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iREVIEWS

STATE-OF-THE-ART PAPER

Cardiac PET: A Versatile, Quantitative Measurement Tool for Heart Failure Management

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Current American Heart Association/American College of Cardiology practice guidelines classify congestive heart failure (CHF) in 4 stages (A, B, C, and D). This review focuses on state-of-the-art and future applications of quantitative positron emission tomography (PET) myocardial perfusion and metabolic imaging in the clinical evaluation and treatment of patients in all CHF stages. Basic physiological and metabolic principles related to the regulation of myocardial blood flow and metabolism at various stages of CHF are briefly reviewed. The advantages of quantitative PET image analysis in contrast to simple qualitative visual analysis of the scans also will be addressed. Finally, potential future clinical applications of quantitative PET for CHF evaluation and treatment will be discussed. (J Am Coll Cardiol Img 2011;4: 292–302) © 2011 by the American College of Cardiology Foundation

Current American Heart Association/American College of Cardiology guidelines recommend consideration of congestive heart failure (CHF) in 4 stages (A, B, C, and D; Fig. 1) (1). Stages A and B represent preclinical CHF (stage A: patient at high risk but without structural heart disease; stage B: structural heart disease present but symptoms/signs of CHF absent). Stages C and D reflect overt CHF (stage C: structural heart disease present with prior or current symptoms of CHF; stage D: refractory CHF requiring specialized intervention). The incidence of CHF in the United States has been increasing steadily in recent years (400,000 new cases every year estimated by the National Heart, Lung and Blood Institute in 1996), and mortality, particularly in stage D, is in excess of 50% per year (2). Accordingly, the syndrome represents a major public health problem. Ischemic heart disease (IHD) and hypertension are the most common causes of CHF, although obesity and diabetes, even in the absence of overt IHD but frequently present together and often with hypertension, are increasingly recognized as common etiologies (2). Quantitative positron emission tomography (PET) imaging plays an important role in both diagnosis of etiology and assessment of treatment of CHF at various stages of the syndrome and provides prognostic information as well. The current state of the art and future directions for quantitative PET imaging in CHF is the focus of this review, which will also address the advantages of the quantitative approach in contrast to simple qualitative visual interpretation of PET cardiac images.

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Quantitative PET Imaging in Patients With CHF: State of the Art

The role for state-of-the-art quantitative PET measurement of myocardial blood flow (MBF) (Fig. 2) and metabolism (glucose and fatty acid) depends on the specific clinical question(s) to be addressed. However, in more general terms, there are several points that should be made concerning the advantages of quantitative versus qualitative simple visual analysis of cardiac PET images in patients with CHF. First, simple visual analysis of PET myocardial perfusion images requires the assumption of a "normal" perfusion or metabolic zone—an erroneous assumption and clearly a major limitation of that approach. Second, simple visual interpretation is by definition subjective and hence liable to all associated shortcomings. Third, it has been shown in a modern clinical trial (PARR 2 [PET and Recovery Following Revascularization]) (3,4) and older observational studies (5–9) that objective measurement of parameters indicative of myocardial viability or myocardial flow reserve are valuable in improving patient management or assessing prognosis in patients with CHF. Such parameters (e.g., quantitative, objective determination and extent of MBF/^{18}F-fluorodeoxyglucose [FDG] "mismatch" and ^{82}Rb myocardial tracer kinetics and measurement of myocardial flow reserve) necessitate state-of-the-art quantitative PET imaging of MBF and metabolism and cannot be obtained by simple visual analysis of static PET images. Finally, potential future clinical applications for PET cardiac imaging in CHF (e.g., risk assessment for sudden cardiac death in patients with ischemic cardiomyopathy; PARAPET [Prediction of Arrhythmic Events With Positron Emission Tomography] trial) (10–13) will depend on adoption of current state-of-the-art quantitative PET methodologies used in such trials for assessment of MBF, glucose metabolism, and sympathetic nervous system function.

Pathophysiology of MBF and Clinical Applications of PET in Left Ventricular Dysfunction and CHF

Ischemic cardiomyopathy. Endothelial dysfunction related to dyslipidemia and oxidant stress (14,15) is known to affect the coronary microcirculation before the onset of overt coronary atherosclerosis and therefore places affected individuals in stage A CHF (high risk, without structural heart disease). Ongoing dyslipidemia, oxidant stress, and resulting endothelial dysfunction commonly progress to overt coronary atherosclerosis (stage B CHF), which in turn may be complicated by acute myocardial infarction and resulting left ventricular (LV) dysfunction or frank CHF (stage C CHF). Extensive myocardial damage from either a single or multiple infarcts may result in refractory CHF requiring specialized treatment or intervention (stage D CHF). Positron emission tomography measurements of absolute myocardial blood flow play an important role in patient management at each stage of CHF related to IHD or predisposing conditions such as obesity, hypertension, diabetes, dyslipidemia, and smoking. PET assessment of myocardial viability (typically with combined MBF and glucose [^{18}F-FDG] metabolism study) is especially important in stages C and D CHF.

The role of PET measurements of MBF in assessment of coronary microvascular function has been reviewed extensively (14–16). Even asymptomatic patients with dyslipidemia without manifest IHD may have abnormal myocardial flow reserve owing to coronary microvascular dysfunction (17). The same is true of patients with obesity, diabetes, and hypertension either alone or in combination (18). A common mechanism in each of these conditions is endothelial dysfunction related to oxidant stress and subsequent reduction in nitric oxide bioavailability (18–21). Depending on whether or not LV hypertrophy is present in association with hypertension, mechanical compressive forces and interstitial fibrosis also may play a role (22). Circulating vasoactive peptides (e.g., endothelin) (23) also may contribute to impairment of coronary microvascular dilator capacity. Finally, it has been shown that evidence of increased serum levels of circulating biomarkers of inflammation increase the risk of developing CHF (24–26) and may do so at least in part via the oxidant stress mechanism noted earlier.

ABBREVIATIONS AND ACRONYMS

CAV = coronary artery vasculopathy
CHF = congestive heart failure
DCM = dilated cardiomyopathy
FDG = fluorodeoxyglucose
FFA = free fatty acid
IHD = ischemic heart disease
IVUS = intravascular ultrasound
LV = left ventricular
MBF = myocardial blood flow
PET = positron emission tomography

Several small observational studies in humans have suggested that PET measurements of absolute MBF and MBF reserve may be useful in providing prognostic information concerning progression from stage A/B to C/D CHF in patients with hypertrophic (5,27) or idiopathic dilated cardiomyopathy (DCM) (7). Although the studies have certain limitations in addition to small sample size, such as reliance on flow reserve ratio as an end point, they nevertheless demonstrated the potential for quantitative measurements of absolute MBF to