Multi-modality imaging: Bird's eye view from the 2020 American Heart Association Scientific Sessions

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This review summarizes key imaging studies that were presented at the American Heart Association Scientific Sessions 2020, which occurred virtually this year due to the pandemic, related to the fields of single-photon emission computed tomography, positron emission tomography, cardiac computed tomography, cardiac magnetic resonance, and echocardiography. The aim of this bird's eye view is to inform readers of the various studies discussed at the meeting from these imaging modalities. Since there was no physical attendance this year, we find that a general overview of imaging will be especially useful. Further, we hope that the presentation of multiple imaging studies in a single synthesized review will stimulate new ideas for future research in imaging. (J Nucl Cardiol 2021;28:492–501.)

Key Words: CAD • heart failure • sarcoid heart disease • amyloid heart disease • inflammation • myocardial ischemia and infarction

Abbreviations	
CAC	Coronary artery calcium
CAD	Coronary artery disease
CCTA	Coronary computed tomography angiography
CFR	Coronary flow reserve
CMR	Cardiac magnetic resonance
CT	Computed tomography
HFpEF	Heart failure with preserved ejection fraction
IMAT	Intermuscular adipose tissue
LGE	Late gadolinium enhancement
LVEF	Left ventricular ejection fraction
MACE	Major adverse cardiovascular events
MBF	Myocardial blood flow
MIBG	Iodine-123 metaiodobenzylguanidine
MINOCA	Myocardial infarction without obstructive coronary disease
MPI	Myocardial perfusion imaging
OCT	Optimal coherence tomography
PCWP	Pulmonary capillary wedge pressure
PET	Positron computed tomography
RHC	Right heart catheterization
SPECT	Single-photon emission computed tomography
SRS	Summed rest score
TAVR	Transcatheter aortic valve replacement
TR	Tricuspid regurgitation

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This bird's eye view from the 2020 American Heart Association Scientific Sessions (AHA 2020), which was held virtually this year due to the COVID-19 pandemic, will review key abstracts presented at the meeting related to imaging following a similar structure to our bird's eye view from previous years.[1–5] This bird's eye view will include sections on single-photon emission computed tomography (SPECT), positron computed tomography (PET), cardiac magnetic resonance (CMR), echocardiography, and cardiac computed tomography (CT). We acknowledge that no review can summarize all the imaging studies that are presented at a large conference of the magnitude of AHA 2020 but we hope that our review will be useful to the readers by shedding light on some of the presented studies.

SPECT

Many exciting abstracts have been presented at AHA 2020 in the field of SPECT. Coronary artery disease (CAD) remains the leading cause of morbidity and mortality. Cardiac CT angiogram (anatomical definition) and stress SPECT myocardial perfusion imaging (MPI) (physiological evaluation) are two of the most commonly used non-invasive modalities to assess for CAD. However, significant coronary calcification and attenuation artifacts are common limitations for CT and SPECT, respectively, hence reducing their diagnostic accuracies. When combined together into a hybrid modality, however, they tend to complement each other's limitations. Indeed, Hachiva et al.[6] showed that such hybrid imaging exhibited greater results in all of sensitivity, specificity, and diagnostic accuracy, particularly among those with severe vessel calcification, and reclassified perfusion abnormalities mostly in the left circumflex territory. Therefore, hybrid imaging provides higher diagnostic accuracy compared to single modalities, ''enabling physicians to make better decisions'' and reduces the need for unnecessary invasive angiography. Cost and radiation dose remain the main challenges to be surmounted.

HEART score is a useful clinical tool to stratify patients presenting with chest pain based on clinical presentation/suspicion, age, risk factors, ECG, and troponin level. During the COVID-19 pandemic, many patients present to the emergency room with chest pain or dyspnea. In a retrospective study, Mason et al.[7] stratified these patients into low risk (HEART score < 4, N = 90, surveillance group) and intermediate to high risk (HEART score ≥ 4, N = 212). All patients in the latter group underwent stress SPECT MPI for further stratification: more than half had an intermediate to high-risk stress SPECT and 43/212 required coronary revascularization. Given the scarce resources during the COVID-19 pandemic, HEART score remains a useful tool to risk stratify patients, while complemented with stress SPECT for those considered higher risk.

The field of radiomics coupled with artificial intelligence is gaining momentum in cardiac imaging, whether by improving diagnostic accuracy or prognosis. In particular, patients with heart failure (HF) are at increased risk for cardiac death. Different independent clinical and imaging predictors have been identified for patient risk stratification; yet, there is always room for improvement. Dual-isotope (201TlCl and 123I-β-methyl-P-iodophenyl-pentadecanoic acid [BMIPP]) SPECT is a powerful imaging modality performed in patients with ischemic heart disease and HF with known prognostic value. Shimizu et al.[8] evaluated the role of machine learning through Random Forest and Deep Learning algorithms among 310 inpatients admitted with HF (mean age 77 years, 53% males), who underwent dual-isotope SPECT imaging. After a mean follow-up of 1.38 years, there were 35 cardiac deaths. Machine learning identified 4 key variables that predicted death (age, left ventricular ejection fraction [LVEF], summed rest score [SRS] of BMIPP, and mismatch score) with areas under the curve of .895 (Random Forest) and .935 (Deep learning), surpassing the traditional Cox regression model (AUC .479-.773). Machine learning is an evolving technology that provides better predictive models than conventional ones using same database, hence providing an opportunity to further refine our models, improve risk stratification, and guide better clinical judgment.

Cardiac iodine-123 metaiodobenzylguanidine (MIBG) imaging is another SPECT modality that predicts cardiac mortality risk in patients with HF with model optimization using machine learning (Fig. 1).[9] A risk score is calculated using MIBG delayed heart-to-mediastinum (H/M) ratio, age, LVEF, and NYHA functional class. Tamaki S et al.[10] tested the same model on patients with HF and preserved EF that were admitted with acute decompensation (PURSUIT-HFpEF prospective observational registry in Osaka, Japan, N = 239). During a follow-up period of 1.6 ± .8 years, 33 patients had all-cause death. Multivariate Cox analysis showed that the 2-year MIBG-based cardiac mortality risk score was an independent predictor of all-cause death ($P = .0009$), and could stratify patients into low, intermediate, and high-risk subgroups (log rank $P < .001$).

MIBG evaluates the cardiac sympathetic innervation, and its clinical application goes beyond ischemic and non-ischemic cardiomyopathy. In a recent study, Kadova et al. used MIBG imaging to evaluate the sympathetic nervous system among symptomatic patients with severe aortic stenosis undergoing TAVR

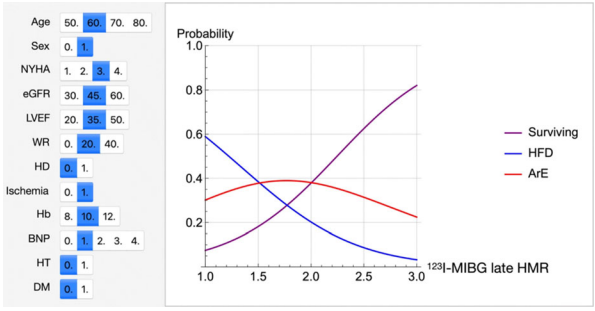

Figure 1. Probability of heart failure death (HFD), arrhythmic events (ArE), survival (no events) against 123I-MIBG heart-to-mediastinum ratio (HMR). Reproduced with permission from Ref. [9].

(transcatheter aortic valve replacement).[11] The authors hypothesized that sympathetic dysfunction is common in severe aortic stenosis and improves with TAVR. In an interesting study, they performed cardiac MIBG SPECT before and after TAVR in 107 patients and followed them for 1 year. An Improvement in the H/M ratio (post–pre) and a high post-TAVR H/M ratio were both associated with reduced major adverse cardiovascular events (MACE). This study demonstrated that cardiac MIBG imaging may be useful for predicting cardiac events after TAVR.

Accelerated sympathetic activity also plays an important role in atrial fibrillation. Using a novel solid-state whole-body scanner (VERITON), Fukunaga et al. attempted to image the sympathetic innervation of the left atrium with MIBG in patients with paroxysmal atrial fibrillation.[12] MIBG images were evaluated before and 3 months after ablation to quantify the neural network of the left peri-atrial cardiac sympathetic activity and its response to ablation. Hence, the ability to image sympathetic nerve modification by catheter ablation might prove to be clinically useful in predicting short and long-term responses to ablation, similar to using late Gadolinium enhancement (LGE) as an assessment of atrial fibrosis using CMR, and expands further on the clinical applications for MIBG SPECT imaging.

PET

The field of cardiac PET imaging of inflammation remains a dynamic and evolving one. There seems to be a common pathway between inflammation, microvascular disease, and cardiovascular events. Souza et al.[13] evaluated the association between intermuscular adipose tissue (IMAT) (often associated with inflammation and a key determinant in cardiometabolic disease), microvascular coronary dysfunction, and cardiovascular outcomes in 669 patients undergoing stress PET with normal perfusion and LVEF. Coronary flow reserve (CFR) was calculated as the stress/rest myocardial blood flow ratio, while IMAT areas (cm^2) were obtained from PET attenuation correction CTs. There was an association between CFR and IMAT after adjusting for age, sex, race, BMI, LVEF, and hypertension (β − .10, P = .047). Moreover, CFR and IMAT were independent predictors of MACE (HR 1.6 per − 1U CFR and 1.5 per +10 cm^2 IMAT, $P \leq .01$], while patients with both abnormal CFR and high IMAT demonstrated the highest risk for MACE (adjusted $P < .02$).

Patients with rheumatoid arthritis often have premature CAD. While inflammation is thought to be a common link between rheumatoid arthritis, coronary microvascular disease, and cardiovascular events, it remains unclear whether a specific inflammatory pathway plays a more determinant role. Weber et al.[14] evaluated 53 patients with rheumatoid arthritis undergoing dynamic stress PET with CFR quantification. Different cytokines, inflammatory markers, and biomarkers of myocardial injury were measured. The severity of CMD correlated with IL-6, sTNFR2, and NT-proBNP but not IL-1β, hsCRP, or troponin.

Leptin provides another pathway for increased atherogenesis in patients with rheumatoid arthritis. Indeed, Bhattaru et al. [15] showed a moderate correlation between leptin levels and FDG uptake in the abdominal aorta in 18 patients with the systemic disease (r = .59, P = .01), a reflection of increased inflammation and atherogenesis.

Increased and persistent inflammatory state is also found among patients with HIV and thought to be a major player in early atherosclerosis and increased MACE seen in patients living with HIV. Statins are known to have pleiotropic effects and decrease inflammation. In a small study,[16] patients with HIV were randomized to placebo (N = 18) or statin treatment (rosuvastatin, N = 17). Treatment with a statin over 6 months resulted in a significant drop in the 18F-FDG bone marrow, spleen, and thoracic aortic uptake, consistent with the decrease in inflammation. Larger studies and longer follow-up are needed with outcome data to validate these findings. Also, not all statins can be used safely in patients on anti-retroviral therapy due to potentially significant interaction.

Cardiac sarcoidosis is an inflammatory cardiomyopathy associated with ventricular arrhythmia, scarring, and sudden cardiac death.[17] The presence of LGE on CMR indicates scarring and reflects increased risk for MACE. Kiko et al.[18] evaluated the prognostic value of hybrid PET/CMR in patients with sarcoidosis (N = 43, median follow-up 3.7 years). The presence of active inflammation with persistent FDG uptake was associated with worse outcomes when analyzing the entire cohort,

but also when stratifying based on LGE. Patients with no LGE and no FDG uptake had no events, while those with both LGE and FDG uptake had the highest event rates.

Chronic psychological stress is strongly linked to cardiovascular disease risk. The amygdala is the stress-associated brain center; increased metabolic activity of this gland is therefore potentially associated with increased inflammation, accelerated atherogenesis, and cardiovascular events. Abohashem et al.[19] measured the amygdala activity with 18FDG PET/CT in 995 individuals, and showed close association between amygdala activity and the genetic predisposition to stress using a validated polygenic risk score for neuroticism (nPRS) (standardized β [95% CI]: .07 [.01, .13], P = .02, after adjusting for age, gender, and 10 principle components of ancestry). Furthermore, amygdala activity predicted myocardial infarction (adjusted odds ratio 1.50, P = .006), and similarly nPRS (adjusted odds ratio 1.12, $P < .001$) that remained significant after additional adjustment for cardiovascular risk factors and psychiatric history (P = .006 and .007, respectively).

In another study from the same group, a polygenic risk score for CAD, which ''integrates information from many sites of DNA variation into a single metric of inherited susceptibility,'' was also shown to be associated with higher amygdala activity on FDG-PET imaging which in turn was associated with 45% increase in risk of myocardial infarction.[20] Finally, the role of amygdala activity as a potential link between sleep apnea, hypertension, and cardiovascular events was also explored from the same database. Using PET imaging to quantify amygdala activity, a close association was found between sleep apnea and amygdala metabolic activity, hence bridging the gap between stress, hypertension, and myocardial infarction.[21]

CMR

The utility of CMR was highlighted in one of the late breaking scientific sessions presented at AHA 2020 evaluating the etiology of myocardial infarction without obstructive coronary disease (MINOCA), a part of the Women's Heart Attack Research Program (HARP) study. Reynolds et al.[22] prospectively evaluated 145 women with MINOCA and showed that 62 of the 116 (53.4%) who had a CMR had myocardial edema or subendocardial LGE in a coronary distribution. Another 24 of 116 (20.7%) were found to have non-ischemic cardiomyopathy,[3] stress-induced cardiomyopathy (4), or myocarditis.[17] Optimal coherence tomography (OCT) found plaque rupture in 57 of 145 patients (39%), keeping in mind these patients were deemed to have non-obstructive CAD on initial angiography. Five patients had coronary thrombus, three with suggestion of coronary vasospasm, and one with spontaneous coronary artery dissection. Overall, a combination of three-vessel OCT and CMR provided a likely diagnosis in 84.5% of women with MINOCA. Interestingly, 44% with ischemic CMR findings had no abnormal OCT findings. This prospective study further supports the class IB recommendation given by the 2020 European Society of Cardiology guidelines[23] in performing a CMR in all patients with MINOCA. An important clinical application of these findings is that a healthy minority of MINOCA patients with non-plaque-related events could avoid long-term antiplatelet and statin therapy.

In the field of hypertrophic cardiomyopathy, a novel cardiac myosin inhibitor that reduces actin–myosin cross-bridge formation, Mavacamten, was shown in 2018 to reduce outflow tract obstruction and improve symptoms in the EXPLORER trial.[24,25] A CMR substudy[26] presented this year showed further evidence this medication can decrease myocardial hypertrophy. In the 17 patients randomized to Mavacamten, there was a mean decrease in myocardial mass index of 17.4 gm/m^2 over the 30-week study period. Interestingly, by CMR measurements of extracellular volume, this was confirmed to be primarily a decrease in intracellular mass. Left ventricular wall thickness was decreased by 2.3 mm. There was also a decrease in left atrial volume index by 10.3 mL/m^2 as well 80% reduction in NT-proBNP, suggesting a favorable effect on hemodynamics. Naturally, one of the concerns of this medication would be inducing myocardial dysfunction and cardiomyopathy. While there was a mean decrease in ejection fraction (− 6.6%), none of the 17 patients who received a CMR had a decrease in ejection fraction to less than 50%.

CMR was also highlighted this year in the early career investigator competition, in an interesting study evaluating myocardial flow reserve in patients with cardiac amyloidosis.[27] It is usually assumed that the cardiac dysfunction in amyloidosis is primarily due to amyloid fibrils contributing to interstitial fibrosis. Chacko et al. studied myocardial perfusion by CMR in 92 patients with amyloidosis (41 with AL and 51 with TTR subtypes). Using adenosine stress and myocardial blood flow (MBF) mapping, they found that these patients had a severe reduction in stress MBF of 1.03 mL/g/min and myocardial perfusion reserve of 1.54. Interestingly, 25 of these patients had endomyocardial biopsy and in these samples, there was severe lumen reduction in 20% of vessels due to amyloid infiltration. The study included a matched cohort, 26 with normal coronaries and 47 with three vessel CAD. The MBF of patient with three vessel disease was

1.32 mL/g/min, further emphasizing the dramatic reduction in flow of the amyloidosis patients. Coronary ischemia is likely an under-recognized component of cardiac amyloidosis.

Another study presented this year looked at one institution's experience in monitoring ascending aortic aneurysm by CMR. In this common clinical scenario, there is some clinical equipoise when it comes to screening interval and imaging study of choice. Callow et al.[28] looked at 941 patients who had serial CMR studies in their imaging database. Of the 342 patients who had annual CMR, the mean progression was .0247 cm, while 206 patients had CMR every 2 years with a mean progression of .0598 cm. They also highlight that Medicare reimbursement was similar between CMR and CT. With the average rate of growth less than 1 mm in both groups they raise the argument that annual screening is too frequent, and that radiation-free CMR has advantages over CT.

Lastly, a trial was presented utilizing exercise CMR to evaluate for heart failure with preserved ejection fraction (HFpEF). It continues to be a challenge in assessing patients with dyspnea as resting echocardiography cannot always exclude cardiac contributions to the patient's symptoms. Pulmonary capillary wedge pressure (PCWP) by right heart catheterization (RHC) is considered the gold standard with HFpEF defined as PCPW $>$ 15 mm Hg at rest or $>$ 25 mm Hg during exercise. Backhause et al.[29] studied 75 patients with dyspnea on exertion and echocardiographic signs of diastolic dysfunction. They compared exercise RHC to real-time CMR with bicycle stress. They looked at time-volume curves for diastolic filling and left atrial emptying as well as long axis strain. Of the 34 patients who had HFpEF defined by exercise RHC, left atrial early and total emptying and not left ventricular diastolic filling correlated with HFpEF. Long axis strain was also impaired at rest and with stress. While exercise CMR has some logistical challenges, this study raises interesting observations that perhaps the left atrial function, and not just size, is an underutilized marker of cardiac hemodynamics, and that exercise CMR can be a valuable tool in assessing suspected HFpEF.

ECHOCARDIOGRAPHY

Numerous interesting abstracts were presented at AHA 2020. We will review here a few representative submissions.

Stress echocardiography has long been used for both establishing a diagnosis as well as risk stratification in patients with suspected and known CAD. Given the modality's relatively low sensitivity, it is of clinical relevance to identify factors that will allow improved risk stratification even in the absence of regional wall motion and/or thickening abnormalities. Bou Chaya et al.[30] retrospectively assessed 2,962 patients who had undergone a negative stress echocardiogram at a single institution. The outcome of interest was evidence of myocardial injury, based on an increase and change in cardiac troponin over a period of 12 months following performance of the stress study. The median age of the population was 58 years, 50% of them were male, 35% were diabetics, 21% had a prior history of CAD, and 1.5% had left ventricular (LV) systolic dysfunction defined as LV ejection fraction (LVEF) less than 50%. Approximately 5% of the patients studied were found to have experienced myocardial injury 12 months following performance of the stress echocardiogram. Factors that correlated with a higher risk of myocardial injury included age over 65 years old, LVEF less than 50%, history of diabetes, and history of end-stage liver disease. These findings highlight the need for multiparametric assessment of patient risk following a negative stress echocardiogram to provide more personalized recommendations for further management and work up.

The first phase EF (EF_1) is a newly introduced marker of early LV systolic function which is measured from end-diastole to maximum aortic valve velocity (peak ventricular contraction).[31] A low EF_1 ($<$ 25%) has been shown to serve as a prognostic marker for aortic valve replacement or death in patients with aortic stenosis. Xie et al. evaluated the prognostic value of EF_1 in 129 patients hospitalized with Covid-19.[32] No deaths were seen in patients with preserved EF_1 while 21 patients with reduced EF_1 expired. Mortality correlated with EF_1, right ventricular strain, and high sensitivity cardiac troponin but not with any other echocardiographic, demographic, or clinical parameters. It should be noted that similar to LV strain, EF_1 may be abnormal even in the presence of overall preserved LVEF and could therefore serve as an early, sensitive marker of LV dysfunction. Further details from the study including how many of the patients studied had a normal vs. low EF_1 and the differential characteristics of the patients based on the presence or absence of normal EF_1 are of interest, and will likely be included in the peer-reviewed manuscript.

The right ventricle has traditionally been called the ''forgotten chamber,'' however, in the past few years interest in the right ventricle has exponentially increased. The left and right atria remain under-appreciated, particularly with respect to their functional parameters. Deeper understanding of the role of the left and right atria, particularly in non-ischemic processes, may not only offer elucidating insight in the pathophysiology of diseases, but also may potentially pave the

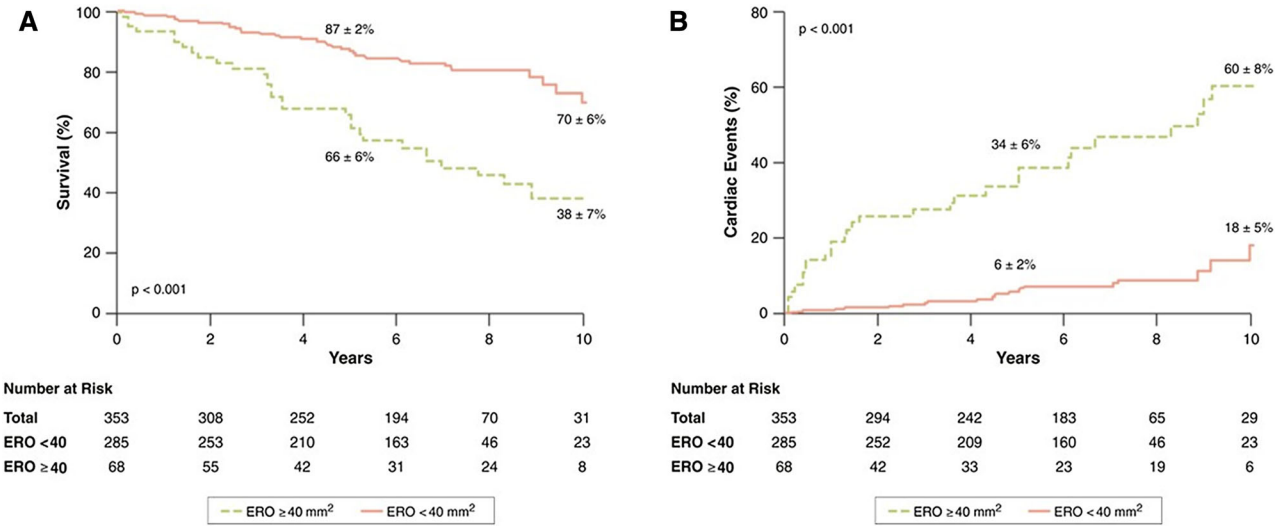

Figure 2. **A** Survival rates in patients with isolated TR, based on whether the effective regurgitant orifice (ERO) is less than or at least .4 cm^2. Of note, an ERO $\geq$ .4 cm^2 denotes severe TR. Each line represents survival rates (± SE) at 5 and 10 years of follow-up. **B** Incidence of combined outcome of cardiac death or heart failure in patients with isolated TR, based on the ERO (severe TR with an ERO $\geq$ .4 cm^2 vs. trivial-moderate TR with an ERO $<$ .4 cm^2). Each line represents cardiac event rates (± SE) at 5 and 10 years. Reprinted with permission from Ref. [34].

path for identifying new algorithms for diagnosis, risk stratification, and treatment monitoring. Cardiac amyloidosis is such a disease example with important recent strides in understanding the underlying pathogenesis, but with significant residual work that needs to be undertaken. Huntjens et al., studied 129 patients diagnosed with cardiac amyloidosis (transthyretin: 23 and light-chain: 106) and performed speckle tracking evaluation of right atrial reservoir strain based on six segments from the apical four-chamber view.[33] The outcome of interest was all-cause death over a 5-year period. During the follow-up period, a total of 60 patients expired. The max right atrial longitudinal strain was measured in 109 patients and it was reduced in non-survivors (8.1% vs. 18.3%, non-survivors vs. survivors, $P < .01$). Reduced values of RA peak longitudinal strain were found to portend a 3.3-fold higher mortality risk (95% confidence interval: 1.83-5.96). These findings suggest that the right atrium may serve as a marker for risk stratification in patients with cardiac amyloidosis.

Tricuspid regurgitation (TR) is now recognized as an important independent prognostic marker for mortality and HF hospitalizations (Fig. 2).[34,35] A new grading scheme that expanded on the severity of TR was recently introduced, adding massive and torrential TR as two additional grades beyond severe TR.[36] So far, the validity of this new classification scheme has not been well validated. Taku et al., retrospectively studied a total of 359 patients with severe TR and divided them in three groups based on the TR vena contracta (VC): those with VC $<$ 11 mm (severe TR), 11 $\leq$ VC $<$ 14 mm (severe-massive TR), and VC $\geq$ 14 mm (massive to torrential).[37] A higher proportion of patients with a TR VC $\geq$ 14 mm were found to have a RA pressure of greater than 15 mm Hg compared to those with a TR VC $<$ 11 mm (odds ratio 1.3; 95% confidence interval 1.01-3.08, $P = .047$). In addition, patients with a TR VC $\geq$ 14 mm were also found to be at higher risk for experiencing cardiac death and heart failure-related hospitalizations ($P = .02$).[8]

The role of the left atrium in risk stratification of patients with hypertrophic cardiomyopathy has not been extensively studied. In a prior study of 242 patients with hypertrophic cardiomyopathy who were followed for a mean of 4.8 ± 3.7 years, a left atrial volume of $\geq$ 37 mL/m^2 and a left atrial strain of $\leq$ 23.4% were found to be independent prognostic markers for new-onset atrial fibrillation, especially in the subset with preserved left atrial diameter ($<$ 45 mm) (Fig. 3).[38] Adding to the limited body of evidence, Saijo et al.,[39] studied a total of 536 patients with hypertrophic cardiomyopathy and found a left atrial contractile strain cutoff of 13.8% to serve as an independent predictor of exercise intolerance (AUC: .68, $P < .001$). In addition, they studied left atrial stiffness using the ratio of E/e' divided by the left atrial reservoir strain and found that a left atrial stiffness less than .41 correlated with a higher likelihood for myectomy ($P = .02$).

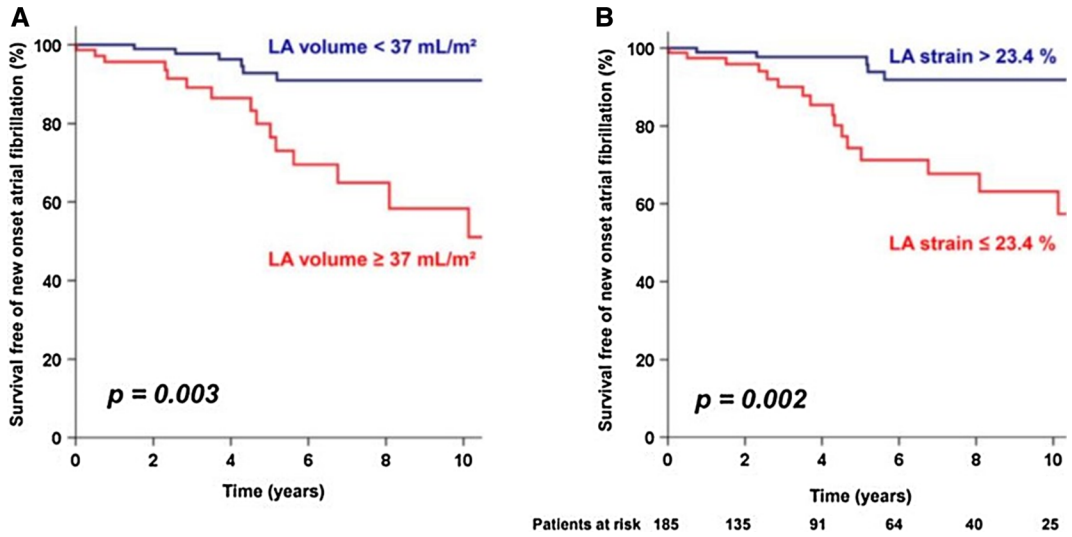

Figure 3. Kaplan–Meier survival curves showing rates of survival free of new-onset atrial fibrillation in patients with HCM and left atrial (LA) diameter less than 45 mm. A LA volume cutoff of 37 mL/m^2 and a LA strain of 23.4% have been shown to serve as independent predictors. Reprinted with permission from Ref. [38].

Following the results of the COAPT trial, MitraClip (Abbott, IL) is now increasingly being performed in patients with secondary mitral regurgitation as a non-surgical alternative.[40] After implantation, it is essential to be able to predict the rise in transmitral pressure gradients to avoid development of clinically significant iatrogenic mitral stenosis. So far, there are no distinct guidelines or echocardiographic criteria to risk stratify patients undergoing evaluation for MitraClip implantation with respect to the likelihood of post-procedural increase in their transmitral gradients. Hadjadj et al.[41] retrospectively evaluated 76 consecutive patients who underwent MitraClip implantation by both 2D (transgastric) and 3D transesophageal and 2D transthoracic echocardiography. They obtained measurements of the mitral valve orifice area prior to MitraClip and they calculated the ratio of the mitral valve orifice area to the LV forward stroke volume based on the LV outflow tract spectral Doppler (VTI). Compared to transthoracic assessment of the mitral valve orifice area, 3D transesophageal assessment (less than 3.9 cm^2) was more accurate in predicting a post-procedural increase in transmitral mean pressure gradients (> 5 mm Hg). In addition to the 3D area, a ratio of the preprocedural 3D mitral valve orifice area to the LV stroke volume less than 96 cm^2/L was also found to be predictive of increased, post-MitraClip mean gradients (> 5 mm Hg) (AUC = .86, 95% confidence intervals: .76-.97, $P < .001$; sensitivity: .84 and specificity: .81).

CT

Multiple important studies, including a late breaking clinical trial, investigating the role of coronary computed tomography angiography (CCTA) and cardiac CT were presented at AHA 2020.

Dr. Gray from Edinburgh presented the results of the RAPID CTA trial (Early Coronary CT Angiography in Patients with Suspected or Provisionally Diagnosed Acute Coronary Syndrome) which was funded by the National Institute for health research in the United Kingdom.[42] The study was a prospective, randomized, open but blinded endpoint clinical and cost effectiveness trial of early CCTA in the management and outcomes of intermediate or high-risk patients who presented to the emergency room with suspected acute coronary syndrome. The study included high-risk patient who were usually excluded from prior acute chest pains trials involving CCTA. Suspected intermediate-to-high-risk acute coronary syndrome was defined as chest pain with the presence of prior CAD, troponin elevation above the 90th percentile or abnormal twelve-lead electrocardiogram. The study enrolled patients between 2015 and 2019 in 37 United Kingdom hospitals. The primary endpoint was all-cause mortality or type I or type IVb myocardial infarction (stent thrombosis) at 1 year.

In the RAPID CTA trial, 877 patients were enrolled in the CTA arm and 871 patients were enrolled in the standard of care arm. The CTA and standard of care groups were comparable in age, gender, and prior cardiovascular risk factors (diabetes 18%, hypertension

47%, and hyperlipidemia 40%). One-third of the patients had known CAD and 57% of the patients had elevated cardiac troponin while nearly 60% of the patients had abnormal electrocardiogram. Notably, CCTA could only be performed in the 87% of the patients that were randomized to CCTA arm due to various technical and clinical reasons with a median radiation dose of 3.1 mSv (interquartile range of 1.9 to 5.5 mSv). It is important to note that half of the patients had normal coronary arteries or non-obstructive CAD. After 1 year of follow-up, there was no difference in the primary endpoint of death or subsequent myocardial infarction between the coronary CT arm or standard of care arm with an adjusted hazard ratio of .91, $P = .65$ (Fig. 4). This finding was consistent across the different prespecified subgroup analysis among diabetics, older patients, females, known CAD or high pretest probability. There was a modest increase in the length of stay 2.2 *vs.* 2.0 days (increase of .21 (95% CI, .05 to .40) days) and healthcare costs ($9,494 *vs.* $8,776) with CCTA in this study. There were no differences in subsequent emergency room visits or admissions with chest pain (Adjusted hazard ratio 1.06 (95% confidence interval .83 to 1.34), $P = .66$). The study clearly illustrates that in this intermediate-to-high-risk cohort, early CCTA had no effect on the overall treatment and prevention of acute coronary syndrome at 1 year. Rather, it was associated a modest increase in the length of stay and healthcare cost.[42]

To continue on the theme of assessment of acute chest pain, a systematic review was presented assessing the role of coronary artery calcium scoring in the evaluation of these patients.[43] The review combined the evidence from 18 studies including 27,719 patients with stable chest pain and 12 studies including 7,184 patients with acute chest pain undergoing simultaneous CCTA and CAC scoring. In these studies, nearly 50% of patients had zero calcium score. The pooled prevalence of obstructive disease in these patients was 3% among stable chest pain patients and 2% among patients with acute chest pain. Thus, the negative predictive value of coronary artery calcium scoring to rule out obstructive disease was about 97% in patients with stable chest pain and 98% in patients with acute chest pain.

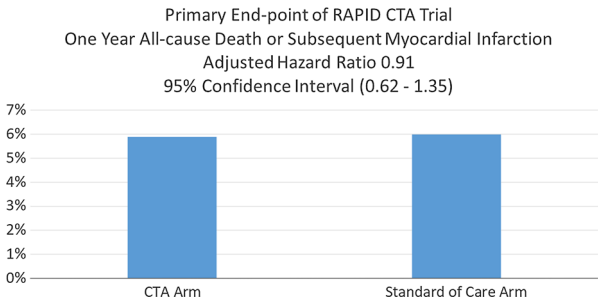

Figure 4. No evidence of differences in any of the individual key secondary outcomes relating to all-cause death, or non-fatal myocardial infarction between CCTA and standard of care in intermediate or high-risk patients presenting to the Emergency Department with suspected or provisionally diagnosed acute coronary syndrome. Figure is based on data from Ref. [42].

Another important multicenter study confirmed the added diagnostic value of CT myocardial perfusion imaging over anatomic assessment of coronary stenosis from coronary CT angiography. This was a seven-center study which included 165 patients with suspected CAD.[44] All studies were interpreted in blinded core Labs. For diagnostic accuracy analysis, CCTA showed an area under the curve (AUC) of .81 (95% confidence interval [CI], .73-.86) on the patient level and .80 (95% CI, .76-.84) on the vessel level. Adding dynamic perfusion data to CCTA significantly increased the AUC to .85 (95% CI, .78-.90; $P = .027$) on the patient level and to .84 (95% CI, .80-.87; $P = .002$) on the vessel level. The study confirms that MPI, which can be obtained by multiple imaging modalities including nuclear techniques and magnetic resonance imaging techniques, will add incremental diagnostic value over anatomical measurements from CCTA and enhance the management of patients with suspected or known CAD.

Plaque analysis is becoming an attractive application for CCTA. The REDUCE-IT (Reduction of Cardiovascular Events with Icosapent Ethyl-Intervention Trial) trial showed that icosapent ethyl (IPE) added to statins reduced initial and total CV events by 25% and 30%. EVAPORATE is a sub-study of REDUCE-IT, and is a randomized, placebo-controlled trial using CCTA to evaluate the effects of IPE as an adjunct to statins on coronary plaque volumes in a cohort with elevated triglycerides.[45] A total of 68 patients completed the 18-month visit. Eicosapentaenoic Acid levels > 26 μg/mL predicted regression of fibro-fatty plaque (logβ: − .75 ± .36), total non-calcified plaque (TNCP) (logβ: − .77 ± .33), and total plaque (TP) (logβ: − .63 ± .28) volumes (mm^3), after adjustment for confounders.

Cardiac CT is also being used for non-coronary applications. A study from the Cleveland clinic evaluated the diagnostic and prognostic value of cardiac CT in patients with confirmed infective endocarditis.[46] The study included 155 consecutive patients with surgically proven infective endocarditis at Cleveland clinic and had contrast-enhanced computed tomography and transesophageal echocardiogram. Cardiac CT and transesophageal echocardiogram were positive in 75% of the patients. The findings on both TEE and cardiac CT predicted outcomes. The presence of pseudoaneurysm or abscess detected by CT and fistula

detected in CT were the only independent predictors of total mortality during follow-up.

Finally, there have been new technological advances in CT technology. The group at Johns Hopkins University evaluated the diagnostic performance of an ultra-high-resolution CT system for the assessment of severe CAD.[47] They included 9 patients, 6 of which has prior coronary stenting who underwent CCTA prior to preplanned invasive angiography. The diagnostic accuracy was 93% on per patient vessel analysis. These are encouraging results in these difficult to image patients with prior stenting or calcifications, but need to be confirmed in studies with a larger sample size and multicenter design.

Disclosure

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