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EDITOR'S PAGE

Resurgence of Novel Research in Nuclear Cardiology

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In years past, the evidence base for conventional nuclear cardiology imaging amassed at a rapid pace and provided robust evidence supporting widespread use of the modality. However, nearly a decade ago, the pace of this research in single-photon emission computed tomography (SPECT) and positron emission tomography (PET) imaging largely halted, which led to much concern that this slower pace of advancement would affect the current high use and reimbursement patterns across the United States. What may have been valid concerns in the past can no longer be stated, as recent clinical research in SPECT and PET imaging has focused both on the area of stable ischemic heart disease and also on broadening the indications for use, including amyloidosis, sarcoidosis, and imaging for cardiac valve infection. Moreover, more recent evidence also includes a focus on validating prior research using novel technology, such as risk stratification with myocardial perfusion PET (1) or with high-efficiency SPECT(2). In this issue of *iJACC*, one such effort is presented from the REFINE SPECT (Registry of Fast Myocardial Perfusion Imaging with Next generation SPECT) registry (3).

The novelty of this report lies not only in the use of more contemporary SPECT imaging, but also in a direct comparison of prognosis associated with visual versus automated quantitative interpretation of rest/stress myocardial perfusion. The data from the REFINE SPECT registry includes a very large series of patients who had undergone myocardial perfusion imaging across multiple centers, thus providing robust and generalizable findings broadly applicable to the field of nuclear cardiology. For many years, experts in the field have long advocated for nuclear imagers to use quantitative interpretation as a guide or aid to their visual interpretation, akin to that of a second reader. Quantitative imaging has found favor in multiple imaging modalities—originally in nuclear imaging and subsequently in CT (4) and CMR (5). CMR studies also show that quantitation might also allow differentiation of epicardial CAD from microvascular disease (6). Quantitation of perfusion has also found a role in prognostication in multiple modalities other than SPECT and PET but with evidence both for (4,7) and against (8) the superiority over visual reads. With this publication by Otaki et al. (3), we now have a definitive report on concordance of prognostic estimates for both visual and automated quantitative interpretation in nearly 20,000 patients who were followed for 4.5 years for the occurrence of major coronary disease events. Certainly, this is 1 of the larger series reporting prognosis following cardiac imaging and collecting contemporary imaging of patients enrolled from 2009 to 2014. Thus, this data fulfills a major gap in the nuclear imaging evidence that was lacking contemporary data on risk stratification. This is incredibly important given the evidence of declining risk in our symptomatic patient cohorts, manifesting in reduced rates of ischemia and obstructive coronary artery disease (9,10). The high predictive accuracy of the presented SPECT findings provide for novel evidence that this modality continues to be highly predictive of cardiac risk.

All of these statements are important, but the vital message from this registry is that not only was the

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quantitation complementary, but further refined the risk estimates in this large patient cohort. In fact, for the 1,062 patients with a normal visual read, annualized event rates ranged considerably from 1.6% to 3.4% for stress total perfusion deficits quantified automatically from 0% to ≥5% of the myocardium. A similar stratification was also reported for those patients with a summed stress score of 0. These data support an important further stratification of risk, which to date has not been appreciated in nuclear interpretation.

These findings are significant, as recent trial evidence reports that patients with lower risk findings may have clinically important (but nonischemic) coronary artery disease. From the National Institutes of Health-sponsored PROMISE (PROspective Multicenter Imaging Study for Evaluation of Chest Pain) trial, the 2-year event rate was significantly higher for patients with a normal stress imaging study compared with a normal coronary computed tomographic angiogram (11). Moreover, approximately one-half of major coronary disease events occurred in patients with physician-interpreted normal stress tests (12). The findings put forth from the REFINE SPECT registry combined with the PROMISE reports support that improvements in risk detection may yield better detection of at-risk patients.

There are a number of limitations of this registry, including the use of revascularization as part of the composite endpoint. Given the predominance of relatively low-risk, stable patients, continued use of late revascularization as an endpoint seems unjustified, as many patients could have protracted evaluations including initial deferment of invasive procedures. In lower-risk patients, the current evaluation pathway may take months and may remain within the window of the index evaluation. Given the large cohort and frequently documented other composite endpoints, the use of revascularization as an event seems superfluous and distracting from the main findings of this report. Moreover, we continue to have a paucity of evidence on stress imaging-guided antianginal and preventive therapies, which are increasingly vital to care when invasive approaches are not supported by randomized trials, such as with the ISCHEMIA (International Study of Comparative Health Effectiveness With Medical and Invasive Approaches) trial (13).

As we see new and emerging evidence supporting the utility of nuclear cardiology, especially in the exciting age of big data and machine learning (14), let us also hope that there are unfolding data from randomized trials that compare its effectiveness with that of cardiac magnetic resonance or coronary computed tomographic angiography. We are also seeing growth in the use of cardiac PET, and it would be fundamental to optimal patient care that trial evidence support the superiority of accuracy and improvement in clinical outcomes when compared with other competitive modalities, including SPECT. This, by far, is the challenge for the nuclear community to raise the bar to a new level!

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