Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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GUEST EDITORS' PAGE

What Is of Recent Interest in Cardiac Imaging?

Insights From the *JACC* Family of Journals

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Despite the coronavirus disease-2019 (COVID-19), a number of high impact papers covered many of the recent advances in cardiac imaging over the last year. The *JACC* family of journals showcases many important original research papers in multiple imaging modalities, and we periodically summarize our favorite results and concepts across various *JACC* journals.

IMAGING IN COVID-19

COVID-19 played an oversized role among research papers, and imaging was no different. Cardiac involvement in COVID-19 is common. Myocardial injury in the form of troponin leak is seen in about one-third of patients hospitalized with COVID-19 (1) and conveys adverse prognosis. A large international cohort study (2) showed that echocardiographic abnormalities identified a high-risk group among those with elevated troponins. Does this injury leave a lasting adverse impact? The earliest cardiac magnetic resonance (CMR) study to answer this (3) showed myocardial edema (54%) and late gadolinium enhancement (LGE) (31%), raising the possibility of longer-term sequela that was confirmed to varying degrees by other studies. COVID-19 also revealed a multisystem inflammatory syndrome in kids where subtle myocardial injury was common even with preserved ejection fraction (4).

The right ventricle was an important marker of poor prognosis in COVID-19 (5). Right ventricular (RV) longitudinal strain in particular seemed better than other measures for predicting outcomes (6) and had importance over clinical and biomarker factors (7). How to keep imaging laboratories open became a pressing issue necessitating novel strategies (8). A particularly controversial issue was how much myocardial damage COVID-19 can inflict in athletes. Early studies showed subtle changes (9). One of the first comprehensive, prospective studies found pericardial involvement in one-third, but frank myocarditis was rare (10), thus providing some evidence to allow cautious participation for recovering athletes (11).

IMAGING IN CORONARY ARTERY DISEASE

Coronary artery disease was an active area of high-quality papers in the *JACC* journals. Fractional flow reserve derived from coronary computed tomography angiography (FFR_{CT}) is promising, but how does it perform in real life? Data from the large international ADVANCE (Assessing Diagnostic Value of Non-invasive FFR_{CT} in Coronary Care) registry confirmed the protective effect of negative FFR_{CT} (12). Machine-learning-based FFR_{CT} remained better than computed tomography angiography (CTA) alone, especially as the calcium burden increased (13). Perfusion imaging generated some interesting data. Automated myocardial perfusion imaging (measured as total perfusion defect) predicted higher major adverse cardiovascular events (MACE) even when visual reads were normal, thereby showing ability to more finely characterize risk than before (14). Another paper from

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the SPINS (Stress CMR Perfusion Imaging in the United States) study found stress CMR is cost effective (cost/quality-adjusted life years) and a good gatekeeper for invasive angiography (15).

Novel imaging strategies were reported. CTA is not usually recommended to evaluate patients with acute coronary syndrome (ACS). A VERDICT (Very Early Versus Deferred Invasive Evaluation Using Computerized Tomography in Patients With Acute Coronary Syndromes) trial substudy revealed very high negative predictive value allowing CTA to be a good gatekeeper for invasive angiography (16); however, we need more information because a very recent randomized, controlled trial (RCT) did not show a big advantage for CTA in patients with suspected ACS (17). Finding an etiology in myocardial infarction with nonobstructive coronary arteries is challenging, and conventional LGE is the standard method to identify myocardial infarction. High-resolution LGE imaging changed the final diagnosis in about one-fourth of patients with myocardial infarction with nonobstructive coronary arteries and was most effective in patients with normal echo and conventional CMR (18). Multisystem imaging is emerging as a powerful technique. A study in psoriasis found that chronic stress associates with noncalcified coronary plaque, possibly through its effects on the hematopoietic system activity and inflammation. Treating psoriasis attenuated these effects, including plaque progression. This might explain, in part, the high risk of cardiac events in psoriasis (19).

A couple of important papers were published regarding coronary plaque imaging. Total atherosclerotic burden but not noncalcified plaque prevalence increased with higher clinical risk profiles, but higher noncalcified plaque volume strongly predicted events in patients with multivessel disease (20). Intravascular imaging can identify vulnerable plaques in ACS, but such information was not traditionally used to guide interventions. A study using 3-vessel intravascular ultrasound with near-infrared spectroscopy in patients undergoing percutaneous coronary intervention for ACS found that intervening was safe, improved lumen size, and provided a nonsignificant trend toward favorable outcomes, thus paving the way for robust RCTs in this area (21).

IMAGING OTHER VASCULAR TERRITORIES

Identifying patients at risk for stroke is challenging, but intraplaque hemorrhage seen on magnetic resonance seems to be one of the strongest markers and better than conventional parameters (22). There is no good way to predict restenosis after peripheral vessel angioplasty, but a nice study shows that persistent femoral arterial inflammation (^{18}F-fluorodeoxyglucose positron emission tomography) and microcalcification (with sodium fluoride) postprocedure increase risk of future restenosis (23).

IMAGING IN HEART FAILURE

There were a number of important papers for imaging in heart failure in the *JACC* family of journals. CMR is excellent for identifying fibrosis, but how should we find it? Fibrosis measured with extracellular volume (ECV) was the strongest predictor of outcomes (24). A normal cardiac echo is often considered to rule out structural heart disease in patients with ventricular arrhythmia, but CMR increasingly is showing that this is not true—a pathology could be identified in about one-fourth of patients with a normal conventional echo study (25). These findings raise important questions for clinical practice, but how much CMR adds over more advanced echo techniques (eg, global longitudinal strain [GLS]) is still unclear. Amyloid imaging had some new information. Echocardiography has modest accuracy when screening for amyloidosis, but using a multiparametric score improves diagnosis efficacy and detection in this treatable cause of heart failure (26). T1 mapping appears to help with amyloid diagnosis without requiring contrast administration. A native T1 <1,036 ms (98% negative predictive value) or T1 >1,164 ms (98% positive predictive value) can simplify diagnosis and triage patients who need gadolinium contrast (27). Scintigraphy is highly sensitive for TTR-amyloidosis, but caution is needed in patients with the Phe64Leu TTR mutation where sensitivity is <11% (28). Last, regression of amyloidosis is a high interest area—treating ATTR amyloid with patisiran reduced ECV in association with lower BNP and less cardiac uptake of amyloid avid tracers, suggesting that ECV can track regression in cardiac amyloid burden (29).

Cardio-oncology remained an area of important findings. A large study found that treatment with doxorubicin or doxorubicin with trastuzumab (but not trastuzumab alone) can progressively worsen diastolic function (80% prevalence at 3 years), which then modestly predicted future left ventricular (LV) systolic dysfunction (30). Identifying early cardiotoxicity with immune checkpoint inhibitors is becoming important. GLS is decreased in patients with immune checkpoint inhibitor myocarditis

irrespective of ejection fraction and portended worse MACE, especially in those with a preserved ejection fraction (31). What is the value of nonparametric CMR imaging in Immune checkpoint inhibitor induced myocarditis? A comprehensive study showed that abnormal T1 and T2 values were common, helped with the diagnosis, and native T1 (unlike T2 values) strongly predicted MACE (32). GLS predicts cardiotoxicity better than ejection fraction, but can a GLS-guided strategy allow for better cardioprotection than usual care? A large RCT showed that GLS-guided cardioprotective strategies were found to be useful—greater use of cardioprotective therapies and possibly lesser cardiotoxicity even though the change in ejection fraction at 1 year was not significantly different (33).

There was new information on atrial myopathy based on atrial fibrillation burden in heart failure with preserved ejection fraction. Left atrial size and function worsen in proportion to atrial fibrillation burden and might constitute a variant of heart failure with preserved ejection fraction with significant effects on the right ventricle and pulmonary circulation (34). A large registry study shows that significant remodeling is still seen commonly after primary percutaneous coronary intervention but predicts rehospitalization and not increased mortality (35). Empagliflozin has protective effects in diabetic and nondiabetic hearts (36), but does it affect myocardial stiffness? A robust animal study showed that its effect on diastolic function in nondiabetic heart failure with reduced ejection fraction is associated with better remodeling, increased nitric oxide, as well as reduction in both interstitial myocardial fibrosis and improved cardiomyocyte stiffness via titin phosphorylation (37). This raises the possibility of new and attractive strategies for intervention.

IMAGING AND MACHINE LEARNING/ ARTIFICIAL INTELLIGENCE

Impactful papers were seen in the domain of machine learning and artificial intelligence. Deep convolutional neural network is revolutionizing imaging, but how good is it compared to highly trained cardiologists? It seems as good for detecting regional wall motion abnormalities and identifying infarction territories as our usual echo images (38). Deep learning can automate tasks better than humans, but can it also self-correct its output? Cardiac function was automatically obtained from CMR images with quality-control not requiring any human interaction (39).

VALVULAR HEART DISEASE

Plasma angiotensin-converting enzyme (ACE)2 is important in many conditions including COVID-19, but a fascinating study now finds its effect on LV remodeling and adverse prognosis in aortic stenosis (40). While an increase in plasma ACE2 is detrimental, myocardial ACE2 seems to inhibit fibrosis. Similarly, fibrosis, best quantitated with extracellular volume fraction, predicted total and cardiovascular mortality in aortic stenosis independent of traditional risk variables including the presence of macroscopic scar (41).

How useful is GLS in predicting postoperative course in chronic aortic regurgitation? Even a mild reduction in preoperative GLS predicts reduced survival, and persistently low GLS on follow-up was additionally prognostic (42). Timing surgical intervention in asymptomatic patients with severe chronic aortic regurgitation is difficult, but LV GLS is proving to be a good marker even in patients with preserved ejection fraction. Worsening GLS allows better reclassification and prognostication (43). Ischemic mitral regurgitation is a major problem, but the effects of mitral regurgitation severity vs size of the underlying infarct remains unclear. A large CMR study shows that for similar mitral regurgitation severity, the size of the underlying scar affected outcomes, showing a role for CMR to better characterize such patients (44).

STRUCTURAL HEART DISEASE

Valve embolization is a dreaded complication of transcatheter mitral valve replacement in valve-in-mitral annular calcification interventions. A new score that grades mitral annular calcification systematically seems to mitigate this risk to some extent (45). Subclinical leaflet thrombosis has generated much interest after transcatheter aortic valve replacement (TAVR), but its natural history is unclear. A serial CT study from the PARTNER 3 (The Safety and Effectiveness of the SAPIEN 3 Transcatheter Heart Valve in Low-Risk Patients With Aortic Stenosis) showed a small prevalence of hypoattenuated leaflet thickening (10% at 30 days to 24% at 1 year) that was 3 times more frequent in TAVR valves, resolved in 50% by 1 year, and had only mild effects on gradients (46). Who are the patients that improve after transcatheter mitral valve repair? Significant improvement in mitral regurgitation and pulmonary artery pressure 1 month postprocedure

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could identify those with greater potential to respond to this therapy (47). Can prolonged transesophageal echocardiography during SHD procedures result in gastrointestinal injuries? A high rate of new post-procedural esophageal/gastric injury was linked to prolonged imaging and significant manipulation in case of suboptimal views (48). RV function is prognostic in many SHDs but surprisingly affects transcatheter tricuspid repair. The procedure improved New York Heart Association functional class in two-thirds of patients, including those with significant RV dysfunction and pulmonary arterial hypertension (49). LV outflow tract calcification adversely influences TAVR outcomes, and a semiquantitative study now clarifies this further. Moderate-to-severe calcification increased risk of rupture for balloon expandable valves while regurgitation and need for second valve was equally high for all valve types (50). Intracardiac echocardiography is attractive for guiding left atrial appendage occlusion because it avoids the requirements associated with transesophageal echocardiography, but how cost effective is it? It appears equally effective in terms of success rates and costs but shortens the time in the catheterization laboratory (51).

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