Magnetic resonance imaging and positron emission tomography as predictors of heart failure

Christoph Klein
Department of Internal Medicine/Cardiology, German Heart Institute, Berlin, Germany

Correspondence: Christoph Klein MD, Internal Medicine/Cardiology, German Heart Institute Berlin, Augustenburger Platz 1, 13353 Berlin, Germany.
Tel: +49 (0)30 45932457; fax: +49 (0)30 45932500; e-mail: klein@dhzb.de

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Abstract

Heart failure is a clinical syndrome of ischemic and non ischemic etiology. Imaging plays a major part in diagnosing its cause, course, and prognosis. In the ischemic heart, positron emission tomography (PET), by, for example, assessing myocardial perfusion and glucose metabolism, and magnetic resonance imaging (MRI), by evaluating myocardial function, myocardial necrosis, and/or inotropic contractile reserve, can predict contractile recovery, and therefore potential improvement of heart failure, after revascularization. In non ischemic cardiomyopathies such as dilative or hypertrophic cardiomyopathy, PET serves as an important tool for the assessment of metabolic changes, whereas MRI serves as the gold standard for measuring cardiac volumes and mass. In addition, late gadolinium enhancement MRI, which assesses regional fibrotic alteration of the myocardium, serves as a potential marker of disease progression and patient prognosis.
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Introduction

Heart failure is a clinical syndrome in which patients have symptoms (eg, shortness of breath at rest or on exercise) and signs (eg, tachycardia, tachypnea, pulmonary râles, or peripheral edema) typical of heart failure, together with objective evidence of a structural or functional abnormality of the heart at rest (eg, cardiomegaly, cardiac murmurs, abnormal echocardiogram, increased natriuretic peptide concentration) [1]. The prevalence of heart failure, whether symptomatic or asymptomatic, is approximately 4% in the population as a whole; however, as the condition is age related, its prevalence is between 10 and 20% in people aged 70–80 years. The prognosis in general is poor, as approximately 50% of patients die within 4 years. The etiology of heart failure is manifold. Coronary artery disease is the most common etiology in the western world, being the initiating cause in approximately 70% of patients. Valve disease and cardiomyopathies each account for 10%. Other causes include hypertension, drugs, toxins, endocrine disorders, and infiltrative disorders. In addition to clinical evaluation, cardiac imaging has a major role in diagnosing heart failure and characterizing its cause, course, and prognosis.

Positron emission tomography

Positron emission tomography (PET) can incorporate positron-emitting radionuclides into biochemical

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molecules and can, therefore, not only image their distribution, but also quantify their uptake. In this way myocardial perfusion, glucose utilization, fatty acid uptake, oxygen consumption, and pre- and postsynaptic neuronal activity can be assessed.

Magnetic resonance imaging

The strength of magnetic resonance imaging (MRI) lies in its intrinsic tissue contrast. It has emerged as the gold standard for measurement of cardiac volumes, mass, and ejection fraction. Tissue characterization is possible with different imaging weighting (T1/T2) and with the application of gadolinium-containing extracellular T1-shortening contrast agents. Myocardial edema, often present in acute inflammation of whatever cause, results in a high signal in T2-weighted imaging [2]. Extracellular, gadolinium-containing contrast agents distribute in the vascular and interstitial spaces, but are excluded from the cellular space. If the interstitial space is enlarged as in myocardial fibrosis (whether for ischemic or non ischemic reasons), or if the ability of the myocyte to exclude the contrast agent is impaired as in acute myocardial infarction, the concentration of the contrast agent is increased in that region, resulting in a high signal in special T1-weighted imaging late after the application of the contrast agent. This is called ''late gadolinium enhancement'' (LGE) [3]. Because of the high spatial resolution, the transmural extent or the distribution, or both, of LGE, and therefore a pathological structural process, can be quantified.

Ischemic heart failure

Besides reducing exercise capacity, coronary artery disease is the major cause of heart failure, as a result of (a) myocardial infarction resulting in necrosis (non viability), or (b) reduced perfusion at rest or impaired perfusion reserve resulting in stunning/hibernation*, both leading to reduced contractile capacity (viability). Distinguishing between these two states is of crucial importance: after revascularization, areas of transmural necrosis will not show any improvement in contractile performance, whereas areas of stunning/hibernation or non transmural infarct may exhibit improved contractile performance leading to an improvement in left ventricular ejection fraction and, thus, a beneficial alteration in the prognosis for the patient.

PET can be used to evaluate myocardial viability. The most widely used technique is the combination of myocardial perfusion using ammonia (NH_3) or water (H_2O) and glucose metabolism using [^{18}F]fluoro-2-deoxy-D-glucose. Dysfunctional areas with normal or reduced perfusion and maintained glucose metabolism are suggestive of hibernating
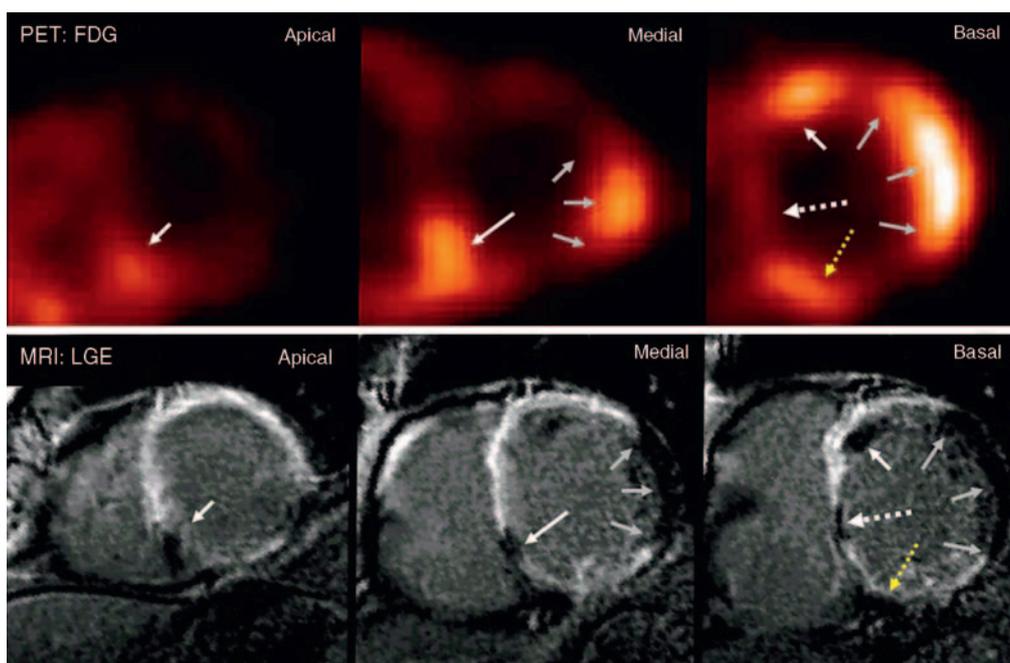

Figure 1. Short-axis views (apical, medial, and basal) of a patient with ischemic cardiomyopathy imaged with [^{18}F]fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (PET) (top row) and with late gadolinium enhancement (LGE) with magnetic resonance imaging (MRI) (bottom row). Areas without FDG uptake correlate with areas of LGE, suggesting non viability, whereas segments without LGE correlate with segments with preserved FDG uptake (arrows), suggesting viability. Because of the high spatial resolution of MRI, there is a clear delineation between viable and non viable myocardium. Small areas of viable myocardium (dotted white arrow, basal slice) and small subendocardial infarcts (dotted yellow arrow, basal slice) can be detected with higher sensitivity.

myocardium or non transmural infarct and have a high chance of contractile recovery after revascularization compared with regions having both reduced perfusion and glucose metabolism. Although the spatial resolution of PET is not sufficient to measure the transmural extent of viable and non viable myocardium, assessment of relative tracer uptake does provide some information. Approximately 50% tracer uptake may serve as the threshold for functional recovery [4]. Several studies have demonstrated sensitivity and specificity of 86–93% and 58–73%, respectively [5]. An exact threshold for the amount of viable dysfunctional myocardium for the prediction of improvement in global myocardial function has not been clearly defined, but it appears to be around 25–30% of viability [6]. Besides contractile recovery, PET can predict outcome [7] and perioperative complications [8].

After the application of extracellular contrast agents, MRI can identify myocardial necrosis that correlates with data derived from PET [9] (*Figure 1*). However, because of its greater spatial resolution, MRI not only enables the exact assessment of the transmural extent of the infarction, but, additionally, is more sensitive in identifying even small subendocardial infarcts [9] and peri-infarct zones [10], which is of prognostic relevance [11]. In the acute and chronic settings, the transmural extent of necrosis is a parameter of functional recovery after revascularization [12,13], as areas with no or any subendocardial infarcts have a high, and areas with a near-transmural infarct a very low, chance of recovery. Thus the transmural extent of LGE is a marker of the progression or reversibility of ischemic heart failure. By adding edema imaging (T2-weighted) in the case of an acute event, the difference between edema and LGE represents the salvaged myocardium [14] and is therefore a marker of the course of myocardial function and prognosis [15] (*Figure 2*). In addition to the detection and identification of the transmurality of infarction, by adding parameters such as wall thickness and inotropic reserve in response to low-dose dobutamine, MRI offers an excellent tool for predicting functional recovery [16], especially in areas with non transmural infarction of intermediate transmurality. Furthermore, after an acute myocardial infarction, infarct size measured by MRI has been found to be a strong predictor of left ventricular remodeling [17]. As for PET, there is no valid information from MRI studies concerning the amount of viable tissue needed for improved heart failure and prognosis. It remains unknown whether the revascularization of small epicardial viable rims without contractile improvement is of any prognostic value – for example in terms of less left ventricular remodeling or electrical stability – but this question is the subject of current research. Although the use of MRI in cardiology is a fairly young discipline for which there are relatively few
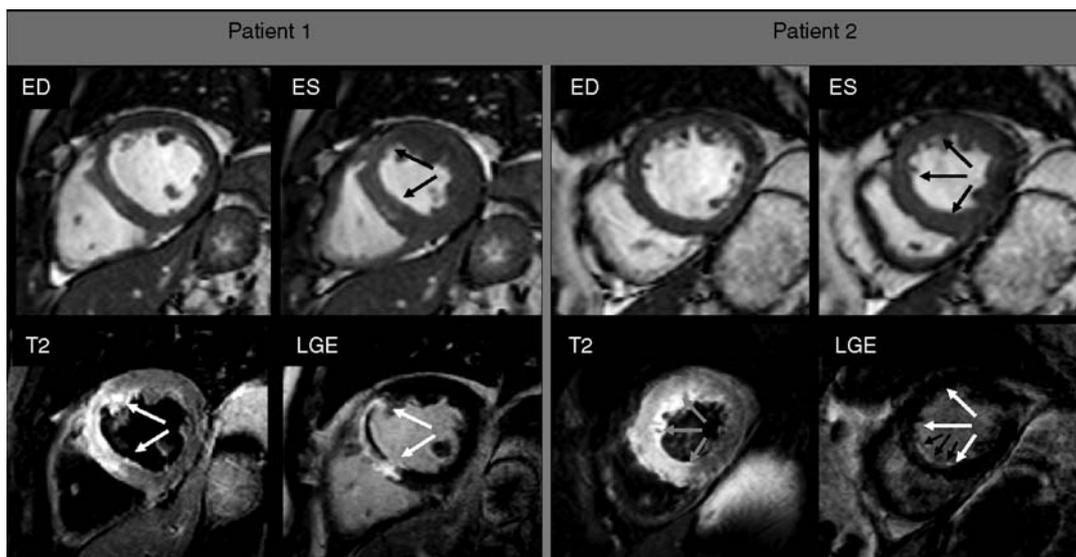

Figure 2. Short-axis view of two patients with acute revascularized anteroseptal myocardial infarction. Both patients have akinesia in the anteroseptal segments (top row, black arrows). The high signal intensity in the T2-weighted images (arrows) suggests myocardial edema, which shows a similar extent of distribution as the wall motion abnormality and therefore represents the area at risk. In patient 2, some of the very high anterior signal, which appears to be subendocardial, is actually blood that is insufficiently suppressed by the ''black blood'' prepulses. In patient 1, late gadolinium enhancement (LGE) (white arrows) is of equal distribution as the area at risk (gray arrows), with additional microvascular obstruction (black subendocardial margin surrounded by LGE). In patient 2, the extent of LGE (black arrows) is much smaller than that of the edema (grey arrows) and located only in the subendocardial layer, without microvascular obstruction. Whereas patient 1 had a transmural infarction with an area of necrosis the size of the occluded vessel territory, with little chance of contractile recovery, patient 2 demonstrates a large area of salvaged myocardium (T2 > LGE), with high probability of contractile improvement (small subendocardial scar only). ED, end-diastolic; ES, end-systolic.

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clinical data, because – in particular – of the greater availability and the high quality of information on function and tissue characterization that it affords, it is very attractive for the assessment of clinical viability and has been classified, alongside nuclear and echocardiographic methods, as a Class I indication [18].

Table I lists the MRI and PET features of different types of myocardial tissues and their prediction of contractile improvement.

Non ischemic cardiomyopathies

Non ischemic cardiomyopathies have unique functional, morphological, and tissue characteristics. It has recently been acknowledged that, in addition to the functional information it provides, MRI can further characterize non ischemic cardiomyopathies by the presence, extent, and pattern of edema/LGE imaging, and detect cardiac involvement of systemic diseases such as sarcoidosis or amyloidosis [19]. LGE is an unspecific marker of increased regional fibrosis. In idiopathic cardiomyopathy, it is present in approximately 30–40% of patients and is a marker of worse prognosis in terms of progressive disease, reduced likelihood of response to medical treatment, and susceptibility to arrhythmogenic events. In hypertrophic cardiomyopathy, functional MRI is more sensitive than echocardiography in detecting areas of hypertrophy [20]. In addition, left ventricular mass [21] and the presence of LGE [22] may be more sensitive markers than, for example, septum thickness for progressive disease and risk for sudden cardiac death. Similarly, MRI can be useful for the diagnosis and prognosis of patients with myocarditis, as the presence of edema and globally and regionally increased uptake of contrast agents suggest myocardial inflammation, whereas certain patterns of LGE may even indicate irreversible myocardial damage and progression to heart failure [23]. One problem that needs to be addressed is that LGE is an unspecific sign of fibrosis of whatever cause. However, the pattern and distribution of LGE and their combination with other functional and morphological features offer clues as to a specific cardiomyopathy. *Figure 3* shows the patterns of LGE in different cardiomyopathies [19]. Although experience remains too limited to allow the drawing of definite clinical conclusions (for example, the need for implantation of an intracardiac defibrillator because of increased risk of sudden cardiac death), MRI offers a tool with which to look deeper into the myocardial changes that occur in non ischemic cardiomyopathies, and is likely to have an impact on clinical management in the near future.

Heart failure is associated with several changes in myocardial perfusion, oxygen metabolism, and

Table I. Patterns of perfusion and metabolism assessed by positron emission tomography (PET), and of late gadolinium enhancement (LGE) and inotropic reserve assessed by magnetic resonance imaging (MRI) in ischemic myocardial dysfunction and prediction of functional recovery after revascularization.

Tissue type	PET Perfusion	PET + FDG Metabolism	MRI LGE	Functional recovery	Inotropic reserve	Functional recovery
Stunned	Normal	Normal to increased	No	Yes	Positive	Yes
Hibernation	Mildly reduced	Increased relative to perfusion	No; non transmural LGE possible	Yes	Positive	Yes
Non transmural infarction	Partly reduced	Partly reduced	0–25% transmurality	High probability	Yes	High probability
			26–50% transmurality	Medium probability	Yes/No	High probability/Low probability
			51–75% transmurality	Medium to low probability	Yes/No	High probability/Low probability
Transmural infarction	Severely reduced	Severely reduced	>75% transmurality	Very low probability	No	No
			100%	No	No	No

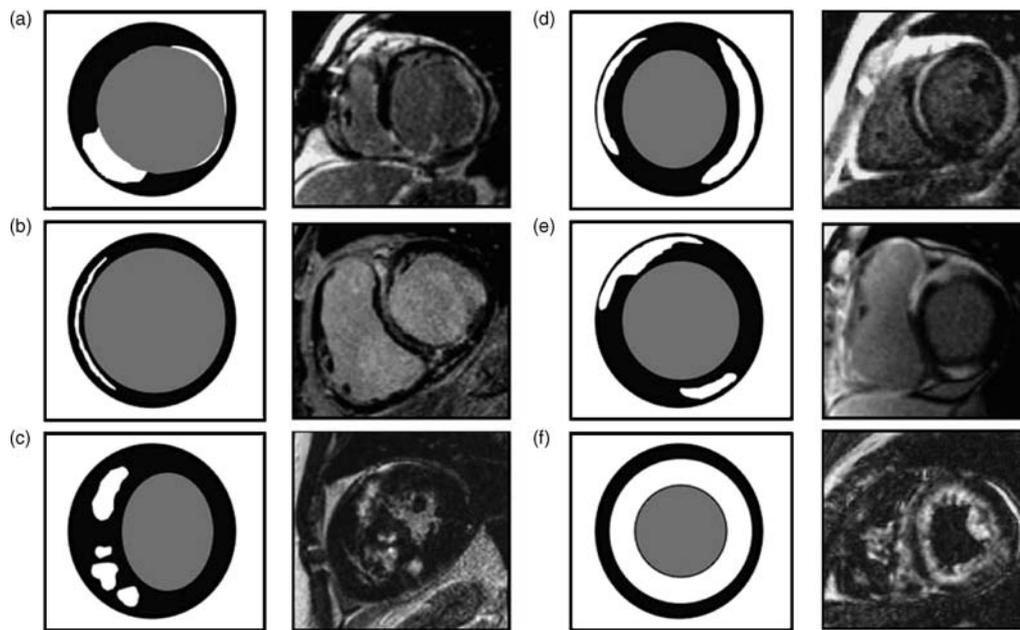FDG, [18F]fluoro-2-deoxy-D-glucose.

Figure 3. Characteristic patterns of late enhancement in specific cardiomyopathies. (a) Ischemic cardiomyopathy: regional thinning with 50% transmural scar in the lateral wall and 100% transmural scar in the inferoseptal wall. (b) Idiopathic dilated cardiomyopathy: mid-wall late enhancement in the basal septum. (c) Hypertrophic cardiomyopathy: patchy late enhancement within septum. (d) Myocarditis: epicardial zone late enhancement in the inferolateral and anteroseptal walls. (e) Sarcoidosis: dense epicardial zone late enhancement. (f) Amyloidosis: diffuse late enhancement progressing from subendocardium to epicardium (this pattern may also be seen in uremic cardiomyopathy and after heart transplantation). (From White and Patel [19], with permission.)

pre- and postsynaptic innervation. In addition to its application in basic research into primary and secondary alterations to innervation and metabolism in heart failure, PET may be able to provide valuable prognostic information in patients with hypertrophic and dilative cardiomyopathies, according to their responsiveness to vasodilators or the presence of scar tissue [24,25].

Conclusion

Whereas PET provides biological information, the strength of MRI lies mainly in assessment of function, morphology, and structural alteration of the myocardium. The combination of both methods may provide the most complete information about the cause and course of heart failure, and may shed more light on the processes underlying functional and morphological abnormalities.

*See glossary for definition of these terms. ■

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