The Additive Value of Combined Assessment of Myocardial Perfusion and Ventricular Function Studies*

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In addition to providing quantitative ventricular function information, gated SPECT and radionuclide angiocardiographic studies can evaluate regional wall motion and ventricular volumes. This review focuses on the combined assessment of myocardial perfusion and left ventricular function. Two clear roles for nuclear imaging in clinical practice include the diagnosis of coronary artery disease and assessment of prognosis in patients with known coronary artery disease. Ventricular function information can help differentiate an attenuation artifact from an infarct and is helpful in diagnosing 3-vessel coronary disease. Additionally, several studies have highlighted the prognostic benefit to combined assessment of myocardial perfusion and ventricular function. Several new modalities have recently been reported that promise to continue to solidify the place of nuclear imaging in the diagnosis and prognosis of coronary artery disease.

Key Words: clinical cardiology; SPECT; myocardial perfusion; nuclear cardiology; ventricular function

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Early cardiac nuclear imaging studies were hampered by an inability to integrate myocardial perfusion imaging with studies of ventricular function. Though myocardial perfusion imaging (1) and radionuclide cineangiography (2) have been possible since the 1970s, it was not until the subsequent decade that the 2 modalities were used simultaneously (3). Since those early reports, other investigators have successfully related the results of using electrocardiogram-gated images to evaluate left ventricular function by comparing their findings with equilibrium-gated blood pool measurements (4), conventional radionuclide measurements (5), and echocardiographic ejection fraction assessments (6–8).

This review focuses on the combined assessment of myocardial perfusion imaging and left ventricular function. Two clear roles for nuclear imaging in clinical practice include the diagnosis of coronary artery disease (CAD) and assessment of prognosis in patients with known CAD. Combined nuclear imaging can play a role in both these areas, and in fact, the addition of left ventricular function data to myocardial perfusion imaging can enhance the clinician’s ability to both diagnose CAD and assess prognosis.

DIAGNOSIS

Assessment of ventricular function has long been recognized as a sensitive means by which to diagnose the presence of CAD, as shown in early studies of first-pass radionuclide angiocardiography (9,10). More recently, studies have evaluated the diagnostic benefit of adding ventricular function information to myocardial perfusion imaging. Borges-Neto et al. studied 167 patients with suspected CAD who underwent myocardial perfusion imaging, radionuclide angiography, and cardiac catheterization. They found that combined nuclear perfusion and functional studies contributed 31% of the diagnostic information beyond that provided by clinical and electrocardiographic data alone when evaluating for the presence of severe CAD; that is, functional studies had an incremental value of 16% and myocardial perfusion imaging provided an additional value of 15% above functional studies (11). Other studies have confirmed the benefit of ventricular function assessment. Flamen et al. evaluated 52 patients undergoing cardiac catheterization after a recent myocardial infarction. All received perfusion imaging as well as first-pass radionuclide angiography. The authors found that ejection fraction, wall motion score, and myocardial perfusion score were all associated with the presence of severe CAD. However, on multivariate analysis, only wall motion score was an independent predictor of severe CAD (12). Similarly, an evaluation of 70 patients undergoing exercise treadmill as well as myocardial perfusion imaging and radionuclide angiography found that stepwise addition of scintigraphic data—perfusion followed by ejection fraction—to the tread-
mill score provided significant incremental value in predicting the extent of CAD (13).

The benefit of ventricular function information is not limited to first-pass radionuclide angiography. An evaluation of 99 patients with suspected CAD who were undergoing gated SPECT in addition to myocardial perfusion imaging found that postexercise wall motion abnormalities added significant incremental value over stress myocardium perfusion alone for the identification of severe CAD in patients with normal resting myocardial perfusion findings. The sensitivity for identifying severe CAD by wall motion abnormality was 78%, versus 49% for myocardial perfusion imaging ($P < 0.0001$), and specificity was not significantly different. The authors suggested that decreases in subendocardial blood flow, as might be seen in severe CAD, could result in severe impairment of myocardial function without causing an observable perfusion defect (14).

Much of the benefit of the addition of ventricular function data to myocardial perfusion imaging may relate to the ability of gated SPECT and radionuclide angiography to help differentiate attenuation from infarct. This finding was confirmed by DePuey et al., who performed myocardial perfusion imaging and gated SPECT on 551 patients. Thirty-three percent of these patients had isolated fixed defects on myocardial perfusion imaging. By using gated SPECT to evaluate these areas of decreased perfusion, the percentage of patients with “unexplained fixed defects,” that is, no clinical myocardial infarction, was decreased from 14% to 3%. About half of these unexplained defects were anterior abnormalities in women, which were believed to be related to breast attenuation. The authors thus concluded that gated SPECT could potentially improve specificity (15). Another evaluation of 285 patients undergoing gated SPECT found that the addition of ventricular function information to myocardial perfusion data decreased the number of “borderline” interpretations from 89 to 29 (16). Similarly, Taillefer et al. studied 115 with known coronary anatomy. They performed thallium myocardial perfusion imaging as well as gated SPECT and found that specificity for coronary stenoses improved by greater than 50%, from 86% to 94%, and that specificity for stenoses improved by greater than 70%, from 84% to 92% (17).

Another potential use of this additional technology is in identifying patients with multivessel CAD who might otherwise be missed by myocardial perfusion imaging. A recent study attempted to evaluate this question. Yamagishi et al. found that the sensitivity for detecting multivessel CAD was increased (from 26.9% to 43.4%, $P < 0.05$) by the addition of ejection fraction by gated SPECT to myocardial perfusion imaging. The authors concluded that the worsening of ventricular function by exercise had the potential to increase the sensitivity of patients with multivessel CAD among those without multivessel patterns of reversible defects (18).

Thus, the diagnostic benefits of nuclear modalities that determine ventricular function cannot be overstated. These benefits encompass enhanced sensitivity and specificity for significant coronary artery stenoses. Furthermore, the addition of ventricular function information to myocardial perfusion imaging can aid in the interpretation of clinically complex studies, such as those involving multivessel disease and attenuation artifacts.

**PROGNOSIS**

An equally, if not more, useful role for the adjunctive use of myocardial perfusion and ventricular function studies is in determining cardiac prognosis. The prognostic value of SPECT alone has long been recognized. Machecourt et al. evaluated the prognostic information gleaned from SPECT myocardial perfusion imaging and found that cardiovascular survival was related to the number of perfusion abnormalities present, with a cumulative 32-mo survival of 83% in patients with 4 or more abnormal cardiac segments (19). Similarly, another group of investigators found that the extent of reversible defects on SPECT added information to clinical and catheterization data (20). Hachamovitch et al. studied 2,200 patients without known CAD and found that SPECT added prognostically even after clinical and exercise variables had been utilized (21).

As with myocardial perfusion imaging, ventricular function assessment has been found—in numerous studies of both radionuclide angiography and gated SPECT—to provide prognostic value. Several early studies provided evidence that evaluation of left ventricular function, specifically by radionuclide angiography, adds significantly to the prognostic value of clinical variables. Pryor et al. at Duke University followed 386 patients for up to 4.5 y. The investigators examined 6 variables, including rest and exercise ejection fraction by radionuclide angiography, change in ejection fraction with exercise, left ventricular wall motion abnormalities, and exercise time and found that exercise ejection fraction was the variable most associated with future cardiac events ($P < 0.01$) (22).

Later studies continued to evince the predictive benefits of radionuclide angiography over clinical variables. The Duke group studied 571 patients with symptomatic CAD and followed them for a median of 5.4 y. The investigators found that the most important radionuclide angiography predictor of mortality was the exercise ejection fraction ($P < 0.00001$) and that, when compared with noninvasive clinical data, radionuclide angiography variables were more predictive of mortality. In fact, the strength of the relationship of the radionuclide angiography variables to mortality was equivalent to a set of cardiac catheterization variables studied (23). A year later, these authors published a further study of 2,042 patients with CAD, examining the relationship of clinical and radionuclide angiography variables to cardiac mortality. They again found that exercise ejection fraction by radio-
nuclide angiocardiography was the single most important predictor of cardiac death (24). The results of the 2 previous studies were confirmed in 1998, when the Duke investigators found, in a study of 863 patients with CAD, that radionuclide angiocardiography was a key predictor of cardiac death when compared with both clinical and catheterization data (25).

Recently, other investigators have examined the ability of radionuclide angiocardiography to add information to myocardial perfusion imaging. Mast et al. studied 240 patients undergoing pharmacologic perfusion studies with adjunctive first-pass radionuclide angiocardiography and found that clinical information, myocardial perfusion data, and radionuclide angiography ejection fraction were all significant predictors of the combined endpoint of death and myocardial infarction. Interestingly, though, they found that the addition of radionuclide angiography ejection fraction to myocardial perfusion imaging data and clinical information added incremental prognostic value but that when the ejection fraction was added first, myocardial perfusion imaging had no incremental prognostic value (26). The predictive power of ejection fraction as determined by radionuclide angiography was also evaluated by Heiba et al., who studied 101 patients undergoing vascular surgery. They found that extent of both ischemic myocardium on perfusion imaging and left ventricular ejection fraction on radionuclide angiography had independent and complementary power to predict cardiac events in this population (27).

The prognostic information gleaned from radionuclide angiocardiography also is available from gated SPECT images. This has been confirmed in 2 separate studies from Cedars-Sinai Medical Center. In the first study, involving 1,680 patients, the authors found that both poststress ejection fraction and end-systolic volume, as determined by gated SPECT, were independent predictors of overall coronary events and provided incremental prognostic information over prescan clinical and myocardial perfusion data in predicting cardiac death and the combination of death and myocardial infarction. They concluded that an ejection fraction of less than 45% and an end-systolic volume of greater than 70 mL placed patients in a “high-risk” category (28). In a second study, the same research group evaluated 2,686 patients with myocardial perfusion imaging and gated SPECT. They found that, whereas the best predictor of nonfatal myocardial infarction was the amount of ischemia present on perfusion imaging, the most powerful predictor of cardiac death was poststress ejection fraction. By integrating the perfusion data with the poststress ejection fraction, they were able to separate patients into tertiles of risk (29).

Finally, it is important to note that valuable prognostic data can be gleaned from negative scan findings as well. Berman et al. reported a 0.2% rate of myocardial infarction or cardiac death in 1,131 patients with normal or equivocal SPECT findings. Of interest, in patients with a high (>85%) prescan likelihood of CAD, the event rate was 0% (30).

Thus, the value of prognostic information gained from myocardial perfusion imaging and radionuclide evaluation of left ventricular ejection fraction cannot be overstated, as these data are additive to clinical, exercise, and even cardiac catheterization variables in predicting risk.

VIABILITY

Combined assessment of function and perfusion can also play a role in determining myocardial viability. Levine et al. performed rest gated SPECT before and after revascularization on 50 patients with CAD and found that the addition of ventricular function information to perfusion data alone increased the accuracy of the test from 85% to 91% (31). This same group also found that rest gated SPECT was equivalent to rest-redistribution thallium studies in the prediction of myocardial viability (32).

CONCLUSION

The role of myocardial perfusion imaging in the diagnosis of CAD and determination of its prognosis is irrefutable. However, perfusion imaging alone has several inherent drawbacks. In the diagnosis of CAD, perfusion imaging often suffers from suboptimal differentiation of infarct from soft tissue or diaphragmatic attenuation artifacts. Additionally, multivessel CAD, with its concomitant global decrease in perfusion, is a well-known Achilles’ heel of nuclear imaging. The addition of ventricular function data—not overall ejection fraction and segmental wall motion—offers potential solutions to both of these vexing problems. At the same time, the data provided by radionuclide cineangiography or gated SPECT can greatly enhance the already additive prognostic information provided by myocardial perfusion imaging.

REFERENCES


