Editorial

How Should We Interpret the Decrease in Annual Volume of Stress Imaging Tests for Evaluation of Suspected or Known Coronary Artery Disease With Fewer High-Risk Test Results?

George A. Beller, MD

In recent years, observations related to the diminution in annual volume of stress imaging tests, the decrease in frequency of abnormal test findings, coupled with a rather high rate of normal coronary angiograms or nonobstructive coronary artery disease (CAD) at coronary angiography, following an abnormal stress imaging test, have intrigued the cardiology specialist community. Similarly, these observations have occurred simultaneously with a decrease in the cardiac event rate after testing and an overall improved prognosis in patients with CAD. Using Medicare data, Levin et al[1] determined the trends in noninvasive imaging use from 2001 to 2013. Total radionuclide myocardial perfusion imaging (MPI) rates per 1000 Medicare beneficiaries rose from 63.4 in 2001 to a peak of 88.0 in 2006 but then declined every year afterward, reaching 10.8 in 2013. Rates for use of stress echocardiography held steady until 2010 and then decreased each year thereafter (12.6/1000 to 10.8/1000). McNulty et al[2] investigated the temporal trends in radionuclide MPI use at Kaiser Permanente Northern California from 2000 to 2011. They found that annual rates of MPI rose steadily from 2000 to 2006 and then abruptly declined by 51% through 2011. Relative declines were greater for outpatients than inpatients and greater for individuals <65 years of age versus those ≥65 years. Interestingly, the volume of stress echocardiography was unchanged from 2007 to 2011.

See Article by Jouni et al

In 2 separate publications, the second in this issue of the journal, Jouni et al[3,4] from the Mayo Clinic report a marked decrease in single-photon computed tomography (SPECT) myocardial perfusion MPI tests from 2003 to 2012 at their institution. The first study comprised patients without known prior CAD referred for SPECT MPI.[3] They found that between 2001 and 2003, 2490 such tests were performed annually. By 2012, the volume of SPECT MPI fell to 1033 per year, a value similar to that for 1995. A similar trend was found for stress echocardiography. In addition, these investigators found that after 2003, more tests showed low-risk results, and the extent of stress perfusion defects and amount of stress-induced ischemia diminished over time. The number of high-risk stress SPECT MPI tests also decreased. For 2011 to 2012, 95.6% of tests were low risk versus 63.9% in 1991 to 1995.

The second Mayo study[4] published in this issue of the journal analyzed temporal trends in SPECT MPI in patients with known CAD (prior myocardial infarction [MI], prior percutaneous coronary intervention, or prior coronary artery bypass grafting). Similar to the findings in patients without known CAD,[3] annual use of SPECT MPI in patients with known CAD increased from an average of 495 tests per year from 1991 to 1995 to 1425 in 2003. The volume then markedly decreased to 552 tests in 2012. As seen in patients tested without prior known CAD, the percentage of high-risk test results decreased over time in these patients with known CAD, from 47.8% in 1991 to 1995 to 8.1% in 2011 to 2012. Conversely, the percentage of low-risk SPECT MPI tests increased. For example, 32.6% of patients who underwent SPECT MPI with a negative stress ECG had a summed stress score of ≥9 in the years 1991 to 1995. This fell to 9.5% of patients exhibiting a high-risk summed stress score in 2011 to 2012. With respect to post–percutaneous coronary intervention or post–coronary artery bypass grafting patients without a prior MI, the number of low-risk SPECT MPI studies (summed stress score, 0–3) more than doubled from 40.5% to 89.4% in this time frame.[4] In patients undergoing stress MPI after MI who were not revascularized, the percentage of low-risk SPECT test results increased from 20.5% in 1991 to 1995 to 63.6% of all tests in 2011 to 2012. Interestingly, the prevalence of CAD risk factors, such as hypertension, dyslipidemia, and diabetes mellitus, increased over time, whereas smoking decreased. Although not specifically monitored, the authors mention that the percentage of patients with known CAD being treated for these risk factors in Minnesota increased in this time period.

The group at Cedars Sinai in Los Angeles were among the first to observe this marked decline in abnormal SPECT MPI studies.[5] They reported a progressive decrease in abnormal SPECT studies from 40.9% in 1991 to 8.7% in 2009. The prevalence of stress-induced SPECT ischemia fell from 29.6% to 5.0%. Similarly, there was an impressive decrease in the patients with moderate to severe ischemia. This decrease in percentage of abnormal SPECT studies occurred as the population referred for testing demonstrated a higher pre-test likelihood of CAD, with a higher percentage of patients tested with hypertension, an elevated

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cholesterol, diabetes mellitus, and obesity. However, there was an increase in the use of aspirin, statins, and antihypertensive drugs over the ≈2 decades of patient imaging. Duvall et al[6] also reported a decrease in abnormal SPECT MPI studies from 54.0% of studies performed in 1996 to 33.7% in 2012. The prevalence of ischemic SPECT studies and the percentage of patients with high-risk ischemia (>10% of the left ventricle) declined as well. As seen in the Cedars Sinai study,[5] this decline in stress-induced ischemia occurred as the number of CAD risk factors increased in the tested population over time. Consistent with these findings, our study in diabetic patients referred for stress MPI between 2006 and 2007 showed an unexpectedly low prevalence of significant ischemia, with only 5.0% of patients having ≥10% left ventricular ischemia.[7] In fact, ≈80% had no inducible ischemia, despite the fact that 40% of the patients had known CAD. For the entire diabetes mellitus cohort, the cardiac death rate was only 0.8% per year at 4.4 years of follow-up. As with the prior studies cited, many of the patients were on statins and antihypertensive drugs when undergoing testing. In the WOMEN trial (What is the Optimal Method for Ischemia Evaluation in Women) that enrolled women who had a Duke Activity Status Index of ≥5 metabolic equivalents, only 6.2% of those randomized to exercise SPECT MPI had a moderate-severely abnormal scan.[8]

More recently, several cardiac imaging trials have been performed comparing functional stress testing with coronary computed tomography angiography (CTA). The PROMISE trial (Prospective Multicenter Imagine Study for Evaluation of Chest Pain) compared a strategy of initial functional stress testing with CTA in 10 003 symptomatic patients with suspected CAD.[9] Patients were enrolled between 2010 and 2013. Only 12.6% of patients in the functional arm had abnormal tests.[9] Similarly, in the CTA arm of the trial, only 11.9% of patients had obstructive CAD. In PROMISE, 45% to 50% of patients tested were on aspirin, and angiotensin-converting enzyme inhibitor or angiotensin receptor blocker and a statin. The rates of abnormal stress test results in the SCOT-HEART (Scottish Computed Tomography of the Heart), CRESCENT (Calcium Imaging and Selective CT Angiography in Comparison to Functional Testing for Suspected Coronary Artery Disease), and CAPP (Cardiac CT for the Assessment of Pain and Plaque) studies were 15.0%, 11.0%, and 19.2%, respectively.[10–12] This low rate of abnormal findings on functional testing in the current era is similar to rates cited above for the observational SPECT MPI studies reported from single centers.

The prognosis of patients after testing has significantly improved during the past 25 years. The end point for the PROMISE trial was a composite of major cardiovascular events, including death from any cause, nonfatal MI, hospitalization for unstable angina, and major complications of cardiovascular procedures or diagnostic testing. In the functional group, only 3.0% of the population had a primary end point event versus 3.3% in the CTA group for a median follow-up of 25 months.[9] A pooled analysis of studies published before 2004 comprising ≈70 000 patients, and the combined annual death or MI rate for patients with an abnormal exercise or pharmacological stress SPECT MPI was 5.9%.[13] A subsequent meta-analysis of studies published between 2001 and 2014[14] found that the annual event rate for death, MI, or revascularization after an abnormal MPI was 5.2%. Of these events, 44% were revascularization. Thus, it seems that not only has the prevalence of high-risk studies and ischemia declined since the early 1990s but also has the subsequent hard event rate after testing. This is also highlighted by the observation in the study by Ouellette et al[15] that 42% of patients with an abnormal stress test had normal coronary arteries or nonobstructive CAD (<50% stenosis) at time of invasive coronary angiography.[15]

What are the possible factors that account for the decrease in annual volume of stress SPECT MPI studies, and the decline in abnormal study results, particularly a marked decrease in high-risk scans? In addition, why has the prognosis of patients with abnormal studies improved? With respect to the volume decrease, test substitution does not seem to be a factor. Jouni et al[4] did not find that stress echocardiography or positron emission tomography MPI increased during the time period surveyed to account for the decrease in SPECT MPI. The volume of SPECT MPI performed by cardiologists in Medicare patients seemed to peak around 2006,[1] dropping slowly until 2009, and then declining rather rapidly beginning in 2010. Levin et al[1] point out that most of the SPECT MPI studies before 2010 were performed in private cardiology offices. In 2010, private cardiology practices began to be acquired by hospitals or just closed. Reimbursement for SPECT MPI was also reduced by bundling of add-on codes, such as ventricular ejection fraction and wall motion analysis, into the primary codes. This reduced the global relative value units for rest and exercise SPECT from 16.48 to 10.53. Concerns arose about self-referral of patients to the physician's private office nuclear cardiology laboratory.

The first publication of the American College of Cardiology appropriate use criteria for SPECT appeared in 2005.[16] This surely had an impact on the reduction in referrals for SPECT MPI, particularly in asymptomatic patients. Many insurance companies with radiology benefits management made it more difficult to order SPECT MPI studies. For 1 insurance company in Virginia, pre-authorization to perform SPECT MPI was required but not for stress echocardiography. Fewer patients with an acute coronary syndrome are now referred for early or pre-discharge functional testing. Such patients now most often undergo direct coronary angiography with percutaneous coronary intervention performed for significant culprit lesions. It is possible that more patients with typical angina are also being referred directly for invasive coronary angiography. Perhaps, as a result of the COURAGE trial (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation),[17] some patients with mild stable angina are being treated medically after initial testing, without repeat testing performed in later months. Similarly, fewer patients are being referred for routine functional testing after uncomplicated percutaneous coronary intervention or coronary artery bypass grafting. Currently, it seems that many patients with suspected CAD, who are low to intermediate clinical risk, are undergoing CTA rather than functional stress testing. The PROMISE study showed similar outcomes for the 2 diagnostic approaches.[9] Finally, it is likely that the recognition of the radiation exposure with SPECT imaging resulted in some decrease in referrals, particularly in younger women.

With respect to the reduction in abnormal SPECT studies, an increased number of low-risk test results, and a concomitant decrease in high-risk findings, a major likely contributing factor is the more effective treatment of risk factors for

CAD, despite the increase in prevalence of obesity and diabetes mellitus in the population. More patients are prescribed statins and antihypertensive drugs. The reduction in ischemia and high-risk test results parallels the improved prognosis in patients on optimal medical therapy.[17,18] In the COURAGE nuclear substudy, the summed stress score was lower on serial images in patients on optimal medical therapy.[19] The role of an improved lifestyle, with fewer individuals smoking, and more individuals exercising and adhering to a heart healthy diet is unclear. This could also be playing a role in the reduction in high-risk findings on SPECT MPI. From the technical standpoint, a reduction in false-positive SPECT scans associated with better image quantification, assessment of regional function on gated images, and attenuation correction may be playing a role in the reduced prevalence of abnormal studies.

In conclusion, Jouni et al[3,4] have made an important contribution to quantifying the temporal trends in volume of SPECT MPI studies for a period of 22 years. They showed a marked reduction of stress SPECT MPI in patients with either suspected or known CAD starting around 2003 with a more precipitous decline beginning in 2006. They confirmed prior observations that the percentage of abnormal stress tests has also declined, particularly high-risk test results. This corresponds to the overall improved outcomes in patients after testing, most recently highlighted by the low event rate in the PROMISE trial.[9] The contributing causes for these observations are multifactorial, as cited above. The decline in procedural volumes is occurring at a time when the technology of cardiac imaging has substantially improved, with enhanced sensitivity, specificity, and overall accuracy of MPI, both with SPECT and positron emission tomography. The latter permits absolute quantification of blood flow and coronary flow reserve, permitting even better risk stratification of patients undergoing testing.[20] Such improved imaging should reduce the number of false-negative and false-positive noninvasive imaging studies, allowing for even better patient management, whether enhancing medical therapy to reduce ischemia, or better selection of patients for revascularization. Finally, radiation exposure has markedly decreased because of advances in SPECT technology (eg, cadmium zinc telluride detectors), greater use of positron emission tomography MPI, and greater use of stress-only SPECT MPI. Functional stress imaging will undoubtedly continue to play an important role in the evaluation and management of patients with suspected or known CAD. What has changed is that the indications for appropriate testing are continually being refined based on cumulative evidence from clinical research studies. The challenge going forward is how best to identify those patients who benefit the most from stress imaging with respect to improved outcomes.

Disclosures

None.

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