MAJOR ACHIEVEMENTS IN NUCLEAR CARDIOLOGY: XI

Advances in positron emission tomography

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INTRODUCTION

The experimental and clinical use of positron emission tomography (PET) has contributed significantly to advance our understanding of heart physiology and pathophysiology for more than 25 years. Initially, it emerged as a powerful investigative tool that allowed in vivo quantification of physiologic processes including myocardial perfusion and metabolism, as well as neuronal and receptor function. However, the wealth of data built by many investigators over the years has allowed PET imaging to now play an important role in the clinical evaluation of patients with known or suspected ischemic heart disease.

This important clinical role is expected to grow with the availability of PET/computed tomography (CT) scanners that allow a true integration (fusion) of structure and function.1 This will allow a comprehensive examination of the heart’s anatomy and function in ways never before possible. The objective of this review is to provide the reader with an update on the current and (potential) future role of PET in clinical cardiology, with a special eye on the great opportunities now offered by PET/CT.

CURRENT ROLE OF CARDIAC PET IN THE EVALUATION OF PATIENTS WITH KNOWN OR SUSPECTED CORONARY ARTERY DISEASE

Preclinical Coronary Artery Disease

The significant advances in our understanding of the mechanisms that initiate and facilitate the progression of coronary atherosclerosis have greatly improved our ability to target therapies aimed at prevention, halting progression or promoting regression of atherosclerosis before it becomes clinically overt. Thus cardiovascular medicine is witnessing a dramatic shift from the “traditional” paradigm of diagnosing obstructive coronary artery disease (CAD) to a “new” paradigm in which the central goal is to detect patients who are at risk for the development of CAD or who already have preclinical (albeit not obstructive) disease.

In this paradigm shift, the traditional relative assessments of regional myocardial perfusion will likely be insensitive to identify preclinical CAD and, thus, be of limited clinical value. It is now clear that endothelial dysfunction is an early event in atherosclerosis that precedes the development of structural changes in the coronary arteries, and it is magnified in the presence of coronary risk factors and obstructive CAD. Consequently, endothelial dysfunction and its resulting consequences on coronary vasoreactivity comprise an attractive diagnostic target, especially for methods that can quantify coronary vasodilator dysfunction noninvasively such as PET. Detection of patients at risk may offer an opportunity for early medical intervention aimed at halting the progression of atherogenesis and ultimately lead to a reduction in cardiovascular events.

Relationship between risk factors and coronary vasoreactivity as measured by PET

There is mounting and consistent evidence that patients with coronary risk factors including dyslipidemia, diabetes, hypertension, and smoking demonstrate abnormal coronary vasodilator function as measured by PET (Figure 1).2 Importantly, these abnormalities are present in patients without clinically overt (obstructive) CAD. These abnormalities have been linked to endothelial dysfunction, an early event in atherogenesis. Thus PET measures of coronary vasodilator function may be useful surrogate markers of atherosclerotic disease activity. Such measurements of impaired coronary vasoreactivity, in patients with and without obstructive CAD, may also have important prognostic implications.3-7 Furthermore, the available evidence also suggests that these measures of coronary vasoreactivity are useful markers with which to monitor therapeutic responses.8-12

Clinical CAD

PET has proven to be a powerful and efficient noninvasive imaging modality with which to evaluate regional myocardial perfusion in patients with known or suspected CAD. Several technical advantages account for the improved diagnostic power of PET including (1)
routine measured (depth-independent) attenuation correction, which decreases false-positive results and, thus, increases specificity; (2) high spatial and contrast resolution (heart-to-background ratio) that allows improved detection of small perfusion defects, thereby decreasing false-negative results and increasing sensitivity; and (3) high temporal resolution that allows fast dynamic imaging of tracer kinetics, which makes absolute quantification of myocardial perfusion (in milliliters per minute per gram of tissue) possible. In addition, the use of short-lived radiopharmaceuticals allows fast sequential assessment of regional myocardial perfusion (eg, rest and stress), thereby improving laboratory efficiency and patient throughput (Figure 2).

Although these technical advantages have been recognized for a long time, the use of PET for routine detection of CAD has only gained momentum in recent years. Recent Food and Drug Administration approval of PET radiotracers (ie, rubidium 82, nitrogen 13 ammonia, and fluorine 18 fluorodeoxyglucose [FDG]) and the subsequent changes in reimbursement are responsible for much of the recent growth in clinical cardiac PET.

**Diagnostic accuracy of PET for detection of obstructive CAD** The experience with PET for detecting obstructive CAD has been extensively documented in 7 studies including 663 patients (Table 1). In these studies regional myocardial perfusion was assessed with N-13 ammonia or Rb-82; the mean sensitivity for detecting greater than 50% angiographic stenoses was 89% (range, 83%-100%), whereas the mean specificity was 86% (range, 73%-100%).

**Comparative studies of PET versus single photon emission computed tomography** Only two studies have performed a head-to-head comparison of the diagnostic accuracy of Rb-82 PET and thallium 201 single photon emission computed tomography (SPECT) in the same patient population. Go et al compared PET and SPECT in 202 patients. Their results showed a higher sensitivity with PET (76% vs 93%) and no significant changes in specificity (80% vs 78% for SPECT vs PET). In another study Stewart et al compared PET and SPECT in 81 patients. They observed a higher specificity for PET (53% vs 83% for SPECT vs PET), and no significant differences in sensitivity (84% vs 86% for SPECT vs PET). Diag-

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**Figure 1.** Bar graph illustrating average coronary flow reserve as determined by PET in patients with dyslipidemia (left) and diabetes (right) without clinically overt CAD.

**Figure 2.** Imaging protocol for the evaluation of regional myocardial perfusion with conventional PET scanners (top) and with PET/CT (bottom).