Optimizing patient centered care in the cardiac intensive care unit: Harness the safety, effectiveness, and incremental value of radionuclide perfusion, function, and molecular imaging

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Cardiovascular disease (CVD) and its sequelae remain the number one cause of death in the USA and globally. Despite a heightened focus on cardiac risk stratification, primary and secondary prevention, and an increasing number of medical and mechanical therapies, CVD and its management have grown in scope and complexity. Nuclear cardiology techniques provide safe and effective evaluation of CVD. Safety is our professional and ethical imperative, and in critically ill patients with cardiovascular, CNS, pulmonary, renal and/or hepatic dysfunction, nuclear cardiology techniques reliably provide safe assessment of diagnosis, prognosis, and treatment response. PredischARGE vasodilator stress testing and its safe, prompt, and effective reversal with either aminophylline, theophylline or caffeine provide an exemplary standard of safety and effectiveness and wide applicability to patients in the field of cardiovascular stress testing.^{1,2} Beyond safety, the quantitative assessment of myocardial relative perfusion, absolute

myocardial blood flow and blood flow reserve, global and regional function, dyssynchrony, ventricular volumes and molecular imaging of sympathetic innervation, dysrhythmia, infiltrative cardiomyopathies and aortopathies, prosthetic valve endocarditis, and cardiac device infection endow the discipline of nuclear cardiology with the signature value of incremental assessment of diagnosis, prognosis, and treatment response in a wide range of cardiac conditions.

In the current issue of the Journal, Schenone et al. provide an overview of the safety and utility of radionuclide imaging of patients in the coronary intensive care unit (CICU).³ The authors note that the evaluation of CICU patients is guided by several considerations: (1) Is the current presentation driven by myocardial ischemia or solely represent a progression of cardiomyopathy?, (2) Do benefits of revascularization outweigh the risks on the basis of myocardium at risk?, and (3) Which vessels/territories would benefit from revascularization? A fourth consideration in their review is the influence of other disease processes that may contribute to the presentation of the acutely ill patient in the CICU. Major take-home points of this Cleveland Clinic review merit further consideration. The versatility of nuclear cardiology applications in CICU is summarized in the Figure.³

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ASSESS FOR MYOCARDIAL ISCHEMIA IN COMPLEX CAD CASES

Global and culprit regional myocardial ischemic jeopardy can be readily quantified by PET and SPECT MPI. Extensive global LV stress-induced ischemia that exceeds the burden of infarction identifies near-term benefit of revascularization.^{4,5} Incremental value of revascularization has been clearly identified by PET measurements of MBF and MFR.^{6–9} Patients with $\geq 10\%$ stress-induced ischemic defect and $MFR \leq 1.8$ on PET MPI have been reported to benefit from revascularization.⁹ Patients with stress MBF < 1.8 ml/min/gr and $MFR < 2.0$ also benefit from revascularization.⁷ A growing literature supports the use of CZT SPECT to obtain MBF and MFR results that correlate highly with those of PET and coronary angiography.^{10,11}

ASCERTAIN CULPRIT ISCHEMIC TERRITORIES AND EXTENT OF HIBERNATING VIABLE MYOCARDIUM TO GUIDE GDMT AND REVASCULARIZATION

A major question confronting management of patients who survive acute myocardial infarction with extensive cardiac dysfunction is whether sufficient ischemic jeopardy exists to provide benefit of revascularization. The Ottawa-FIVE sub-study of the PAAR2

trial is unique in the literature in providing a robust, meaningful study design to evaluate this question. This secondary analysis of this interventional trial evaluated the effect of revascularization on primary cardiovascular outcome events as a function of the extent of hibernating viable myocardium (HVM) defined by “mismatched” PET resting myocardial perfusion defects associated with increased myocardial FDG uptake representing myocardial glycolysis associated with regional ischemia. The study showed that revascularization was increasingly effective in reducing primary cardiovascular outcome events with progressive increases in the extent of HVM $\geq 7\%$ LV myocardium.¹² Similar to the diagnostic accuracy of PET perfusion metabolism mismatch, HVM can comparably be evaluated by rest-redistribution thallium-201 imaging.¹³ An opportunity exists to confirm with randomized controlled trials the threshold of HVM by either technique, including CZT SPECT ultra-low-dose thallium-201 rest-redistribution imaging. Nevertheless, compelling observational data have stimulated clinical application of assessment of HVM, rather than “viability” without evaluation of hibernation prior to revascularization by radionuclide PET and SPECT imaging of perfusion, cellular energy metabolism, and myocyte membrane function evidenced by cation redistribution. Importantly, future studies that attempt to quantify the benefit of revascularization

should consider the substrate of global ischemic burden as the sum of stress-induced ischemia and resting ischemia in dysfunctional, viable myocardium that SPECT and PET myocardial perfusion, function, and metabolic imaging can identify.

EVALUATE FOR MYOCARDIAL ISCHEMIA, SCARRING, AND INFLAMMATION AS TRIGGERS FOR VT

CICU patients with monomorphic VT associated with predominant scar on SPECT or PET MPI suggest the value of antiarrhythmic therapy, VT ablation, and/or ICD implantation. CICU patients with polymorphic VT/VF with large areas of ischemia by SPECT or PET MPI are likely to benefit from ischemia-guided revascularization. Malignant polymorphic VT/VF in CICU patients with evidence of active inflammatory cardiac sarcoidosis (CS) can be refractory to standard anti-arrhythmic therapy or revascularization and benefit from intensive immunosuppression and implantation of a dual chamber ICD. These cases of malignant polymorphic VT/VF associated with active inflammatory myocardial sarcoidosis without scar may not be identified by cardiac MRI. The residual risk of VT and VF on immunosuppressive therapy can be uniquely identified by resolution of FDG uptake on serial CS PET imaging, thereby facilitating timely tapering and discontinuation of immunosuppressive therapies, limiting numerous adverse effects and enhancing quality of life associated with these lifesaving therapies.

RULE OUT INFILTRATIVE AND INFLAMMATORY PROCESSES AS REASONS FOR AV BLOCK AND/OR HF

Intense, heterogeneous FDG uptake on PET scan after prolonged (12-18 hour) fasting preceded by very low-carbohydrate high-fat meals identifies active inflammatory CS in most cases in the presence or absence of scar in an atypical (non-vascular) distribution.¹⁴ Extensiveness of FDG uptake and RV uptake contribute to adverse prognosis. In addition to aforementioned polymorphic VT refractory to anti-dysrhythmic therapy, the classic presentations of active inflammatory sarcoidosis include high-degree AV block and HFrEF. HF may result from extensive CS infiltration, also suggestive of myocarditis, or from myocardial stunning associated with atrial and ventricular tachyarrhythmias. The presence of AV block or HF unexplained by myocardial infarction or ischemia in CICU patients suggest the value of fasting FDG PET in combination with resting PET or hybrid CZT SPECT MPI to diagnose active CS inflammation and scar, to initiate timely immunosuppressive therapy and limit progression of cardiac degeneration.

ASSIST IN THE DIAGNOSIS OF INFECTIVE ENDOCARDITIS IN COMPLEX CASES

Schenone et al. review the role of fasting FDG PET imaging to evaluate prosthetic valve endocarditis in cases where echocardiography is inconclusive or suggests aortic root abscess.¹⁵ Detection of IE has high sensitivity and limited specificity; and diagnostic accuracy can be optimized by follow-up testing with an indium-111 WBC scan.¹⁶ Most patients with a prosthetic valve and no evidence of infection exhibit prosthetic F18-FDG valve uptake 1 year after surgery, mostly with a diffuse homogeneous uptake and occasionally diffuse heterogeneous or focal which may simulate CS.¹⁷ In CICU patients, focal F18-FDG uptake can reflect other non-infectious conditions including thrombi, non-calcified atherosclerotic plaque, vasculitis, tumor, and foreign body reactions. The interpretation of an abnormal uptake on either F18-FDG PET/CT or WBC scans as a major criterion for the diagnosis of IE is supported by the European Society of Cardiology for the management of IE.¹⁸ Schenone et al. suggest that the diagnosis and management of endocarditis in complex patients utilize hybrid PET/CT imaging and a multi-disciplinary endocarditis team including surgical, infectious disease, and cardiology consultants.

The presence of high-degree AVB and clinical and echocardiographic features of cardiac amyloidosis suggest the utility of technetium-99m pyrophosphate for sensitive and specific for the non-biopsy detection of transthyretin cardiac amyloidosis.

DISCRIMINATE INFLAMMATORY AORTOPATHIES FROM ACUTE AORTIC SYNDROME IN SELECTED CASES

The association of intense FDG uptake in the aorta associated with elevations of CRP with CTA evidence of aortic wall thickening and presence of negative blood cultures for bacteria or fungus is strongly suggestive of aortitis. Further investigation is needed to clarify the significance of frequent findings of fasting FDG uptake in the ascending, arch, and descending aorta on routine fasting CS scans alone or in combination with classical findings of CS.

ADVANTAGES OF NUCLEAR CARDIOLOGY IMAGING IN THE CICU

Minimal patient cooperation is required. Imaging times are brief. CICU patients can be imaged with instrumentation and devices such as pacemakers, ICD, and balloon pumps.

Imaging is not precluded by kidney or liver failure; vasodilator stress testing can be routinely performed in moderate-to-severe COPD and mild-to-moderate asthma.

In summary, the greatest values of nuclear cardiology include safety, effectiveness, and incremental value of diagnosis, prognosis, and assessment of treatment response. CICU patients can benefit greatly from nuclear cardiology, and diagnostic SPECT and PET imaging can be safely and effectively performed in patients with multi-organ failure and in the presence of cardiac devices such as pacemakers, ICD, or intra-aortic balloons. Advances in digital PET and CZT SPECT instrumentation provide similar spatial resolution, safe and effective low-dose imaging and rapid imaging results. This overview by our colleagues at the Cleveland Clinic reminds us that clinicians must understand current and future nuclear cardiology applications to optimize safety and outcomes for these acutely ill patients in the CICU who confront risks of imminent worsening of cardiovascular morbidity and mortality with downstream testing and interventions.

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