: Myocardial function versus perfusion

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ARTICLE INFO

Article history:
Received 29 September 2014
Accepted 8 October 2014
Available online 18 October 2014

Keywords:
Myocardial viability
Myocardial hibernation
Non-invasive imaging
Myocardial stunning

ABSTRACT

Coronary artery disease (CAD) is the most prevalent and single most common cause of morbidity and mortality [1] with the resulting left ventricular (LV) dysfunction an important complication. The distinction between viable and non-viable myocardium in patients with LV dysfunction is a clinically important issue among possible candidates for myocardial revascularization. Several available non-invasive techniques are used to detect and assess ischemia and myocardial viability. These techniques include echocardiography, radionuclide images, cardiac magnetic resonance imaging and recently myocardial computed tomography perfusion imaging. This review aims to distinguish between the available non-invasive imaging techniques in detecting signs of functional and perfusion viability and identify those which have the most clinical relevance in detecting myocardial viability in patients with CAD and chronic ischemic LV dysfunction. The most current available studies showed that both myocardial perfusion and function based on non-invasive imaging have high sensitivity with however wide range of specificity for detecting myocardial viability. Both perfusion and function imaging modalities provide complementary information about myocardial viability and no optimum single imaging technique exists that can provide very accurate diagnostic and prognostic viability assessment. The weight of the body of evidence suggested that non-invasive imaging can help in guiding therapeutic decision making in patients with LV dysfunction.

1. Introduction

Because of high mortality rate and increasing prevalence of heart failure and the need to tailor therapy to the etiology and stage of the condition, testing of patients with heart failure will become increasingly common [2]. Non-invasive imaging can help identify viable segments of myocardium that have greater likelihood of improving functionally when an adequate blood supply is restored. Echocardiography, radionuclide images, cardiac magnetic resonance imaging and recently myocardial computerized tomography perfusion imaging are used to detect and assess ischemia and myocardial viability. These imaging modalities detect signs of myocardial viability through contractile reserve in response to low dose dobutamine, intact cell membrane or residual glucose utilization.

2. Definition and historical perspective of myocardial viability

Myocardial viability is the myocardium with a potentially reversible contractile dysfunction in patients with chronic CAD. Myocardial stunning is defined as a prolonged contractile myocardial dysfunction after a transient acute ischemia, whereas dysfunctional myocardium which improves after coronary revascularization is defined as myocardial hibernation [3,4]. Myocardial viability has been clinically recognized for more than 40 years ago. The term 'myocardial viability' adopted by clinicians relies on a clinical phenomenon that is potentially salvageable with treatment using revascularization, drugs or devices. The prognostic benefit is measured by patient's survival and symptomatic improvement or with cardiac function measurements.

For more than four decades, several observational trials have identified the reversible myocardial dysfunction post revascularization in patients with CAD and showed that ischemic LV dysfunction is not always irreversible. In 1973, Chatterjee et al. reported improved myocardial wall motion abnormalities following revascularization in the CAD patients in the absence of myocardial scar [5]. A year later, Horn et al. (1974) concluded that myocardial wall motion abnormalities improved by inotropic stimulation with epinephrine infusion in patients with CAD and LV asynergy [6]. Rahimtoola and Braunwald in the mid eighties used the term myocardial hibernation to describe a condition of abnormal resting ventricular function because of chronic hypoperfusion in CAD patients [3,4,7,8]. As a result of coronary blood flow reduction, acute and chronic adaptations of the myocardium prevent irreversible myocardial damage.

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http://dx.doi.org/10.1016/j.ijcha.2014.10.008

3. Imaging techniques employed for viability assessment

Several non-invasive imaging modalities are used to assess myocardial viability and to identify markers of functional recovery. These imaging modalities have different diagnostic accuracy and limitations [9]. Assessment of systolic function and contractile reserve within areas of dysfunction are based on the imaging of dysfunctional myocardium using dobutamine stress echocardiography, Doppler tissue imaging and dobutamine stress cardiac magnetic resonance (CMR). Assessment of perfusion is based on the documentation of cell integrity using contrast echocardiography and nuclear techniques (SPECT and PET) by perfusion tracers or a combination of metabolic and perfusion tracers, respectively. Moreover, delayed enhancement CMR imaging and more recently multi slice computer tomography (MSCT) delayed enhancement imaging can define necrotic myocardium. For diagnostic and prognostic viability assessment, the relative merits of non-invasive myocardial function imaging as compared to myocardial perfusion imaging are discussed.

3.1. Non-invasive myocardial function imaging

3.1.1. Dobutamine stress echocardiography

Dobutamine stress echocardiography (DSE) is the most widely used modality and most extensively studied test for the assessment of myocardial viability. Contractile reserve is the most common criterion used to detect viable myocardium. Usually low dose Dobutamine is used by infusion of 5–10 mcg/kg/min Dobutamine which increases contractility in dysfunctional but viable myocardium while nonviable myocardium does not show this contractile reserve. In 1997 a meta-analysis by Bax et al. pooled 37 studies showed an overall sensitivity of 84% and specificity of 81% as compared with other imaging techniques, DSE has an overall similar sensitivity and the highest specificity [10]. In addition, pooled data by Bax et al. (2001) evaluated the detection of hibernating myocardium and utilized myocardial perfusion images and DSE [11]. However, most of these studies did not compare imaging techniques in the same patients [12]. FDG-PET, reinjection thallium SPECT, and DSE had the highest negative predictive values while rest–redistribution thallium SPECT and technetium sestamibi SPECT had lower values. The highest positive predictive value was seen with DSE with intermediate values for other forms of radionuclide myocardial perfusion imaging of 84% versus 75% except reinjection thallium SPECT which had the lowest value. However, DSE had the lowest negative predictive values in comparison with FDG-PET and reinjection thallium SPECT of 69% versus 80%. Furthermore, for the prediction of an improvement in LV ejection fraction (EF) after revascularization, DSE had the highest positive and negative predictive values compared with nuclear imaging (77% versus 70% and 85% versus 78%, respectively) [11]. Similar results have recently been confirmed by Schinkel et al. (2007) [13].

3.1.2. End diastolic wall thickness

End diastolic wall thickness (EDWT) may provide the simplest method to identify myocardial viability. This approach uses a cut-off value of $\geq$5.5–6 mm in most studies to determine whether a segment is viable [14]. Echocardiography and CMR can be used to measure the EDWT with the advantage of CMR that provides accurate measurements of the entire LV wall. In a meta-analysis study that used echocardiography and nuclear imaging [15], EDWT predicted functional recovery with a sensitivity of 94% but low specificity of 48% which were comparable to CMR-based wall thickness measurements results reported in a recent meta-analysis [16].

3.1.3. Myocardial strain imaging

More information on myocardial viability can be obtained by strain and strain rate. Strain is the deformation of an object relative to its original length and strain rate is the gradient of velocities between two points in space. Strain and strain rate imaging can be obtained either from color tissue Doppler imaging or 2D speckle tracking [17]. Echocardiography and CMR can be used to quantify myocardial strain and strain rate. Strain rate imaging, 2D speckle tracking and myocardial tagging may improve accuracy in detecting myocardial viability. In a study by Hoffmann R et al. (2002), strain rate imaging in combination with low dose dobutamine was used to improve assessment of viable myocardium in 37 patients with ischemic cardiomyopathy. An increase of peak systolic strain rate of $\geq$0.23/s had a sensitivity of 83% and specificity of 84% [18]. In addition, adenosine speckle tracking could be used to discriminate viable from non-viable myocardium with stress. In a recent small trial by Ran et al. (2012), 36 patients who had sustained previous MI and EF of 40% ($\pm$6%) were assessed and showed that using adenosine stress, radial myocardial strain more than 9.5% had a sensitivity of 83.9% and a specificity of 81.4% for detecting viable myocardium, whereas a change of longitudinal strain more than 14.6% displayed a sensitivity of 86.7% and a specificity of 90.2%. Peak-systolic circumferential strain however, had little effect on viability assessment. The study concluded that 2D speckle tracking imaging combined with adenosine stress echocardiography could be reliable method to detect viable myocardium [19].

3.1.4. Dobutamine stress CMR

Dobutamine stress CMR is based on the same principle as in the DSE that determines the contractile reserve of dysfunctional myocardium by administrating low dose dobutamine of 5–10 mcg/kg/min, viable myocardium will show an increased contractile function and non-viable myocardium will remain unchanged [20]. A recent meta-analysis by Romero et al. (2012) pooled nine studies assessing low dose dobutamine stress CMR showed that mean weighted sensitivity and specificity for low dose dobutamine stress CMR were 81% and 91%, whereas the PPV and NPV were 93% and 75%, respectively. Low dose dobutamine stress CMR showed the highest specificity in comparison with LGE and end-diastolic wall thickness [16].

Low dose dobutamine stress CMR and DSE are comparable as shown by Baer et al. (2000) in head to head study comparing dobutamine stress CMR and dobutamine stress transoesophageal echocardiography for predicting recovery of ventricular function post revascularization in patients with chronic CAD [21]. Both tests were highly accurate where the respective values of sensitivity and specificity for echocardiography were 82% and 83%, whereas for the CMR were 86% and 92%, respectively. A small study by Wellnhoffer et al. enrolled 29 patients suggested that low dose dobutamine stress CMR was superior to LGE in predicting improvement in wall motion of dysfunctional segments with 1–74% transmural extent of myocardial infarction after revascularization [22]. In addition, a study by Bove et al. demonstrated a similar improvement in percentage of wall thickness and LV function with low dose dobutamine in segments with 1–50% transmural infarction after revascularization [23]. Other studies suggested that the combination of LGE and low dose dobutamine stress CMR may offer a more reliable method of assessing myocardial viability [24,25]. A recent study demonstrated that combination of CMR viability parameters, contractile reserve by low dose dobutamine, EDWT and scar quantification improved the prediction of function recovery [26].

3.2. Non-invasive myocardial perfusion imaging

3.2.1. Myocardial contrast echocardiography

Myocardial contrast echocardiography (MCE) uses intravenous contrast agents composed of high molecular weight inert gases which produce microbubbles which behave like red blood cells and stay in the vascular space thus allow direct visualization of myocardial perfusion. The intensity of myocardial contrast reflects the myocardial blood flow. Therefore, dysfunctional segments are classified as viable when segments have normal or patchy perfusion and nonviable when segments have no perfusion [15].