A quick glance at selected topics in this issue

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''A quick glance at selected topics in this issue'' aims to highlight contents of the *Journal* and provide a quick review to the readers. (J Nucl Cardiol 2019;26:355–8.)

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Abbreviations			
CAD	Coronary Artery Disease	LV	Left Ventricle
MPI	Myocardial Perfusion Imaging	FDG	^{18}F-fluorodeoxyglucose
SPECT	Single Photon Emission Computed Tomography	CZT	Cadmium Zinc Telluride
PET	Positron Emission Tomography	CAC	Coronary Artery Calcium

''A quick glance at selected topics in this issue'' aims to highlight contents of the *Journal* and provide a quick review to the readers. We realize that many of you do not have time to read all journals or attend all national meetings. For that reason, every issue of the JNC includes 2 types of literature reviews. One summarizing recent key nuclear cardiology articles that have been published in journals other than ours (https://doi.org/10.1007/s12350-019-01610-5) while the second outlines select publications in the general cardiovascular disease literature that have relevance to our field (https://doi.org/10.1007/s12350-019-01611-4).

Another entry is the historical corner that looks at the career and scientific contributions of a pioneer in Nuclear Medicine instrumentation, Dr. Hal O. Anger (https://doi.org/10.1007/s12350-018-1384-7). He invented the scintillation well counter to measure radiotracer activity in blood and tissue samples and the gamma camera. These manuscripts are complimented by a great selection of original articles with accompanying editorials, brief reports, 'What is this image' and 'Images that Teach,' and a CME review paper by Henry Gewirtz (https://doi.org/10.1007/s12350-018-1270-3) that discusses the 'Coronary circulation: Pressure/flow parameters for assessment of ischemic heart disease.' Reviewed is the physiology of the coronary circulation and the available invasive (e.g., fractional flow reserve, etc.) and non-invasive (e.g., PET-derived myocardial blood blow and coronary flow reserve, etc.) metrics of the physiological status of the coronary circulation with potential strengths and weaknesses. Many of the original articles also have PowerPoint slides. The abstract of the lead original article 'The utility of ^{82}Rb PET for myocardial viability assessment: comparison with perfusion-metabolism ^{82}Rb-^{18}F-FDG PET' by Moody and colleagues from Ann Arbor, Michigan, has also been translated into Spanish, Chinese, and French in response to requests from the international readership. PowerPoint slides from this paper can be found by https://doi.org/10.1007/s12350-019-01615-0. The review article by Lee and colleagues on 'Advances in imaging

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instrumentation for nuclear cardiology' (https://doi.org/10.1007/s12350-017-0979-8) includes discussions on SPECT, SPECT/CT, CZT scanners, PET/CT, PET/MRI, motion correction in cardiac PET etc. Also included in the issue by Al-Mallah and colleagues (https://doi.org/10.1007/s12350-019-01603-4) is a summary of key imaging studies that were presented at the American Heart Association Scientific Sessions 2018 in Chicago related to the fields of nuclear cardiology (planar, SPECT and PET), cardiac computed tomography, cardiac magnetic resonance, and echocardiography.

Our comments on a few selected papers noted below are therefore only the tip of the iceberg. These manuscripts were selected randomly and we sincerely believe all original articles serve a purpose, provide great value, and have undergone an intense peer review.

FDG PET is the most sensitive non-invasive test for distinguishing scar from hibernating myocardium in patients with severe coronary artery disease and impaired left ventricular function. However, FDG PET is time consuming and resource intensive. ^{82}Rb, a potassium analog has been studied as a marker of myocardial tissue integrity but with equivocal results. Moody et al. from Ann Arbor, Michigan (https://doi.org/10.1007/s12350-019-01615-0), attempt to define the relationship between ^{82}Rb kinetics and myocardial viability compared with conventional ^{82}Rb and FDG perfusion-metabolism PET imaging in a pilot study with 120 patients referred for evaluation of myocardial viability prior to revascularization and 37 normal volunteers. Dynamic ^{82}Rb 3D PET data were acquired at rest, whereas FDG 3D PET data were acquired after metabolic preparation using a standardized hyperinsulinemic-euglycemic clamp. The authors noted that the ^{82}Rb kinetic parameters k2 and partition coefficient (KP), reliably differentiated hibernating myocardium from scar. The ^{82}Rb partition coefficient is readily estimated using the same protocol and kinetic model commonly used for myocardial blood flow, and can be obtained at no additional cost, imaging time, or radiation exposure. The results demonstrate the feasibility of using ^{82}Rb kinetics to differentiate scar from hibernating myocardium.

FDG PET/CT has been used to identify active cardiac inflammation from sarcoidosis. Tuominen and colleagues from Tampere, Finland (https://doi.org/10.1007/s12350-017-0940-x), retrospectively attempt to identify patients with suspected cardiac sarcoidosis, who are most likely to benefit from PET imaging. The investigators found that in a cohort of 137 patients with suspected cardiac sarcoidosis, the highest frequency of pathologic cardiac PET findings (RV and/or LV uptake) was seen in female patients with a history of advanced AV-block and cardiac arrhythmias (ventricular tachycardia and atrial fibrillation).

Myocardial ischemia is known to contribute to arrhythmogenesis and present-day clinical risk stratification for ventricular arrhythmias is far from perfect. Ghannam et al. (https://doi.org/10.1007/s12350-017-0975-z) studied the relationship of rubidium-82 PET MPI-derived quantification of myocardial blood flow to arrhythmic events in 159 patients with implantable cardiac defibrillators. They noted that after adjustment for LV ejection fraction, age, and sex, impaired stress myocardial blood flow was associated with an increased risk of ventricular arrhythmias in this high-risk population, whereas residual EF, summed rest, and summed stress scores were not. The authors make a case for incorporation of stress myocardial blood flow in future models of ventricular arrhythmia risk assessment.

The size of myocardial infarction is predictive of subsequent morphological changes and clinical outcome. Ghotbi and colleagues from the University of Copenhagen, Denmark (https://doi.org/10.1007/s12350-017-0993-x) investigated whether Rubidium-82 PET MPI-derived measurements of resting blood flow and extent of severe hypoperfusion in the subacute phase of STEMI can predict final infarct size, LVEF, and regional wall motion as measured by cardiac magnetic resonance (CMR) at 3-month follow-up. 35 STEMI patients undergoing primary percutaneous coronary intervention (PCI) were included prospectively. Rest PET MPI was performed the day after PCI (median 36 hours) when patients were clinically stable. The authors report that PET MPI seems to forecast the degree of wall motion impairment (LVEF) and amount of scar. Resting blood flow measurements by PET were significantly lower in patients with reduced LVEF at 3-month follow-up compared to those with preserved LVEF. The investigators make the case for a single rest PET MPI that would take less than 15 minutes to perform the day after a STEMI which could add useful prognostic information.

MPI is a useful CAD risk stratification tool in chronic kidney disease (CKD) patients. Nakamura and colleagues from Japan (https://doi.org/10.1007/s12350-017-0880-5) report results of a Japanese multicenter, prospective cohort study investigating the ability of MPI to predict cardiac events in 529 advanced CKD patients without definitive CAD. The mean estimated GFR was 29.0 ± 12.8 (mL/minute/1.73 m^2). Major cardiac events were analyzed for 3 years after registration. A total of 60 cardiac events (3 cardiac deaths, 6 sudden deaths, 5 non-fatal myocardial infarctions, 46 heart failure hospitalization cases) occurred. They found that the event-free survival rate was lower among patients with kidney dysfunction, higher summed stress score, and higher C-

reactive protein (CRP) values. Thus, from a practical point of view, the authors suggest that CKD patients with eGFR <15 mL/minute/1.73 m^2 or CRP ≥0.3 mg/dL should be assessed with MPI. In these patients, if the summed stress score is ≥8, their cardiac prognosis may be worse. Thus, advanced renal dysfunction combined with MPI abnormalities provided additional prognostic information that is superior to either marker alone.

Wu et al. from China (https://doi.org/10.1007/s12350-017-0952-6) compared the diagnostic performance of resting CZT SPECT to conventional SPECT (C-SPECT) in the assessment of left ventricular myocardial scar, contractile function, and mechanical synchrony in 59 heart failure patients. All patients underwent resting 99mTc-MIBI gated MPI using a CZT-SPECT camera and a C-SPECT camera, respectively, and ^{18}F-FDG PET myocardial metabolism imaging within three days. They found that CZT SPECT provided comparable data to C-SPECT for measuring LV perfusion, scar, function and synchrony (latter measured with histogram band width and standard deviation) at a considerable reduction in imaging time (3 minutes versus 12 minutes).

Patient-centered testing is aimed at selecting the right test for the right patient. Salimi et al. from the University of Vermont Medical Center (https://doi.org/10.1007/s12350-017-0911-2) investigated nurse-driven protocols of stress tests towards the goal of patient-centered cardiac testing. A protocol nurse reviewed records before scheduling all non-imaging (Exercise Treadmill) and nuclear (MPI) stress tests (N=3071). The nurse also communicated with patients and ordering providers as needed. The authors found that compared to their prior process of script-driven scheduling of stress tests by non-medically trained scheduling staff, the nurse-driven approach led to protocol changes in 37% of patients, which included change in stress testing modality (e.g., SPECT to PET MPI due to high BMI), or choosing a stress first approach, or changing location of stress for clinical or safety reasons or for care coordination. Additionally, the nurse-driven approach reduced the number of tests that could not be performed by 56% and cancelations by 71% ($P < 0.001$). The authors propose that an optimal patient-centered approach might include a combination of electronic point-of-ordering tools and expert nurse review of stress protocols.

Nuclear imaging (Planar with or without SPECT) using bone-avid radiotracers (e.g., 99mTc-3,3-diphosphono-1,2-propanodicarboxylic acid-Tc-DPD or 99mTc-Pyrophosphate-Tc-PYP) has been shown to be effective in the diagnosis of transthyretin cardiac amyloidosis. Cappelli and colleagues from Italy (https://doi.org/10.1007/s12350-017-0922-z) assessed the diagnostic accuracy of planar imaging with another bone-specific radiotracer, 99mTc-HMDP in a cohort of 65 patients with biopsy-proven cardiac amyloidosis. All patients with transthyretin cardiac amyloidosis had cardiac uptake of Tc-HMDP based on visual/qualitative evaluation. Quantitative assessment using the heart retention-to-whole body retention ratio (HR:WBR) showed that patients with transthyretin cardiac amyloidosis had a significantly higher HR:WBR ratio compared to patients with light-chain cardiac amyloidosis. A positive 99mTc-HMDP scintigraphy showed a 100% sensitivity and 96% specificity for identifying transthyretin cardiac amyloidosis. Thus, 99mTc-HMDP could also be considered as an effective radiotracer to correctly identify patients with transthyretin cardiac amyloidosis.

Vasodilators including adenosine or regadenoson are often used for pharmacologic stress testing. These vasodilators may trigger atrioventricular block (AVB). Andrikopoulou et al. (https://doi.org/10.1007/s12350-017-1081-y) performed a meta-analysis to study the incidence of de novo AVB with these agents. A total of 34 studies were included in the final analysis. Overall AVB included first-, second-, and third-degree AVB, whereas high-grade AVB included second- and/or third-degree AVB. The estimated incidence of overall and high-grade AVB was 3.81% and 1.93%, respectively. The incidence of overall AVB (8.58% vs. 0.3%) and high-grade AVB (5.21% vs. 0.05%) was higher with adenosine compared to regadenoson.

SPECT MPI is a widely used and proven diagnostic and prognostic tool in CAD. Coronary artery calcium (CAC) scoring is a non-invasive technique to estimate the amount of coronary atherosclerosis. Simultaneous CAC scoring together with MPI may offer additional diagnostic and prognostic information. Yokota and colleagues from Isala hospital, Zwolle, The Netherlands (https://doi.org/10.1007/s12350-017-1067-9) evaluated whether high CAC scores are associated with increased referral for invasive angiography following normal SPECT MPI. 2286 consecutive patients (mean age 60 ± 12, 39% male) with normal SPECT were assessed. All patients underwent simultaneous CAC scoring and were categorized into four groups based on their CAC score: CAC = 0 (n = 694), CAC 1 to 100 (n = 891), CAC 101 to 400 (n = 368), and CAC >400 (n = 333). The decision to perform angiography was at the discretion of the treating physician. Follow-up angiography was confined to the first 60 days after SPECT. Occurrence of major adverse cardiovascular events (MACE i.e., late revascularization, myocardial infarction or death) was recorded. Overall, 100 patients (4.4%) underwent early angiography with increasing rates in higher CAC score groups (1.0%, 2.6%, 8.4%, and 11.7% respectively, $P < 0.001$). A CAC score > 400 was independently associated with referral to angiography and was an independent predictor for MACE. In conclusion, this observational study

suggests that CAC scores (especially high scores > 400) influence clinical decision making and increases the early referral for invasive coronary angiography in stable low- to intermediate-risk patients with normal MPI.

We encourage the readers to look at the several other articles in the Journal with accompanying scholarly and informative editorials that not only put the findings in perspectives but also outline future directions. We would like to hear your comments as we strive to gain knowledge and in the process, improve patient care.

Disclosure

Pradeep Bhambhvani, Fadi G. Hage, and Ami E. Iskandrian have no COI with this work.