



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;26:1047–50.)

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

“A quick glance at selected topics in this issue” aims to highlight contents of the *Journal* and provide a quick review to the readers. Recently, we have also started to provide the quick glance write-up in an audio format as well via the JNC/ASNC Podcast (<https://soundcloud.com/jnc-podcast/quick-glance-july-august-2019-hage-bhambhani>), which can be accessed on iTunes, Spotify, and most podcast manager applications. 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 two 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/s12350-019-01772-2>), while the second outlines select publications in the general cardiovascular disease literature that have

relevance to our field (<https://doi.org/10.1007/s12350-019-01763-3>).

Another entry is the historical corner that looks at the career and scientific contributions of a pioneer in tomographic and nuclear imaging, David Kuhl, MD (1929-2017) (<https://doi.org/10.1007/s12350-018-1427-0>). 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 Bravo from the Hospital of the University of Pennsylvania, Philadelphia, PA (<https://doi.org/10.1007/s12350-018-1298-4>), which discusses the ‘Role of PET MPI in Hypertrophic Cardiomyopathy.’ Many of the original articles also have accompanying PowerPoint slides. The abstract of the lead original article ‘¹⁸F-sodium fluoride PET assessed microcalcifications in culprit and nonculprit human carotid plaques’ by Hop and colleagues from the Netherlands, 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 doi: <https://doi.org/10.1007/s12350-018-1325-5>.

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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.

Plaque thickness and intraplaque inflammation and microcalcification are important contributors to plaque vulnerability and thus have become targets of various molecular imaging techniques for noninvasive risk stratification of patients with carotid artery stenosis. Several studies have shown the feasibility of ^{18}F -sodium fluoride (^{18}F -NaF) PET for imaging vulnerable atherosclerotic plaques by virtue of its binding to microcalcifications within the plaque. In contrast, established calcifications are considered as the end-stage products of atherosclerosis and are associated with plaque stability. Hop and colleagues from the Netherlands (<https://doi.org/10.1007/s12350-018-1325-5>) compare in vitro ^{18}F -NaF PET uptakes between 17 culprit (symptomatic stenosis, $\geq 50\%$) and 6 nonculprit (asymptomatic stenosis, $\geq 70\%$) carotid plaques from 23 stroke patients. Renal arteries without macrocalcifications from 15 healthy kidney donors were studied as negative controls. The data showed that ^{18}F -NaF uptake between culprit and nonculprit carotid plaques was comparable, while the uptake in plaques was significantly higher than that in control renal arteries. ^{18}F -NaF activity was increased in areas without calcification on CT, and most of the CT calcifications showed minimal ^{18}F -NaF uptake. Also ^{18}F -NaF uptake on PET images matched with area of histologically proven calcifications. Areas with negligible ^{18}F -NaF uptake did not show any histological evidence for calcification. This supports the idea that microcalcifications visualized with ^{18}F -NaF PET, and typical calcifications visualized on CT may reflect different stages of the calcification process in the atherosclerotic plaque. Hence, ^{18}F -NaF PET has the potential to identify potentially vulnerable carotid plaques with ongoing calcification.

Diabetics are at greater risk for adverse cardiovascular outcomes and have a fourfold higher risk of developing CAD compared to their nondiabetic counterparts. Thus, several publications and guidelines designate diabetes mellitus (DM) as a CAD risk equivalent. Morales et al (<https://doi.org/10.1007/s12350-017-1114-6>) examine the DM cardiac risk equivalence from the perspective of stress SPECT MPI. The investigators look at the cardiovascular outcomes (cardiac death or nonfatal MI) of 17,499 patients referred for stress SPECT-MPI. Patients were stratified into four categories: non-DM without CAD ($n = 9133$), non-DM with CAD ($n = 3906$), DM without CAD ($n = 2768$), and DM with CAD ($n = 1692$). These four groups were further subdivided based on stress SPECT-MPI results

into normal or abnormal myocardial perfusion. Cardiac events occurred in 872 patients (5%), with event-free survival best among non-DM without CAD, worst in DM with CAD, and intermediate in non-DM with CAD and DM without CAD. After multivariate adjustment, risk for cardiovascular events remained comparable between DM without CAD and non-DM with CAD ($P = .74$). In addition, nuclear imaging results confirmed the similarity between these pair groups. Annualized event rates for subjects with normal perfusion were 1.4% and 1.6% for non-DM with CAD and DM without CAD, respectively ($P = .48$) and 3.5% ($P = .95$), for both abnormal groups. The study findings support DM as a CAD equivalent and suggest that MPI provides additional prognostic information in these patients.

The introduction of combined PET/MR imaging systems has opened up new avenues for assessment of myocardial perfusion and viability. However, myocardial perfusion and metabolism imaging acquisition mandates accurate attenuation correction (AC) of the PET-emission data. Segmented MR-based AC (MR-AC) maps are the current AC method of choice for integrated PET/MR imaging. The AC maps are based on segmentation algorithms, which segment the images into four tissue types (fat, soft tissue, background, and lung tissue). Lassen and colleagues from the Medical University of Vienna, Vienna, Austria (<https://doi.org/10.1007/s12350-017-1118-2>) investigate the frequency and the test–retest reproducibility of artifacts in MR-AC (DIXON-AC) maps acquired as part of PET/MRI protocols and assess the impact of these artifacts on the quantitative accuracy of PET myocardial perfusion (^{13}N -NH₃) and metabolism (^{18}F -FDG) measurements in a cohort of 20 patients with advanced CAD and heart failure. Four distinct artifact subtypes were noted—susceptibility, truncation, tissue inversion, and respiratory misalignment. The authors noted a high frequency of MR-AC artifacts (90%) in this study; however, the majority of the artifacts observed in the clinical PET/MR imaging protocol did not affect the quantitative assessment of the myocardium but potentially could question the validity of studies involving patients with cardiac-assisting devices. In conclusion, the authors suggest a thorough examination of DIXON-AC maps and correction of misalignment and susceptibility artifacts in the vicinity of the myocardium to ensure reliable cardiac PET/MR results.

Left ventricular assist device (LVAD) implantation is a standard treatment for end-stage heart failure. It is used either as a bridge to transplant, as a bridge to recovery, or as a destination therapy. However, LVAD infection represents a major and frequently occurring complication (incidence 17–22%), especially involving

the percutaneous driveline connecting the intracorporeal pump with the extracorporeal control unit. Diagnosis of a driveline infection remains challenging and without a clinical gold standard. Timely, correct, and complete treatments of a cardiac device infection are of utmost importance for prognosis as delay increases morbidity and mortality. Kanapinn et al from the University Hospital of the Ruhr-University Bochum, Bad Oeynhausen, Germany (<https://doi.org/10.1007/s12350-017-1161-z>) evaluate the potential of a baseline ^{18}F -FDG PET/CT (prior to an infection) for the diagnosis of an LVAD-related infection and establish an anatomy-based, reproducible method of semiquantitative measurement for ^{18}F -FDG PET/CT uptake at five distinct anatomic regions along the driveline (for a HeartWare device) and 3 regions (with a HeartMate II device). The difference in SUV max between the first and the second ^{18}F -FDG PET/CT was calculated for each of the regions ($\Delta\text{SUV}_{\text{max}}$). The highest difference was also ascertained (highest $\Delta\text{SUV}_{\text{max}}$). In addition, qualitative uptake pattern along the driveline was also assessed. Thirty patients who had undergone two ^{18}F -FDG PET/CT's, first after implantation and without signs of infection, and at a second time, with suspicion of a device infection were enrolled. Mean difference in SUV max for all five positions between the first and the second PET/CT along the driveline was significantly higher in patients with an LVAD-related infection compared to those without infection ($P < .05$). A SUV max threshold of 3.88 resulted in a sensitivity and specificity of 100%. Thus, the authors make a case for improved diagnosis of LVAD infection by comparing to a baseline ^{18}F -FDG PET/CT and using a distinctive SUV max threshold.

Yalcin and colleagues (<https://doi.org/10.1007/s12350-017-1155-x>) compare agreement between results of myocardial blood flow (MBF) and myocardial flow reserve (MFR), obtained using two software programs, PMod (that permits manual segmentation of the heart) and QPET (that has automated segmentation) in 76 hypertrophic cardiomyopathy (HCM) and 10 non-HCM patients who underwent rest and pharmacologic stress ^{13}N -ammonia PET MPI for CAD evaluation. All HCM patients had asymmetric septal hypertrophy, and 50% had evidence of left ventricular outflow tract obstruction, whereas non-HCM patients had normal wall thickness and ejection fraction. Data analysis revealed only modest agreement between the two software programs in HCM patients, but excellent agreement in the small cohort of non-HCM patients. PMod yielded significantly higher values for global and regional stress-MBF and MFR than for QPET in HCM. The authors infer that the observed differences in global and regional MBF values obtained by PMod and QPET could be attributed to anatomic characteristics specific to HCM,

namely, variability in degree and location of LV hypertrophy, small LV cavity size, and hypercontractility of HCM hearts. Thus, the two software programs cannot be interchangeably used for MBF/MFR analyses in HCM patients.

The advent of high-sensitivity solid-state of Cadmium-Zinc-Telluride (CZT) detector cameras and advances in software development have enabled reductions in imaging time and/or patient radiation dose without compromising image quality and diagnostic performance in nuclear cardiac imaging. Barone-Rochette et al from France (<https://doi.org/10.1007/s12350-018-1189-8>) examine the diagnostic accuracy of exercise or pharmacologic stress thallium-201/rest technetium-99m-sestamibi sequential dual-isotope high-speed MPI (DI-HS-MPI) performed using a CZT camera (Discovery NM 530c) against invasively determined fractional flow reserve (FFR) in 54 patients with known or suspected CAD. Patients were scheduled for DI-HS-MPI within 14 days before invasive coronary angiography (ICA). Significant CAD was defined by the presence of $\geq 90\%$ stenosis/occlusion or fractional flow reserve ≤ 0.80 for coronary stenosis $\geq 50\%$. When compared to ICA and FFR, the sensitivity, specificity, and diagnostic accuracy of MPI for the detection of significant CAD were 92.8%, 69.2%, and 81.4%, respectively, on a patient basis, and 83.7%, 90.4%, and 88.8% by coronary territory. The results indicate that stress thallium-201/rest technetium-99m-sestamibi sequential DI-HS-MPI accurately detected the presence of significant CAD as measured by FFR. Advantages of the dual isotope MPI technique include faster imaging time and clinic through put (less than 30 minutes), and favorable Thallium-201 kinetics (has higher extraction fraction than $^{99\text{m}}\text{Tc}$ -labeled tracers).

Significant associations have been demonstrated between atherosclerotic cardiovascular disease and several genes involved in the renin-angiotensin-aldosterone system (RAAS). Angelidis and colleagues from Greece (<https://doi.org/10.1007/s12350-017-1181-8>) are the first to investigate the effects of six RAAS gene polymorphisms on myocardial perfusion using stress-rest SPECT MPI in 810 patients with known or suspected CAD. After adjusting for all demographic and clinical data, an abnormal summed stress score (SSS) was significantly associated with the D allele of angiotensin-converting enzyme (ACE) gene. Given the strong association between the ACE polymorphism and abnormal SSS, this finding may be important for the preventive management of asymptomatic patients and opens a new window for further research.

LV remodeling is associated with adverse cardiovascular events. Hence, early identification of LV remodeling might be of clinical value for risk

stratification of patients with suspected CAD. Gaudieri et al (<https://doi.org/10.1007/s12350-017-1090-x>) evaluate the prognostic value gated SPECT MPI derived LV shape index (LVSI) in 646 patients with suspected CAD and normal myocardial perfusion and LVEF. An automated software program-derived LVSI ≤ 0.54 at end-systole was considered normal. During follow-up, 25 events (cardiac death, nonfatal myocardial infarction, or unstable angina requiring coronary revascularization) occurred (3.8% cumulative event rate). Event-free survival was lower in patients with abnormal end-systolic LVSI (more rounded shape of the heart, $P < .001$). Diabetes was an independent predictor of high end-systolic LVSI even after matching for demographic characteristics and risk factors. Age ($P = .021$), diabetes ($P = .048$), and end-systolic LVSI ($P < .001$) were independent predictors of cardiac events. Thus, end-systolic LVSI provided added prognostic information over traditional cardiac risk factors and may identify patients with early-stage LV remodeling who are at a higher risk of adverse cardiac events, even in the presence of normal myocardial perfusion.

CHF is a life-threatening syndrome with high morbidity and mortality rates. Approximately 50% of deaths are related to sudden cardiac death (SCD). In order to prevent SCD in CHF patients, current guidelines recommend an implantable cardioverter-defibrillator (ICD) in patients with a LVEF $< 35\%$, NYHA class II or III and treated with optimal medical therapy. Recent studies suggest that several ICD recipients experience inappropriate shocks and ICD-associated infectious complications. Furthermore, some arrhythmic deaths happen in patients who were classified as low risk for arrhythmic cardiac death and had no ICD indication. Thus, current ICD selection criteria in CHF patients, largely driven by LVEF, are suboptimal. Quantitative myocardial ^{123}I -mIBG parameters have been shown to be of prognostic value in CHF. De Vincentis and

colleagues (<https://doi.org/10.1007/s12350-018-1258-z>) evaluate the efficacies of both planar and SPECT ^{123}I -mIBG imaging to predict arrhythmic events (AE, defined as an episode of sustained ventricular tachycardia, resuscitated cardiac arrest, appropriate ICD discharge, or SCD) in 170 CHF patients and whether ^{123}I -mIBG scintigraphy could predict appropriate ICD therapy. During a median follow-up of 23.3 months, 69 patients experienced an AE. SPECT-derived early summed score (ESS) was the only independent predictor of AE. Planar ^{123}I -mIBG imaging-derived parameters failed as independent predictors of appropriate ICD therapy. Interestingly, the late H/M (heart-to-mediastinum) ratio in relation to AE and appropriate ICD therapy had a 'bell-shaped' curve, i.e., patients with intermediate late H/M ratios (range 1.2-1.6) were more likely to have an AE and appropriate ICD therapy compared to patients with low and high late H/M ratios. This seemingly counterintuitive finding implies that it is not those with the largest ^{123}I -mIBG abnormalities that tend to be at the highest risk for events, but the highest risk is, instead, with patients with intermediate ^{123}I -mIBG abnormalities.

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 their relevant 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

There are no conflicts of interest in respect of this work.

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