A quick glance at selected topics in this issue

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Abbreviations		LV	Left ventricle
CAD	Coronary artery disease	CZT	Cadmium zinc telluride
MPI	Myocardial perfusion imaging	FDG	Fluorine-18 fluorodeoxyglucose
SPECT	Single-photon emission computed tomography		
PET	Positron emission tomography		

“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 have also started to provide the quick glance write up in an audio format via the JNC/ASNC Podcast, which can be accessed on iTunes, Spotify, and most other podcast manager applications. Every issue of the journal has multiple entries with differing objectives. We realize that many of you do not have time to read all journals or attend all national meetings. For that reason, 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/s12350-020-02121-4>), while the second outlines select publications in the general cardiovascular disease literature that

have relevance to our field (<https://doi.org/10.1007/s12350-020-02153-w>). Another entry in the current issue is the historical corner that looks at the career and scientific contributions of a giant in nuclear cardiology George A. Beller (Born 1940) (<https://doi.org/10.1007/s12350-020-02115-2>). 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 an a CME review paper, which currently is on ‘The role of cardiac imaging in the management of non-ischemic cardiovascular diseases in human immunodeficiency virus infection’ by Aljizeeri and colleagues (<https://doi.org/10.1007/s12350-019-01676-1>). Many of the original articles also have accompanying PowerPoint slides. The abstract of the lead original article, ‘Association between vertebral bone mineral density, myocardial perfusion, and long-term cardiovascular outcomes: A sex-specific analysis’ by Fiechter and colleagues from Switzerland, 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 searching <https://doi.org/10.1007/s12350-019-01802-z>.

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Relevant to the ongoing Coronavirus pandemic are 2 timely Nuclear Cardiology practice documents. These include ‘Adapting to a novel disruptive threat: Nuclear Cardiology Service in the time of the Coronavirus (COVID-19) Outbreak 2020 (SARS REBOOT)’ by Loke et al. from Singapore (<https://doi.org/10.1007/s12350-020-02117-0>) and ‘Guidance and Best Practices for Nuclear Cardiology Laboratories during the Coronavirus Disease 2019 (COVID-19) Pandemic: An Information Statement from ASNC and SNMMI’ by Skali et al. (<https://doi.org/10.1007/s12350-020-02123-2>). The issue’s Case Presentation Corner looks at the identification and typing of cardiac amyloidosis by non-invasive imaging in 2 patients with light chain and transthyretin subtype cardiac amyloidosis, respectively (<https://doi.org/10.1007/s12350-019-01982-8>).

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

Osteoporosis is generally considered a female disorder and bone mineral density (BMD) has been identified as a risk factor for congestive heart failure. Fiechter and colleagues from Switzerland (<https://doi.org/10.1007/s12350-019-01802-z>) study the sex-specific association between bone mineral density, myocardial perfusion, and long-term cardiovascular outcomes in a cohort of 491 aged (65.9 ± 10.7 years) patients (32.4% women) who had undergone rest and adenosine stress ^{13}N -ammonia PET/CT for evaluation of CAD. Three measurements of thoracic spine BMD (in Hounsfield units, [HU]) per vertebra were performed on the acquired CT images. Results showed that reduced BMD was a significant predictor of major adverse cardiac events ($P = 0.015$). Event-free survival was also significantly reduced in patients with low (≤ 100 Hounsfield units) compared to those with higher BMD ($P = 0.037$). BMD was significantly lower in patients with abnormal myocardial perfusion or impaired left ventricular ejection fraction ($P < 0.05$). Surprisingly, this difference was noticed in men, but not in women.

Hyafil et al. from France (<https://doi.org/10.1007/s12350-018-01557-z>) compare the diagnostic performance of 82-Rb-PET-MPI and 99m-Tc-SPECT-MPI in 313 overweight individuals ($\text{BMI} \geq 25$) and women for the detection of myocardial ischemia. All individuals underwent 99m-Tc-SPECT-MPI with CZT cameras and 82-Rb-PET-MPI in 3D mode. Individuals with at least one positive MPI were referred for coronary angiography with FFR measurements. A criterion for positivity was a composite endpoint including significant stenosis on coronary angiography or, in the absence of coronary angiography, the occurrence of an acute coronary event

during the following year. The diagnostic performance of both techniques was good. Sensitivity for the detection of myocardial ischemia was higher with 82-Rb-PET-MPI compared with 99m-Tc-SPECT-MPI (85% vs. 57%, $P < 0.05$); specificity was equally high for both imaging techniques (93% vs. 94%, $P > 0.05$). 82-Rb-PET allowed for a more accurate detection of high-risk coronary artery disease/balanced ischemia than 99m-Tc-SPECT-MPI (AUC = 0.86 vs. 0.75, respectively; $P = .04$). Total effective radiation dose was significantly lower with 82-Rb-PET-MPI in comparison to 99m-Tc-SPECT-MPI in both men and women and those with a $\text{BMI} < 35$ or ≥ 35 . Thus, 82-Rb-PET offers significant advantages over 99m-Tc-SPECT-MPI with CZT camera for the detection of myocardial ischemia in overweight individuals and women with low-to-intermediate prevalence of CAD.

As low as reasonably achievable (ALARA) is the basis of reducing radiation exposure associated with prudent medical imaging. Al Badarin and colleagues from the Saint Luke’s Mid America Heart Institute, Kansas City, MO (<https://doi.org/10.1007/s12350-018-01576-w>) examine the real-world impact of differing intensity of radiation safety practices on effective radiation dose associated with MPI within a single large health system. MPI exams were performed at multiple sites throughout the health system, including four large, hospital-based laboratories within the Kansas City metropolitan area and five affiliated, community-based sites in surrounding rural communities. Sites with ‘basic radiation safety practices’ included those that implemented changes in radiotracer usage (i.e., elimination of Thallium-based protocols) or adopted stress only protocols on conventional SPECT cameras without adjunctive use of advanced post-processing software ($n = 5$). Sites with ‘advanced radiation safety practices’ included those that additionally implemented hardware- or software-based interventions, such as incorporation of solid-state detector cameras, PET scanners, or installation of advanced post-processing software onto standard Anger cameras ($n = 4$). The authors report that use of ‘advanced radiation safety practices’ was associated with significantly lower mean effective radiation dose compared to ‘basic radiation safety practices’ (7 ± 5.6 mSv and 16 ± 5.4 mSv, respectively; $P < 0.001$) and had a greater likelihood of achieving effective radiation dose < 9 mSv, as recommended by ASNC. The main drivers for the reduction in effective radiation dose were use of stress only solid-state detector SPECT, followed by use of stress only solid-state detector + advanced post-processing software, followed by use of PET, and elimination of thallium protocols ($P < 0.0001$ for all comparisons).

FDG PET/CT is increasingly used for imaging of inflammatory cardiac diseases. However, because normal myocardium can use both glucose and free fatty acids (FFAs) for its metabolic needs, physiologic myocardial FDG uptake can interfere with the recognition of pathologic/inflammatory FDG uptake. Ideally, for cardiac inflammation imaging, physiologic myocardial glucose uptake should be completely suppressed, leaving only pathologic FDG uptake in the heart. Optimal patient preparation protocols are not well established. Larson et al. from Bethesda, Maryland and Ann Arbor, Michigan (<https://doi.org/10.1007/s12350-019-01786-w>) discuss a patient preparation protocol consisting of a low-carbohydrate high-fat diet (LCHF), fasting, and unfractionated heparin (UFH) to maximally suppress physiologic myocardial glucose uptake and improve image quality. They also examine correlations between glucose and FFA biomarker metabolism and adequate suppression of myocardial FDG uptake, and develop a reliable method to evaluate the adequacy of myocardial glucose suppression. A LCHF was followed the day prior to FDG PET followed by an overnight fast. Rest MPI was performed with 82Rb in the morning. Thereafter a test meal drink (Unsweetened almond milk mixed with 30 mL of vegetable oil. Atkins™ Milkshake was an alternate drink) was consumed. Approximately 4 hours later, 30 IU/kg of unfractionated heparin was administered as three boluses (10 IU/kg) at 10 minutes preceding and 5 and 20 minutes following FDG injection. FFA, triglycerides (TG), and glucose were measured in the fasting state, immediately before UFH administration and on completion of UFH administration. C-peptide and insulin levels were also measured before and after UFH administration. The authors noted that this preparation resulted in suppression of physiologic myocardial glucose uptake in 95% of patients. Using this protocol, normal myocardial FDG uptake was consistently less than ascending aorta background (ratio of SUVmax myocardium to SUVmean blood pool of 0.75 (septal) and 0.70 (lateral), respectively). Insulin, C-peptide, and glucose levels were modestly related to myocardial and blood pool FDG uptake. TG and FFA levels were not significantly related to myocardial FDG uptake. Thus, comparison of myocardial SUVmax to ascending aorta blood pool SUVmean may be useful for assessment of adequacy of metabolic preparation and in developing quantitative thresholds for normal and abnormal FDG myocardial uptake.

Diagnosis of CAD in patients with advanced lung diseases is challenging, because of non-specific ischemic symptoms and limitations in physical ability and testing. ECHO is limited by hyperinflation in COPD and non-selective vasodilator stress testing poses a risk

for bronchoconstriction. Thus, coronary angiography (CAG) is frequently used for the detection of obstructive CAD in these patients. Schiopu and colleagues from Germany (<https://doi.org/10.1007/s12350-019-01851-4>) demonstrate the feasibility and accuracy of SPECT-MPI with regadenoson in 102 patients being considered for lung transplantation. All patients underwent SPECT-MPI and CAG. Regadenoson was well tolerated in all patients. No patient developed an exacerbation of the underlying lung disease after the SPECT-MPI. 14 patients experienced mild regadenoson-related symptoms. Obstructive CAD was detected in about 20% of patients with end-stage lung disease (ELD), and SPECT-MPI findings were used in these patients to guide decision about coronary revascularization. Thus, the study showed that regadenoson stress SPECT-MPI is safe and well tolerated in patients with ELD and is a useful tool to give guidance on coronary revascularization.

Routine screening for cardiac allograft vasculopathy (CAV) is necessary after orthotopic heart transplantation (OHT). Lazarus et al. from the University of Michigan, Ann Arbor (<https://doi.org/10.1007/s12350-018-01466-1>) show that Regadenoson stress PET MPI is well tolerated and safe in 123 OHT patients. No serious adverse events occurred. There were no life-threatening arrhythmias or hemodynamic changes. Common side effects related to regadenoson were observed, dyspnea being the most frequent (66.7%). Other symptoms included nausea and flushing, dizziness, headache and chest discomfort, palpitations and fatigue. Regadenoson was safe and tolerable even in OHT patients with severe chronic kidney disease (eGFR < 30).

Sudden cardiac death (SCD) is a leading cause of mortality in chronic heart failure patients with reduced ejection fraction (HFrEF). Hence, identifying HFrEF patients at high risk of SCD is important. Cardiac I-123-metaiodobenzylguanidine (MIBG) imaging provides prognostic information in patients with HFrEF. The novel AdreView myocardial imaging for risk evaluation in heart failure (ADMIRE-HF) risk score is useful to predict serious arrhythmia risk in patients with chronic HFrEF. ADMIRE-HF risk score is derived from the sum of the point values of LVEF, Heart-to-Mediastinal (H/M) ratio, and systolic blood pressure. The early repolarization pattern (ERP) in the standard 12-lead ECG is characterized by an elevation of the J point in at least two inferior or lateral leads. Moreover, ERP has also been shown to be associated with an increased risk of sudden cardiac death (SCD) in HFrEF patients. Ikeda-Yorifuji and colleagues from Osaka General Medical Center, Japan (<https://doi.org/10.1007/s12350-019-01639-6>) examine the combined prognostic value of ADMIRE-HF risk score and presence of ERP for predicting SCD in 90 patients with HFrEF. During a

median follow-up of 7.5 (4.5–12.0) years, 22 patients had SCD. LVEF and H/M ratio were lower with a greater washout rate in patients with SCD. The ERP-positive rate was significantly higher in patients with than without SCD. On multivariate analysis, ADMIRE-HF risk score and ERP were independently associated with SCD. Patients with both intermediate/high ADMIRE-HF score and ERP had a higher SCD risk than those with either and none of them. The study verified the prognostic value of ADMIRE-HF risk score for the prediction of SCD. Also the combination of ADMIRE-HF risk score and ERP provided incremental prognostic information for predicting SCD in HFrEF patients.

MPI is a validated technique for the assessment of LV function. The performance of LV functional assessment using gated SPECT-MPI relies on the accuracy of segmentation, i.e., delineation of epicardial and endocardial boundaries on the perfusion images. Current automated methods extract the epicardial and endocardial boundaries based on general assumptions and rules with empirical parameters. This method is easy and fast to implement; however, it can neglect the anatomic variations and pathologic abnormalities among different patients. Wang et al. (<https://doi.org/10.1007/s12350-019-01594-2>) propose and apply a novel machine-learning based method to automatically segment the LV myocardium by delineating its endocardial

and epicardial surface, and measure its volume in gated MPI on 32 normal and 24 abnormal patients and compare it with those delineated and approved by physicians (latter referred to as the ground truth). The results demonstrated very good agreement between the methods. The comparative results indicate feasibility of the novel machine-learning-based method in accurately quantifying LV myocardium volume changes over the cardiac cycle without manual intervention and holds promise for clinical use.

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

The authors declare that they have no conflict of interest with this work.

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