Prognostic Value of Coronary Computed Tomographic Angiography in Comparison With Calcium Scoring and Clinical Risk Scores

Summary: In recent years, coronary computed tomography angiography (CCTA) has emerged as a new noninvasive imaging modality for the detection and in particular exclusion of coronary artery stenosis. In addition, CCTA has the unique advantage of not only depicting the vessel lumen but also the surrounding tissue and has been shown to detect noncalcified plaques. Some studies suggest an incremental value of the detection of these plaques for the prediction of subsequent cardiac events over clinical risk assessment and calcium scoring. In this study of 2223 mostly symptomatic patients undergoing CCTA for diagnostic purposes, the authors confirmed the good prognostic value of CCTA on the basis of findings of plaque and stenosis for major cardiac events, including death, myocardial infarction, and late coronary revascularization over 28 months. Moreover, they demonstrated that these findings are incremental in prediction of major cardiac events when compared with calcium scoring and clinical risk assessment (Morise score). The results of this study suggest that CCTA not only has excellent diagnostic value for the detection of stenosis but also has incremental prognostic value and particularly enables restratification of symptomatic patients at intermediate risk for obstructive coronary artery disease.

Conclusions: In patients with suspected CAD, CCTA not only detects coronary stenosis but also improves prediction of cardiac events over and above conventional risk scores and calcium scoring. This may result in a reclassification of cardiovascular risk in a substantial proportion of patients.1

Features of Disrupted Plaques by Coronary Computed Tomographic Angiography: Correlates With Invasively Proven Complex Lesions

Summary: Coronary computed tomographic angiography (CTA) can accurately detect the presence of coronary atherosclerosis and assess its impact on luminal narrowing. Although CTA also has plaque characterization capabilities, there are only scant data regarding the ability of CTA to delineate features of frank plaque disruption. Given the use of CTA for the evaluation of patients with acute chest pain, identifying features indicative of complex ruptured plaque has considerable clinical implications. This study was designed as a “proof-of-concept” to establish whether CTA has the capability to identify morphological features of plaque disruption and to validate these findings using invasive coronary angiography as the reference standard.

Conclusions: In this highly selected group of patients with unstable angina, CTA can delineate features of plaque disruption, including ulceration and intraplaque dye penetration, which are specific markers of invasively identified complex plaque. Further studies are needed to confirm the generalizability of the results and to explore the clinical and prognostic implications of these findings.2

Bright-Blood T2-Weighted MRI Has Higher Diagnostic Accuracy Than Dark-Blood Short Tau Inversion Recovery MRI for Detection of Acute Myocardial Infarction and for Assessment of the Ischemic Area at Risk and Myocardial Salvage

Summary: T2-weighted MRI has diagnostic and clinical utility for detecting myocardial edema in patients with known or suspected acute myocardial infarction. T2-weighted MRI also enables estimation of the ischemic area at risk and myocardial salvage in patients with acute myocardial infarction. The T2-weighted MRI method that is most widely used is dark-blood short tau inversion recovery (STIR). However, dark-blood STIR is prone to artifacts from motion, subendocardial blood stasis, and technical issues with scan timing or surface coil sensitivity. All of these problems with dark-blood STIR may contribute to diagnostic uncertainty with this method. Based on recent technical developments, an alternative bright-blood T2-weighted MRI approach has emerged. Therefore, the authors compared the diagnostic accuracy of a new bright-blood T2-weighted MRI method with standard dark-blood STIR in patients with acute myocardial infarction. They found that compared with dark-blood STIR, bright-blood T2-weighted MRI was associated with higher consensus agreements between observers for identification of myocardial edema and a higher rate of detection of the culprit coronary artery. The dark-blood method also underestimated the area at risk compared with infarct size. The results support the use of bright-blood T2-weighted MRI instead of STIR for the assessment of myocardial edema.

Conclusions: Bright-blood T2-weighted MRI has higher diagnostic accuracy than dark-blood T2-weighted MRI. Additionally, dark-blood T2-weighted MRI may underestimate area at risk and myocardial salvage.3
Dynamic Changes of Edema and Late Gadolinium Enhancement After Acute Myocardial Infarction and Their Relationship to Functional Recovery and Salvage Index

Summary: Late gadolinium enhancement (LGE) and edema imaging are used to assess acute myocardial injury, area at risk, and salvaged myocardium after reperfusion. LGE is currently considered the gold standard for myocardial infarct visualization both in acute and chronic myocardial infarction and an accurate predictor of recovery of wall motion after revascularization. The present study shows that cardiac magnetic resonance features of acute myocardial infarction are dynamic and change for both LGE and edema. After revascularization, edema is shown to peak within the first week after reperfusion. LGE performed in the first 24 hours does not necessarily indicate irreversible injury; these results show that 51% of the segments with transmural LGE at 24 hours after reperfusion recovered function at 6 months. A detailed knowledge of the early dynamic changes of both LGE and edema imaging is crucial in assessing final infarct size and myocardium salvage, especially when designing clinical trials using cardiac magnetic resonance.

Conclusions: Myocardial edema is maximal and constant over the first week after myocardial infarction, providing a stable window for the retrospective evaluation of area at risk. By contrast, myocardial areas with high signal intensity in LGE images recede over time with corresponding recovery of function, indicating that acutely detected LGE does not necessarily equate with irreversible injury and may severely underestimate salvaged myocardium.

Prognostic Value and Determinants of a Hypointense Infarct Core in T2-Weighted Cardiac Magnetic Resonance in Acute Reperfused ST-Elevation–Myocardial Infarction

Summary: CMR can provide a wide range of prognostic information in acute STEMI by detecting infarct size, MO, and myocardial salvage. Additionally, a hypointense core of infarcted myocardium in T2-weighted CMR has been used as a noninvasive marker for IMH. However, the clinical significance of such findings has not yet been established. The present study is the largest study thus far to assess determinants and the prognostic significance of hypointense infarct cores in T2-weighted CMR. A hypointense core within the AAR of reperfused infarcted myocardium in T2-weighted CMR is a frequent finding in reperfused STEMI patients and is closely related to infarct size, impaired LV function, and late MO. Moreover, hypointense infarct cores are a strong indicator of MACE at 6-month clinical follow-up and may serve as a new CMR marker of severe reperfusion injury. However, further validation is necessary to conclusively ascertain the relationship between hypointense infarct cores and IMH, and large, multicenter studies are warranted to further investigate the prognostic significance of hypointense infarct cores.

Conclusions: A hypointense infarct core within the area at risk of reperfused infarcted myocardium in T2-weighted CMR is closely related to infarct size, microvascular obstruction, and impaired left ventricular function, with subsequent adverse clinical outcome.

Incremental Prognostic Value of Cardiac Computed Tomography in Coronary Artery Disease Using CONFIRM: COrony Computed Tomography Angiography Evaluation for Clinical Outcomes: An InteRnational Multicenter Registry

Summary: The prognostic value of cardiac computed tomographic angiography has been demonstrated in single center studies; however, large multicenter studies validating the prognostic value of CCTA and LVEF are lacking. Using a large international multicenter registry (CONFIRM Registry) of 27,125 patients, the authors sought to confirm the independent and incremental prognostic value of coronary artery disease (CAD) severity measured using 64-slice CT over left ventricular ejection fraction (LVEF) and clinical variables. Multivariable analysis of 14,064 patients, confirmed that LVEF≤50% (hazard ratio, 2.74 [2.12–3.51]) and CAD severity (hazard ratio, 1.58; 95% confidence interval, 1.42–1.76) were predictors of all-cause mortality and CAD severity had incremental value over LVEF and clinical variables.

Conclusions: The results demonstrate that CCTA measures of CAD severity and LVEF have independent prognostic value. Incorporation of CAD severity provides incremental value for predicting all-cause death over routine clinical predictors and LVEF in patients with suspected obstructive CAD.

Development and Validation of a Predictive Screening Tool for Uninterpretable Coronary CT Angiography Results

Summary: Coronary CT angiography (CCTA) is a versatile technique that has evolved rapidly. At the same time, understanding the strengths and weaknesses of this new diagnostic test are prerequisites to ensuring appropriate use of this technology. In clinical practice, CCTA results often are inconclusive or nondiagnostic secondary to poor image quality because of patient characteristics, such as obesity, arhythmias, older age, and diabetes. In this study, the authors examined CCTA data sets from a large multisite registry for patient factors that predict increased risk of uninterpretable CCTA study results. Based on these data, the authors created a tool to predict the likelihood of obtaining an uninterpretable CCTA scan result, which may provide guidance in the appropriate selection of patients for CCTA.

Conclusions: The URS can categorize patients who are likely to have at least 1 uninterpretable major coronary segment on CCTA. This may aid in appropriate patient selection for CCTA and avoiding radiation exposure in those likely to have an uninterpretable study.

Prognostic Value of Routine Cardiac Magnetic Resonance Assessment of Left Ventricular Ejection Fraction and Myocardial Damage: An International, Multicenter Study

Summary: Cardiac magnetic resonance (CMR) is considered the reference standard for assessment of left ventricular ejection fraction (LVEF) and myocardial damage. However, few studies have evaluated the relationship between CMR findings and patient outcome, and of these, most are small and none multicenter. The authors performed an international, multicenter study to assess the prognostic importance of routine CMR in patients with known or suspected heart disease. Consecutive patients from 10 centers in 6 countries who underwent routine CMR assessment of LVEF and myocardial damage by cine- and delayed-enhancement CMR, respectively, were screened. A total of 1560 patients were enrolled (age, 59±14 years; 70% men). Mean LVEF was 45±18%, and 1049 (67%) patients had hyperenhanced tissue on delayed-enhancement CMR indicative of damage. During a median follow-up time of 2.4 years, 176 (11.3%) patients died. Patients who died were more likely to be older, have coronary artery disease, have lower LVEF, and have more segments with hyperenhanced tissue. In multivariable analysis, age, LVEF, and number of segments with hyperenhanced tissue were independent predictors of mortality. The number of segments with hyperenhanced tissue provided incremental prognostic value beyond clinical data and LVEF. Even in patients with near-normal LVEF, significant damage identifies a cohort at high risk for early mortality. In this study, the authors demonstrated that in a large population from several CMR...
centers, unique CMR information on myocardial damage from ischemic and nonischemic etiologies provides independent and incremental prognostic value.

Conclusions: Both LVEF and amount of myocardial damage as assessed by routine CMR are independent predictors of all-cause mortality. Even in patients with near-normal LVEF, significant damage identifies a cohort with a high risk for early mortality.8

Thin-Cap Fibroatheroma as High-Risk Plaque for Microvascular Obstruction in Patients With Acute Coronary Syndrome

Summary: Thin-cap fibroatheroma (TCFA) is characterized as a plaque with a large necrotic core with an overlying thin fibrous cap (<65 μm) infiltrated by macrophages. Even though the importance of TCFA on prediction of future acute coronary syndrome (ACS) events is well recognized from previous pathological studies, this knowledge cannot be readily extended to patients without adequate intravascular devices for assessing thin fibrous cap. Even though optical coherence tomography has been introduced as a high spatial resolution imaging modality that allows for the detailed assessment of atherosclerotic plaques including TCFA, the treatment of TCFA is not yet established. In this study, the authors found that stenting for TCFA was more frequently associated with microvascular obstruction (MVO) assessed by MRI in patients with ACS (ruptured plaque, 27% versus nonrupture with TCFA, 43% versus non-TCFA and nonrupture, 9%; P=0.012). Furthermore, the prevalence of MVO increases as cap thickness decreases. These results suggest that percutaneous coronary intervention for TCFA could easily disrupt thin fibrous caps and squeeze out the contents of the necrotic core to coronary flow. TCFA should be recognized as vulnerable plaque not only for epicardial coronary occlusion but also for MVO in patients with ACS.

Conclusions: TCFA is more frequently associated with MVO after PCI. TCFA is a high-risk plaque for MVO after PCI in patients with ACS.9

Clinical Value of Absolute Quantification of Myocardial Perfusion With 15O-Water in Coronary Artery Disease

Summary: The standard interpretation of perfusion imaging is based on the assessment of relative perfusion defects. This approach has limitations, particularly in the detection of multivessel disease and microvascular dysfunction. Using PET, it is possible to overcome these handicaps by measuring myocardial blood flow in absolute terms. The authors investigated 104 patients with a moderate (30% to 70%) pretest likelihood of coronary artery disease. The patients underwent PET during adenosine stress using15O-water and dynamic imaging. Absolute myocardial blood flow was calculated from which both standard relative uptake images and images exhibiting quantitative myocardial blood flow were produced. The patients and the main vessel regions then were classified as normal or abnormal and compared against the reference of conventional angiography with fractional flow reserve. In patient-based analysis, the positive predictive value, negative predictive value, and accuracy of quantitative blood flow in the detection of obstructive coronary artery disease were 86%, 97%, and 92%, respectively. The corresponding values with relative uptake analysis were 61%, 83%, and 73%, respectively. In region-based analysis, the receiver operating characteristic curves confirmed that the absolute quantification was superior to relative assessment. In particular, the specificity and positive predictive value were low using just relative differences in flow. Only 9 of 24 patients with 3-vessel disease were correctly assessed using relative analysis. The measurement of myocardial blood flow in absolute terms has a significant clinical impact on the interpretation of myocardial perfusion. As expected, multivessel disease is more accurately detected.10

Conclusions: The measurement of myocardial blood flow in absolute terms has a significant impact on the interpretation of myocardial perfusion. As expected, multivessel disease is more accurately detected.10

Pulmonary Vascular Resistance as Assessed by Bicycle Stress Echocardiography in Patients With Atrial Septal Defect Type Secundum

Summary: By measuring pulmonary artery pressures and cardiac output during bicycle stress echocardiography, a pulmonary artery pressure (PAP)-flow relationship can be constructed for each patient. The slope of the PAP-flow plot represents the response of the pulmonary vasculature to increased flow and may identify patients with altered pulmonary hemodynamics which would have been missed at rest. This study showed steeper PAP-flow plots in patients with an atrial septal defect closed later in life, indicating that longstanding volume overload of the pulmonary circulation causes subclinical pulmonary vascular lesions with a decrease in cross-sectional area of the pulmonary vessels. The relation between the slope of the PAP-flow plot and peak oxygen consumption raises the question whether lowering the slope of the PAP-flow plot would increase exercise capacity in these patients.

Conclusions: In patients with an open ASD, the slope of PAP-flow was higher and total PVR did not change from rest to peak exercise. In patients with an ASD closed later in life, the slope of PAP-flow was higher and total PVR did not change from rest to peak exercise, indicating altered pulmonary hemodynamics in these patients.11

Echocardiographic Evaluation Before Bidirectional Glenn Operation in Functional Single-Ventricle Heart Disease: Comparison to Catheter Angiography

Summary: There has been increasing interest in noninvasive evaluation alone in patients with single-ventricle circulation before undergoing bidirectional Glenn operation. The authors studied the ability of echocardiography to visualize and assess the relevant vascular anatomy in this patient population. Echocardiography was found to perform poorly compared with catheter angiography. The branch pulmonary arteries were successfully imaged by echocardiography in under two-thirds of patients, and the majority of pulmonary artery stenoses found at catheterization were not visualized by echocardiography. The aortic arch was imaged more readily by echocardiography, with the majority of arch obstructions identified. Sedation did not appear to improve the performance of echocardiography for assessment of the pulmonary arteries. Given the clinical importance of identification and treatment of obstructions to pulmonary blood flow in the single ventricle circulation, the authors conclude that echocardiography alone before bidirectional Glenn operation is insufficient to image the relevant vascular anatomy.

Conclusions: In a large cohort of patients presenting for BDG, evaluation by echocardiography frequently failed to image the PAs and missed the majority of PA stenoses. Sedation did not appear to improve the performance of echocardiography for evaluation of the PAs. Echocardiography cannot be relied on as the sole investigation before BDG.12

Impact of Gender and Age on Cardiovascular Function Late After Repair of Tetralogy of Fallot: Percentiles Based on Cardiac Magnetic Resonance

Summary: Knowledge of range and distribution of biventricular size, function, and mass is crucial for individual assessment by cardiac magnetic resonance after repair of tetralogy of Fallot. This study demonstrated
significant gender differences in a large, contemporary cohort of children and adults aged 8 to 59 years. Biventricular volumes and mass were significantly larger in male patients, whereas biventricular ejection fraction was higher in female patients; timing and mode of repair and postrepair pulmonary regurgitation fraction was not different between genders. Sex-specific reference percentiles, established for the age range from 8 to 40 years, suggest that the time course of changes in ventricular function and mass may significantly differ from those seen in healthy subjects, certainly for the right ventricle, but also for the less-affected left ventricle. These data suggest that ignoring gender may result in female patients experiencing relatively more severe ventricular dilatation (eg, when planning pulmonary valve replacement). Gender- and age-specific volumetric cardiac magnetic resonance reference data are needed to plan individual follow-up and to design future longitudinal outcome studies.

Conclusions: Significant gender differences of biventricular volumes, function, and mass by CMR exist late after repair of TOF, suggesting that age and gender cannot be ignored when discussing thresholds. Gender-specific percentiles may present a more relevant framework of reference for an individual patient at a given age and suggest a gradual decline of biventricular systolic function over time.13

Cardiac Magnetic Resonance Imaging for Noninvasive Assessment of Cardiovascular Disease During the Follow-Up of Patients With Kawasaki Disease

Summary: Kawasaki disease (KD) was first reported 40 years ago in Japan and is the most important cause of acquired heart disease in childhood. This acute pediatric vasculitis is associated with the development of coronary artery aneurysms that may cause myocardial ischemia and infarction at a young age. In 2004, the American Heart Association published guidelines for the follow-up of patients with KD. Echocardiography is recommended for routine coronary artery surveillance, but it can only visualize the proximal coronary arteries and becomes progressively more difficult as a child grows. Coronary artery lesions, therefore, can be missed when relying on echocardiography only. According to the guidelines, nuclear stress testing and conventional coronary angiography are advised for patients with KD with persistent coronary artery aneurysms but carry risks associated with radiation exposure and the invasive nature of angiography. Cardiac magnetic resonance is a noninvasive and radiation-free imaging modality that overcomes these disadvantages. The present study applied a comprehensive cardiac magnetic resonance protocol during the follow-up of 63 patients with KD aged ≥8 years to detect coronary artery aneurysms, reversible ischemia, and myocardial infarction, all in 1 procedure. The results support cardiac magnetic resonance as a safe and informative imaging modality to identify coronary artery aneurysms (including lesions missed by prior echocardiography), ischemia, and myocardial infarction in a single imaging procedure. As a safe, noninvasive, and radiation-free imaging method for coronary artery surveillance, cardiac magnetic resonance warrants consideration for incorporation in future guidelines for long-term follow-up of patients with KD.15

Conclusions: A comprehensive CMRI protocol including adenosine stress testing is feasible to identify coronary artery pathology, ischemia, and myocardial infarction in former patients with KD and compares favorably with echocardiography. CMRI may be used as a noninvasive and radiation-free imaging method for coronary artery surveillance during the long-term follow-up of patients with KD.14

Right Ventricular Injury in ST-Elevation Myocardial Infarction: Risk Stratification by Visualization of Wall Motion, Edema, and Delayed-Enhancement Cardiac Magnetic Resonance

Summary: Cardiac magnetic resonance (CMR) is a useful tool to evaluate left ventricular myocardial damage after reperfused ST-elevation myocardial infarction. It provides detailed prognostic information by visualizing edema, infarct size, and microvascular obstruction. Recently, CMR has also been introduced for detection of right ventricular injury (RVI); however, the prognostic significance of such findings has not yet been established. RVI is typically detected by echocardiography and/or ECG, but wall motion impairment of the inferior RV wall is difficult to visualize in echocardiography, and ECG changes of RVI may be transient. This work demonstrates the value of CMR value for not only diagnosis but also prognosis in demonstrating and quantifying RVI after ST-elevation myocardial infarction. Similar to the left ventricle, myocardial salvage index can be calculated for the RV. RVI is a strong indicator for major adverse cardiac events when no complete RV myocardial salvage is achieved after angioplasty.

Conclusions: RVI detected by cardiac magnetic resonance is a strong and independent predictor of clinical outcome after acute reperfused STEMI.15

Sex Differences in Myocardial Salvage and Clinical Outcome in Patients With Acute Reperfused ST-Elevation Myocardial Infarction: Advances in Cardiovascular Imaging

Summary: Studies have highlighted important sex differences in the pathophysiology, presentation, treatment, and outcome of ischemic heart disease. It has been also speculated that the efficacy (myocardial salvage) of primary percutaneous coronary intervention (PCI) in high-risk patients with ST-elevation myocardial infarction (STEMI) appears to be sex-dependent. Whether sex disparities in clinical care and death after STEMI are still present in the current PCI era remains a matter of constant debate and has important clinical implications. In this study, the authors analyzed the relationship between sex and outcomes as well as sex and myocardial salvage in an unscreened and consecutive population of patients with STEMI exclusively reperfused by primary PCI. This study is the first using cardiac MRI for assessment of sex-specific reperfusion therapy efficacy. The authors observed no sex-associated differences in myocardial salvage and reperfusion injury. Although women STEMI patients had higher unadjusted in-hospital and 30-day mortality rates than did men, multivariate analysis revealed that these differences were likely because of disparities in baseline risk. Thus, these data highlight that sex by itself, in the current PCI era, does not independently predict death after STEMI and that once women are referred for cardiac catheterization, revascularization practices, success, and complications are similar to those in men.

Conclusions: The efficacy of primary percutaneous coronary intervention (myocardial salvage) in patients with STEMI is not sex dependent. Although women STEMI patients had worse unadjusted in-hospital and 30-day clinical outcomes than did men, multivariate analysis revealed that the observed sex-based differences in early death after STEMI were likely related to differences in baseline risk and clinical characteristics.16


Summary: Although both coronary CT angiography (CTA) and exercise treadmill testing (ETT) can be used to evaluate low- to intermediate-risk patients, there is a paucity of studies that directly compare these tests in patients with acute chest pain. The goal of this study was to examine how data from ETT can identify patients who have
coronary plaque or stenosis, using CTA as the reference standard. In addition, the authors were interested in identifying patient characteristics that could be used in selecting between ETT and CTA. In keeping with prior work and supporting the poor correlation of coronary anatomy and myocardial ischemia, the authors observed that the ETT results had a low sensitivity to identify the presence of coronary artery stenosis. However, interestingly, the specificity was high, in part reflecting the absence of posttest referral bias in this cohort. The authors also observed that the ETT results were not useful for excluding the presence of coronary atherosclerosis as even among individuals who achieved 13 metabolic equivalents, 21% had plaque. In the study, coronary stenosis was not present among men <40 years old or women <50 years old or individuals who achieved at least 13 metabolic equivalents on ETT. Therefore, younger individuals or those who were expected to have a high exercise capacity may benefit from initial ETT testing instead of CTA. On the other hand, testing with CTA or myocardial perfusion imaging may be considered for patients who are older or who have multiple risk factors.

Conclusions: Among low- to intermediate-risk patients with acute chest pain, a positive ETT has a limited specificity but high sensitivity for the detection of >50% stenosis by CTA. Although patients with a high number of clinical risk factors are more likely to have obstructive coronary artery disease, those who are young or who would be expected to have a very high exercise capacity are unlikely to have coronary stenosis and therefore may benefit from initial ETT testing instead of CTA.
all-cause mortality and provided incremental prognostic value over other well-established clinical and ECG predictors. Therefore, these findings underscore that LV GLS assessed with 2D speckle-tracking echocardiography may be used as a novel index of LV longitudinal function and also as a predictor of all-cause mortality in patients with chronic ischemic cardiomyopathy.

**Conclusions:** The assessment of LV GLS with speckle-tracking echocardiography is significantly related to long-term outcome in patients with chronic ischemic cardiomyopathy.21

**Nonculprit Plaques in Patients With Acute Coronary Syndromes Have More Vulnerable Features Compared With Those With Non–Acute Coronary Syndromes: A 3-Vessel Optical Coherence Tomography Study**

**Summary:** Patients with acute coronary syndrome (ACS) have a higher rate of recurrent ischemic events. Although it has been speculated that nonculprit plaques in ACS patients would have higher levels of plaque vulnerability, this concept has not been proven due to the lack of diagnostic modality. In the current study, an attempt was made to prove this hypothesis in vivo, using a high-resolution intravascular imaging modality: optical coherence tomography. Indeed, nonculprit lesions in the ACS subjects, as compared with non-ACS, have features consistent with plaque vulnerability: larger lipid volume, thinner fibrous cap, and a higher prevalence of thin-cap fibroatheroma, thrombus, macrophage, and superficial microvessels. This study supports the concept that ACS is a pan-vascular process with a higher prevalence of vulnerable plaques in nonculprit sites, which explains the higher recurrent ischemic events. Therefore, a more aggressive plaque stabilizing treatment such as cholesterol lowering and/or anti-inflammatory therapy may have additional value in ACS patients.

**Conclusions:** Nonculprit lesions in patients with ACS have more vulnerable plaque characteristics compared with those with non-ACS. Neovascularization was more frequently located close to the lumen in patients with ACS.22

**Prediction of Arrhythmic Events in Ischemic and Dilated Cardiomyopathy Patients Referred for Implantable Cardiac Defibrillator: Evaluation of Multiple Scar Quantification Measures for Late Gadolinium Enhancement Magnetic Resonance Imaging**

**Summary:** Scar signal quantification on late gadolinium enhancement myocardial magnetic resonance has been proposed to have use for the prediction of arrhythmic events in patients with ischemic cardiomyopathy eligible for implantable cardiac defibrillators (ICD). For this noninvasive tool to have widespread clinical value it would ideally be applicable to ischemic and nonischemic referral populations, predict highly relevant clinical outcomes (such as appropriate ICD therapy, resuscitated cardiac arrest, and sudden cardiac death), and demonstrate associations independent of other validated risk markers, such as ejection fraction. In the current study of 124 consecutively referred patients, the authors demonstrate that total scar burden by signal quantification is a reproducible imaging biomarker that appears to meet these desired criteria. While being sensitive to distinct thresholds for ischemic and nonischemic subcohorts, the quantification of total scar burden identifies patients at an elevated risk of future arrhythmic events. These findings support a need for the expanded investigation of this imaging modality to identify patients most likely to benefit from ICD implantation.

**Conclusions:** Myocardial scar quantification by LGE-CMR predicts arrhythmic events in patients being evaluated for ICD eligibility irrespective of cardiomyopathy etiology.23

**Characterizing Myocardial Edema and Hemorrhage Using Quantitative T2 and T2* Mapping at Multiple Time Intervals Post ST-Segment Elevation Myocardial Infarction**

**Summary:** Cardiovascular MRI has gained clinical importance in the noninvasive assessment of myocardial injury parameters including myocardial edema, hemorrhage, microvascular obstruction, and infarct size post acute myocardial infarction. The authors prospectively characterized the evolution of these parameters post reperfused acute myocardial infarction at both early and late time points. They noted that edema is still present in infarcted tissue at 3 weeks, whereas hemorrhage resolves faster. Noninfarcted segments can demonstrate edema in the acute phase as well, perhaps indicative of more severe myocardial injury. The presence of hemorrhage in the acute phase makes edema quantification challenging due to susceptibility effects. In addition, both hemorrhage and microvascular obstruction are associated with worse left ventricular remodeling. Gaining this knowledge about the temporal resolution of myocardial damage and its impact on remodeling processes using quantitative techniques is potentially important in grading severity, evaluating treatment strategies, and improving clinical outcomes.

**Conclusions:** Quantification of myocardial edema and hemorrhage by T2 and T2* mapping is feasible post acute myocardial infarction and demonstrates that hemorrhage resolves faster than edema. Noninfarcted segments can also demonstrate edema in the acute phase possibly due to global hyperemia.24

**Diagnostic Accuracy of Cardiac Positron Emission Tomography Versus Single Photon Emission Computed Tomography for Coronary Artery Disease: A Bivariate Meta-Analysis**

**Summary:** Positron emission tomography (PET) and single photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI) are both established techniques for noninvasively diagnosing coronary artery disease. PET MPI has technical benefits in detecting sensitivity and spatial resolution compared with SPECT MPI and may also allow diagnostic imaging with lower radiation exposure. Clinical differences in diagnostic accuracy remain under investigation. A literature search of English-language studies yielded 117 diagnostic accuracy studies of MPI for detecting 50% angiographic coronary stenosis but only 5 direct comparisons of PET and SPECT. These were systematically reviewed and scored for methodological quality before meta-analysis using techniques designed for analyzing the relationship between sensitivity and specificity. Both PET and SPECT MPI were more commonly performed after pharmacological, as opposed to exercise, stress. Pooled specificity was higher for PET MPI at 92.6% compared with 88.3% for SPECT MPI. Pooled specificity was lower, without a clear difference between PET and SPECT MPI. Type of stress (exercise or pharmacological) and differences in radiotracer used did not seem to affect diagnostic accuracy. More research, especially in head-to-head comparisons, will be needed to identify patient groups most likely to benefit from PET MPI.

**Conclusions:** In a meta-analysis of 11,862 patients, PET MPI demonstrated a higher sensitivity for coronary artery disease than SPECT MPI. No difference in specificity was detected in the pooled analysis of PET and SPECT MPI.25
Prognostic Impact of Hyperglycemia in Nondiabetic and Diabetic Patients With ST-Elevation Myocardial Infarction: Insights From Contrast-Enhanced Magnetic Resonance Imaging

Summary: Previous studies have suggested that hyperglycemia on admission is a risk factor for increased mortality in patients with acute ST-elevation myocardial infarction (STEMI). However, data regarding the relationship between hyperglycemia and myocardial damage in STEMI are scarce. This largest cardiac magnetic resonance study to date evaluating the relationship of diabetes mellitus status and elevated glucose levels on admission on myocardial damage in STEMI patients reperfused by primary percutaneous coronary intervention has 2 essential findings: (1) STEMI patients with preexisting diabetes mellitus are at greater risk for major adverse cardiovascular events despite having similar infarct sizes and extent of reperfusion injury than patients without known diabetes mellitus. (2) Elevated glucose levels on admission are associated with greater myocardial damage (larger infarcts, more pronounced reperfusion injury, left ventricular dysfunction) and an increased risk of clinical events at long-term follow-up. However, hyperglycemia was a stronger indicator of myocardial injury in STEMI patients without previously recognized diabetes mellitus than in those with established diabetes mellitus. Thus, this study confirms and expands previous findings by demonstrating that the amount of myocardial injury does not explain the substantially higher mortality rates in diabetic patients with STEMI. Moreover, the authors could demonstrate that the relationship between hyperglycemia and myocardial damage is different in STEMI patients with and without known diabetes mellitus.

Conclusions: The higher mortality rate in diabetic versus nondiabetic STEMI patients is not explained by more pronounced myocardial damage. Hyperglycemia on admission is associated with greater myocardial injury and an increased risk of major adverse cardiovascular events at long-term follow-up. However, hyperglycemia has a stronger relationship to myocardial injury in nondiabetic compared with diabetic patients.

Systemic-to-Pulmonary Collateral Flow, as Measured by Cardiac Magnetic Resonance Imaging, Is Associated With Acute Post-Fontan Clinical Outcomes

Summary: Systemic-pulmonary collateral (SPC) flow is a well-recognized phenomenon in single ventricle patients after superior cavo-pulmonary connection. The clinical impact of these vessels following Fontan completion is not clear. The authors have recently described a novel method of quantifying SPC flow by cardiac magnetic resonance (CMR) imaging using phase-contrast velocity mapping techniques. They retrospectively reviewed the acute post-Fontan clinical course of 44 patients who had their burden of SPC flow quantified by CMR imaging prior to Fontan completion. Overall, these patients had a mean SPC flow volume of 1.5±0.9 L/min/m², which comprised 31±11% of total aortic flow and 44±15% of total pulmonary venous flow. The authors found significant linear associations between increasing amounts of SPC flow and duration of chest tube and hospitalization after Fontan. After adjusting for Fontan type and the presence of a fenestration, there was an increased odds of both prolonged chest tube duration and prolonged hospitalization, based on increasing amounts of all measures of SPC flow. It is unclear from these data whether the presence of SPC flow is the primary driver of a more complicated post-Fontan course, or whether the presence of SPC flow is a marker of underlying unfavorable anatomy or physiology. Future prospective study is needed to better understand the “natural” history of SPC flow in single ventricle patients through the staged surgical pathway, and to examine the efficacy and durability of catheter-based embolization on SPC flow and its effects on longer-term clinical outcomes.

Conclusions: Increasing SPC flow before Fontan, as measured by CMR imaging, is associated with increased duration of hospitalization and chest tube following Fontan completion.

Quantifying Pulmonary Regurgitation and Right Ventricular Function in Surgically Repaired Tetralogy of Fallot: A Comparative Analysis of Echocardiography and Magnetic Resonance Imaging

Summary: Patients with tetralogy of Fallot represent a growing population of congenital heart disease. Clinicians seek to quantify pulmonary regurgitation and right ventricular function over successive appointments in patients with TOF to identify those in need of intervention or pulmonary valve replacement. To date, though echocardiography is the most valuable tool, it has fallen short in consistent quantification of pulmonary regurgitation and right ventricular function. In this study, the authors describe an echocardiographic tool with which to assess pulmonary regurgitation in tetralogy of Fallot that only modestly correlates with measurements made by cardiac magnetic resonance. In addition, echocardiographic measures of right ventricular function showed limited performance when compared with those derived from cardiac magnetic resonance. Although these echo measures still fall short of the reliability set by CMR for decision making, these results help motivate ongoing investigative efforts to improve echocardiographic assessment of the postoperative patient with tetralogy of Fallot.

Conclusions: This study suggests that the diastolic and systolic time-velocity integrals ratio may make a modest contribution to the overall assessment of PR in patients with repaired tetralogy of Fallot and warrants further investigation. However, echocardiography continues to have a limited ability to quantify PR and RV function as compared with CMR.

Ascending Aortic and Main Pulmonary Artery Areas Derived From Cardiovascular Magnetic Resonance as Reference Values for Normal Subjects and Repaired Tetralogy of Fallot

Summary: Ascending aorta and main pulmonary artery cross-sectional areas can be measured reproducibly in children and young adults using cardiovascular MRI. Great vessel sizes measured this way increase predictably with body surface area in both normal hearts and repaired tetralogy of Fallot, but great arterial growth characteristics in tetralogy are remarkably different from normal. Aortic growth out of proportion to normal is seen in tetralogy after repair and may be a hazard for some of these patients in the long term. For them, cardiovascular magnetic resonance could play an important role in early identification of disproportionate aortic dilation. In this series, male sex, pulmonary valve atresia, and previous surgical palliations emerged as predictors for larger ascending aorta areas in tetralogy. These factors may have implications for risk stratification and surveillance strategies in this population. The main pulmonary artery in repaired tetralogy, although smaller, on an average, than normal controls, is not small to the same extent as the aorta is large. Percentile charts for expected great vessel areas as a function of body surface area in normal subjects and in surgically modified tetralogy were generated for clinical reference.
Conclusions: This study provides cardiac magnetic resonance reference Z scores for great vessel areas in normal children and adolescents in comparison with a large contemporary cohort of repaired TOF. Male sex, pulmonary atresia, and previous palliations emerged as predictors for larger AO dimensions in TOF. 29

Cardiac Allograft Function During the First Year after Transplantation in Rejection-Free Children and Young Adults

Summary: Heart transplantation (HT) is an established therapy in children with end-stage heart failure. Although severe early graft dysfunction after HT is rare, mild ventricular dysfunction is common even without rejection and may persist for years. Pulsed-wave tissue Doppler imaging (PW-TDI) is geometry-independent and allows quantification of both left ventricular and right ventricular (RV) function during systole and diastole. In this study, the authors analyzed serially performed PW-TDI studies in 44 pediatric HT recipients (median age at transplant 7.3 years) who remained rejection-free during the first year post-transplant to investigate the natural history of recovery of ventricular function. The authors used data from PW-TDI studies in 380 healthy children to transform patient data into age-adjusted z scores to allow better interpretation of raw PW-TDI data in the study children. They found biventricular systolic and diastolic dysfunction early after HT with most significant impairment in RV systolic function and RV and LV early-diastolic filling. Although other aspects of left ventricular and RV function normalized in 6 to 9 months, RV systolic function remained abnormal 1 year-post-transplant. Serial cardiac catheterization studies showed that RV and left ventricular filling pressures were elevated early after HT and declined gradually during the first year. These findings provide important insights into the natural history of recovery of biventricular function in pediatric HT recipients and improve our understanding of RV dysfunction in these patients. The authors suggest that a better understanding of ventricular function in rejection-free patients may also help in developing a PW-TDI-based rejection-surveillance protocol in pediatric HT recipients.

Conclusions: Pediatric HT recipients have biventricular dysfunction using pulsed-wave tissue Doppler imaging early after HT with most significant impairment in RV systolic function and RV and LV early-diastolic filling. Although other aspects of LV and RV function normalize in 6 to 9 months, RV systolic function remains abnormal 1 year-post-transplant. 30

Trabeculated (Noncompacted) and Compact Myocardium in Adults: The Multi-Ethnic Study of Atherosclerosis

Summary: Diagnosis of left ventricular noncompaction cardiomyopathy remains challenging in daily practice. Using standard morphological cardiac MRI criteria of trabeculated and compacted myocardium (T/M ratio) of >2.3, overdiagnosis of left ventricular noncompaction cardiomyopathy has been suggested. The present study evaluated T/M ratio in a large population-based cohort of 1000 subjects; 323 of these subjects were free of cardiac disease. In the subset of individuals free of cardiac disease, 43% of subjects had at least 1 region with T/M ratio >2.3. This suggests that T/M ratio alone for left ventricular noncompaction cardiomyopathy diagnosis may have low specificity. Measurement of T/M ratio varied using different imaging planes (long axis versus short axis), indicating a standardized measurement is needed. T/M ratio did not vary with age, sex, ethnicity, height, or weight; therefore, no adjustment to these demographic parameters is required.

Conclusions: A ratio of T/M of >2.3 is common in a large population-based cohort. These results suggest re-evaluation of the current cardiac MR criteria for left ventricular noncompaction may be necessary. 31

Interplay of Coronary Artery Calcification and Traditional Risk Factors for the Prediction of All-Cause Mortality in Asymptomatic Individuals

Summary: Current guidelines recommend the use of coronary artery calcium (CAC) scoring for select intermediate-risk patients. In the present study, the authors followed 44052 consecutive asymptomatic individuals for a median of 5 years. Subjects without risk factors (obtained from patients) but elevated CAC had a significantly higher event rate than individuals with multiple risk factors but no CAC. Conversely, the absence of CAC was associated with a favorable prognosis even among those with multiple risk factors. These findings suggest a potential benefit of CAC over traditional risk assessment to tailor primary prevention therapy. However, further studies based on prospectively collected and quantitative data on risk factors are needed to determine whether CAC in the absence of risk factors enable more effective treatment and reduce overall healthcare costs.

Conclusions: By highlighting that individuals without RFs but elevated CAC have a substantially higher event rates than those who have multiple RFs but no CAC, these findings challenge the exclusive use of traditional risk assessment algorithms for guiding the intensity of primary prevention therapies. 32

Normal Left Ventricular Myocardial Thickness for Middle-Aged and Older Subjects With Steady-State Free Precession Cardiac Magnetic Resonance: The Multi-Ethnic Study of Atherosclerosis

Summary: Left ventricular myocardial thickness is altered in certain cardiomyopathies. In some conditions, such as hypertrophic cardiomyopathy, left ventricular myocardial thickness is the major imaging factor used in establishing the presence or absence of disease. In this study, the authors determined that normal myocardial thickness varies with myocardial region/segment. In addition, the image acquisition plane may affect measurement of myocardial wall thickness. This study provides normal left ventricular myocardial thickness by region/segment as measured in both the short and long axis acquisition planes. These results indicate that gender-specific cutoffs that vary by myocardial region/segment may be defined to help establish the presence or absence of disease. In addition, body size, ethnicity, and left ventricular function affect left ventricular myocardial thickness measurements.

Conclusions: Normal values for wall thickness are provided for middle-aged and older subjects. Normal LVMT is lower for women than men. Observed values vary depending on the imaging plane for measurement. 33

Appropriate Use Criteria For Stress Single-Photon Emission Computed Tomography Sestamibi Studies: A Quality Improvement Project

Summary: In a previous study, the authors reported the application of the published American College of Cardiology Foundation appropriate use criteria for stress single-photon emission computed tomography (SPECT) imaging to patients at Mayo Clinic
(Rochester, MN) in 2005 and 2006. This study reports the results of a subsequent internal quality improvement project focused on physician education, including a presentation at Medical Grand Rounds, a publication in the staff newsletter, meetings with physician administrators, and focused presentations to pertinent department/divisions of ordering physicians. Remeasurement of the appropriateness of SPECT studies was then performed using previously published methods. Unfortunately, the rate of inappropriate SPECT studies did not decrease as hoped but in fact showed a borderline increase (P=0.06). Thus, this quality improvement project did not achieve the desired reduction in the rate of inappropriate stress SPECT studies in a single academic medical center.

Conclusions: This quality improvement project, focused on feedback, physician education, and remeasurement, did not reduce the rate of inappropriate stress SPECT studies in a single academic medical center. Similar limited interventions focused on physician education alone may have limited benefit. More extensive intervention may be necessary to improve the quality of care with appropriateness criteria.34

Incremental Prognostic Significance of Combined Cardiac Magnetic Resonance Imaging, Adenosine Stress Perfusion, Delayed Enhancement, and Left Ventricular Function Over Preimaging Information for the Prediction of Adverse Events

Summary: Cardiac MRI (CMR) is unique in its ability to provide assessment of hemodynamics, ventricular structure and function, valvular structure and function, myocardial viability, and stress perfusion. Various CMR-derived data are known to provide important prognostic information. However, the relative incremental prognostic value of 4 CMR components (vasodilator stress perfusion, myocardial delayed enhancement, aortic blood flow, and left ventricular volumes) is unclear. The authors followed up 908 patients for a mean of 2.6±1.2 years after they underwent combined 4-component CMR for suspicion of coronary stenosis and/or ischemia. In total, 101 cardiac events were observed, including 30 cardiac deaths, 36 noncardiac deaths, 5 nonfatal myocardial infarctions, and 19 late revascularizations. Normal 4-component CMR was followed by a 2.4% annual cardiac event rate (±0.4% for cardiac death) whereas abnormal CMR had an event rate of 5.6% to 7.0%. The risk of cardiac events increased significantly with increasing number of abnormal CMR components. After the authors adjusted for pre-CMR data, the addition of left ventricular ejection fraction, aortic flow, delayed enhancement, and stress perfusion data all added incremental prognostic power. CMR components were additive, not redundant, in predicting risk. Future studies may define how each CMR component is best applied in clinical practice.

Conclusions: CMR analysis of ventricular volume, aortic flow, myocardial viability, and stress perfusion all add incremental value for prediction of adverse events over pre-CMR data and can be combined to further enhance prognostication. Normal combined CMR confers a low risk of subsequent cardiac events.35

Role of Cardiovascular Magnetic Resonance as a Gatekeeper to Invasive Coronary Angiography in Patients Presenting With Heart Failure of Unknown Etiology

Summary: Identifying the underlying etiology in patients with new onset heart failure and no overt features of underlying coronary artery disease, eg angina, can be challenging. Invasive coronary angiography (CA) carries tangible risks and does not provide tissue characterization. In this prospective study of 120 patients (powered to display noninferiority), late gadolinium enhanced cardiovascular magnetic resonance (LGE-CMR) showed equivalence to CA when determined against a gold standard consensus panel who considered data from all the investigations. Diagnoses ascribed by LGE-CMR and CA were also validated against clinical outcomes at a median of 3.7 years. LGE-CMR is ideally placed as a gatekeeper to CA because it is safer, uniquely provides biventricular function and tissue characterization data, and is economically viable. LGE-CMR and CA were equivalent in diagnostic accuracy (97% versus 95%) and the data suggests that 73% of patients would have appropriately avoided CA, being spared the risks and costs of this investigation. Importantly, no patient with prognostically important coronary artery disease would have been denied CA and any subsequent revascularization as LGE-CMR had a negative predictive value of 100%. The data also suggests the need for a paradigm shift in the classification of patients with heart failure to reflect not just coronary anatomy, but also myocardial tissue characterization. This study therefore challenges the traditional dichotomy of ischemic versus nonischemic cardiomyopathy by revealing subgroups of patients with features of both ischemic and nonischemic etiologies.

Conclusions: This study showed that LGE-CMR is a safe, clinically effective, and potentially economical gatekeeper to CA in patients presenting with heart failure of uncertain etiology.36

Myocardial Structure, Function, and Scar in Patients With Type 1 Diabetes Mellitus

Summary: Type 1 diabetes mellitus is associated with a relatively high prevalence of cardiovascular disease and clinical and silent myocardial infarction compared with the nondiabetic population, leading to alterations in cardiac structure and function. In the present study, the authors evaluated the relationship of cardiovascular disease risk factors, including hemoglobin A1c levels and diabetic nephropathy, to myocardial structure, function, and scar by cardiac MRI in 1017 patients of the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications (DCCT/EDIC) study. The DCCT/EDIC study is the first large-scale cohort of patients with type 1 diabetes mellitus. Patients had a mean clinical evaluation period of 22 years preceding cardiac magnetic resonance. The authors found that macroalbuminuria and mean hemoglobin A1c (over ≥22 years of follow-up) were significant risk factors for alterations in left ventricular structure and function and for having myocardial scar. The prevalence of myocardial scar by cardiac magnetic resonance was 4.3% compared with only 1.4% in patients with clinically recognized myocardial infarction. The concordance of scar and clinical history was relatively low. These findings suggest that modifiable cardiovascular disease risk factors and glycemic control play a significant role in relationship to cardiovascular morbidity and mortality in patients with type 1 diabetes mellitus.

Conclusions: In addition to traditional cardiovascular disease risk factors, elevated mean hemoglobin A1c and macroalbuminuria were significantly associated with alterations in left ventricular structure and function. The prevalence of myocardial scar was 4.3% in this subcohort of DCCT/EDIC participants with relatively preserved renal function.37

Improved Cardiac Risk Assessment With Noninvasive Measures of Coronary Flow Reserve

Summary: Quantitative estimates of myocardial blood flow and coronary flow reserve integrate the fluid dynamic effects of epicardial
Atherosclerosis and microvascular function. The present study demonstrates that coronary flow reserve improves stratification of risk of cardiac and all-cause mortality beyond clinical risk factors, left ventricular ejection fraction, extent of myocardial ischemia and scar, and stress-induced left ventricular ejection fraction augmentation. Patients with coronary flow reserve <1.5 were at 5.6-fold increased risk of cardiac mortality compared with those with coronary flow reserve ≥2.0. Among patients whose clinical risk factors, left ventricular ejection fraction, and stress imaging findings placed them at intermediate risk of cardiac death (1% to 3% per year), 35% were reclassified as either high risk (>3% cardiac mortality per year) or low risk (<1% cardiac mortality per year). These findings demonstrate that incorporation of coronary vasodilator function assessment into stress testing by quantification of coronary flow reserve improves risk stratification in patients with known or suspected coronary artery disease.

Conclusions: Noninvasive quantitative assessment of coronary vasodilator function with positron emission tomography is a powerful, independent predictor of cardiac mortality in patients with known or suspected coronary artery disease and provides meaningful incremental risk stratification over clinical and gated myocardial perfusion imaging variables.38

Performance of the Traditional Age, Sex, and Angina Typicality–Based Approach for Estimating Pretest Probability of Angiographically Significant Coronary Artery Disease in Patients Undergoing Coronary Computed Tomographic Angiography: Results From the Multinational Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry (CONFIRM)

Summary: During the initial evaluation of a patient with chest pain, many clinicians use the age, sex, and angina typicality–based pretest probabilities currently cited in professional society practice guidelines (guideline probabilities) to direct decisions for subsequent diagnostic testing and treatment. However, guideline probabilities were derived from patients clinically referred to invasive angiography and have not been validated in patients undergoing noninvasive testing. In this multinational study, the investigators analyzed the performance of guideline probabilities in 14048 consecutive patients, including 8106 patients with chest pain, referred for coronary computed tomographic angiography. Computed tomographic angiography was used to determine the presence of angiographically significant coronary artery disease. In patients with chest pain, guideline probabilities significantly overstated the overall prevalence of ≥50% diameter stenotic coronary artery disease (51% versus 18% observed by computed tomographic angiography) and ≥70% diameter stenotic coronary artery disease (42% versus 10%). Overestimation was particularly pronounced in patients with atypical angina and typical angina across all sex, age, and risk factor subgroups. The large differences between observed and predicted disease prevalence persisted in sensitivity analyses adjusted for potential inaccuracies of coronary computed tomographic angiography. Results from this study illustrate a major limitation in the practice of applying disease prevalence derived from invasive coronary angiography to populations undergoing initial noninvasive evaluation for coronary artery disease and highlight the need for updating probabilities of angiographically significant coronary artery disease in such populations.

Conclusions: In this multinational study of patients referred for coronary computed tomographic angiography, determination of pretest likelihood of angiographically significant CAD by the invasive angiography-based guideline probabilities greatly overestimates the actual prevalence of disease.39

Coronary Computed Tomographic Angiography and Risk of All-Cause Mortality and Nonfatal Myocardial Infarction in Subjects Without Chest Pain Syndrome From the CONFIRM Registry (Coronary CT Angiography Evaluation for Clinical Outcomes: An International Multicenter Registry)

Summary: This is the first registry analysis to evaluate the additive contribution of coronary computed tomographic angiography (cCTA)–defined coronary artery disease compared with clinical risk factors and coronary artery calcium score in a large international multicenter cohort of individuals without chest pain syndrome. Although the overall prevalence of obstructive coronary artery disease was generally low, the authors’ prognostic models revealed an independent prediction of cCTA-defined coronary artery disease for incident mortality and the composite outcome of all-cause mortality and nonfatal myocardial infarction. However, the ability of these findings to improve risk stratification for the prediction of all-cause mortality beyond information derived from coronary artery calcium score was not observed. cCTA offered minimal statistical improvement in risk prediction and reclassification for a composite end point of death and myocardial infarction. Given the ability of cCTA to identify atherosclerotic plaque components beyond calcified plaque, including fibrous, fibrolipoid, and lipid plaque, future studies examining these plaque characteristics in asymptomatic individuals undergoing cCTA and coronary artery calcium score may be useful to further investigate the present study findings.

Conclusions: Although the prognosis for individuals without CPS is stratified by cCTA, the additional risk-predictive advantage by cCTA is not clinically meaningful compared with a risk model based on CACS. Therefore, at present, the application of cCTA for risk assessment of individuals without CPS should not be justified.40

Prognostic Value of High-Dose Dipyridamole Stress Myocardial Contrast Perfusion Echocardiography

Summary: Dipyridamole real-time contrast echocardiography (DipRCE) has considerable advantages over other imaging stress-tests, including no irradiation, spatial and temporal resolution, short test duration, immediate availability of results at the bedside, and the ability to perform stress and rest images in the same setting. The addition of myocardial perfusion (MP) imaging over standard wall motion (WM) analysis during DipRCE improves the sensitivity to detect coronary artery disease (CAD), but its risk reclassification potential to predict hard cardiac events in large numbers of patients with known or suspected CAD remains unknown. The authors studied 1252 patients with DipRCE and followed them for a median of 25 months. A total of 59 hard events (4.7%) occurred during the follow up (24 deaths, 35 myocardial infarctions). Reversible MP defects added incremental prognostic value and risk reclassification benefit to predict hard events, after adjustment for clinical data, ejection fraction, and WM analysis. A normal MP response during DipRCE identified a low-risk patient group (close to 1% yearly hard event rate) with a better outcome than patients with a normal WM but abnormal MP response. An ischemic WM response, which was always accompanied by MP defects, predicted the highest risk of hard events. Patients with a normal MP response can be reassured regarding their low risk of future 1 or 2-year hard events, regardless of their clinical risk factors or previous CAD history. MP should not simply substitute...
WM analysis during DipyRCE, but the 2 variables are complementary and may have different clinical implications for the cardiologist.

**Conclusions:** MP imaging using real-time perfusion echocardiography during dipyridamole real-time contrast echocardiography provides independent, incremental prognostic information regarding hard cardiac events in patients with known or suspected coronary artery disease. Patients with normal MP responses have better outcome than patients with normal WM; patients with both reversible WM and MP abnormalities have the worst outcome.41

**Association Between Coronary Vascular Dysfunction and Cardiac Mortality in Patients With and Without Diabetes Mellitus**

**Summary:** Patients with diabetes mellitus are at increased risk of adverse cardiac events even in the absence of overt myocardial ischemia or scar compared with patients without diabetes mellitus. Coronary flow reserve (CFR) is a quantitative measure of coronary vascular dysfunction, which is an early manifestation of coronary artery disease. CFR can be measured noninvasively with positron emission tomography. The present study establishes that CFR is associated with increased rates of cardiac mortality among both diabetics and nondiabetics and results in similar improvement in risk discrimination and reclassification for both cohorts. In both cases, ≥1 in 3 patients has a clinically relevant change in assessed risk based on CFR, even after accounting for clinical risk factors and traditional stress imaging findings. Intriguingly, diabetic patients without known coronary artery disease with visually normal stress tests but impaired CFR experience a 2.8%/y cardiac mortality rate, comparable to that for patients with known coronary artery disease (2.0%/y). Conversely, diabetic patients without known coronary artery disease and visually normal stress tests who have preserved CFR experience cardiac mortality rates comparable to those of nondiabetic patients free of coronary artery disease with normal stress imaging findings (0.3%/y versus 0.5%/y, respectively). These findings offer important insights into the mechanism of increased cardiac risk among diabetics and the classification of diabetes mellitus as a cardiac risk equivalent.

**Conclusions:** Coronary vasodilator dysfunction is a powerful, independent correlate of cardiac mortality among both diabetics and nondiabetics and provides meaningful incremental risk stratification. Among diabetic patients without CAD, those with impaired CFR have event rates comparable to those of patients with prior CAD, whereas those with preserved CFR have event rates comparable to those of nondiabetics.42

**Computed Tomography Coronary Angiography in Patients With Acute Myocardial Infarction Without Significant Coronary Stenosis**

**Summary:** Almost 10% of patients with acute myocardial infarction have normal or nonsignificant coronary stenosis at coronary angiography. The absence of critical stenosis may challenge the diagnosis, however atherosclerosis may be present also in angiographically nondiagnostic angiography. The extent of left ventricular scar quantified by late gadolinium enhancement cardiac magnetic resonance has been shown to predict overall mortality in patients with coronary artery disease independently of LV ejection fraction. In the present study, 64 consecutive patients (average age, 66±11 years; male sex, 51) with coronary artery disease who had undergone late gadolinium enhancement cardiac magnetic resonance imaging (LGE-CMR) can accurately and reproducibly identify areas of myocardial scar, and the amount of left ventricular scar burden. The primary end point was appropriate ICD therapy (as a surrogate for sudden cardiac death). During a mean follow-up period of 19 months, 19 (30%) patients received appropriate ICD therapy. In an analysis including clinical, biochemical, and CMR variables, the number of transmural scar segments had the strongest association with the occurrence of appropriate ICD therapy. Furthermore, the burden of ventricular arrhythmias was significantly associated with scar burden.

**Conclusions:** CTCA detects coronary plaques in nonstenotic coronary arteries that are underestimated by CA, and identifies a different distribution of plaque types in IRAs and non-IRAs. It may therefore be valuable for diagnosing coronary atherosclerosis in acute myocardial infarction patients without significant coronary stenosis.43

**Echocardiographic Predictors of Outcome in Eisenmenger Syndrome**

**Summary:** Although echocardiography provides accurate information on cardiac anatomy and physiology, as well as prognosis data in patients with idiopathic pulmonary arterial hypertension, only few data exist on the prognostic power of echocardiographic parameters in adults with Eisenmenger syndrome, which was the subject of this study. These data from a single center on a large contemporary cohort of adults with Eisenmenger syndrome showed that echocardiographic indices of right ventricular function (tricuspid annular plane systolic excursion, ratio of right ventricular effective systolic to diastolic duration) and right atrial area are predictive of mortality, assessed either alone or even more so in a composite score. Because the assessment of functional class remains difficult, especially in patients with congenital heart disease, the authors believe that this score may be used in the risk stratification of Eisenmenger patients and could influence the decision to initiate or escalate therapy.

**Conclusions:** Echocardiographic parameters of right ventricular function and RA area predict mortality in Eisenmenger patients. A new composite echocardiographic score, described herewith, may be incorporated into the noninvasive, periodic assessment of these patients.44

**The Extent of Left Ventricular Scar Quantified by Late Gadolinium Enhancement MRI Is Associated With Spontaneous Ventricular Arrhythmias in Patients With Coronary Artery Disease and Implantable Cardioverter-Defibrillators**

**Summary:** The identification of patients at high risk for sudden cardiac death remains a challenge in the application of implantable cardioverter-defibrillator (ICD) therapy. Late gadolinium enhancement cardiac MR can accurately and reproducibly identify areas of myocardial scar, and the amount of left ventricular scar quantified by LGE-CMR has been shown to predict overall mortality in patients with coronary artery disease independently of LV ejection fraction. In the present study, 64 consecutive patients (average age, 66±11 years; male sex, 51) with coronary artery disease who had undergone LGE-CMR before receiving an ICD were studied. The extent of left ventricular scar on LGE-CMR was characterized in terms of percent scar, scar surface area, and number of transmural scar segments. The primary end point was appropriate ICD therapy (as a surrogate for sudden cardiac death). During a mean follow-up period of 19 months, 19 (30%) patients received appropriate ICD therapy. In an analysis including clinical, biochemical, and CMR variables, the number of transmural scar segments had the strongest association with the occurrence of appropriate ICD therapy. Furthermore, the burden of ventricular arrhythmias was significantly associated with scar burden.

**Conclusions:** In this pilot study, the extent of myocardial scar characterized by LGE-CMR was significantly associated with the occurrence of spontaneous ventricular arrhythmias. The authors hypothesize that scar quantification by LGE-CMR may prove a valuable risk stratification tool for the occurrence of ventricular arrhythmias, which may have implications for patient selection for ICD therapy.45
Validation of Intravascular Ultrasound–Derived Parameters With Fractional Flow Reserve for Assessment of Coronary Stenosis Severity

Summary: The authors assessed optimal intravascular ultrasound (IVUS) criteria for predicting functional significance of intermediate coronary lesions. Overall, 201 patients with 236 coronary lesions underwent IVUS and invasive physiological assessment preintervention. Fractional flow reserve (FFR) was measured at maximal hyperemia induced by intravenous adenosine infusion. FFR < 0.80 at maximum hyperemia was seen in 49 (21%) of the overall 236 lesions. The independent determinants of FFR were minimal lumen area (MLA; β = 0.020; 95% confidence interval [CI], 0.008–0.031; P < 0.002), plaque burden (β = −0.003; 95% CI, −0.003 to 0.001; P = 0.001), lesion length with a lumen area < 3.0 mm² (β = −0.003; 95% CI, −0.005 to −0.001; P < 0.005), and LAD location (β = −0.035; 95% CI, −0.055 to −0.016; P = 0.001). The best cutoff value (with a maximal accuracy) of the MLA to predict FFR < 0.80 was < 2.4 mm² with a diagnostic accuracy of 68% (90% sensitivity, 62% specificity, and area under the curve = 0.756; 95% CI, 0.696–0.810; P < 0.001). Among 117 lesions with an MLA ≥ 2.4 mm², 112 (96%) had an FFR ≥ 0.80, and all but 1 showed FFR ≥ 0.75. Conversely, 44 (37%) lesions with an MLA < 2.4 mm² had an FFR < 0.80. IVUS-derived MLA ≥ 2.2 mm² may be useful to exclude FFR < 0.80, but poor specificity limits its value for physiological assessment of lesions with MLA < 2.4 mm². Thus, FFR or some other functional assessment may be necessary to accurately identify ischemia-inducible intermediate stenoses.

Conclusions: IVUS-derived MLA ≥ 2.4 mm² may be useful to exclude FFR < 0.80, but poor specificity limits its value for physiological assessment of lesions with MLA < 2.4 mm². Thus, FFR or stress tests may be necessary to accurately identify ischemia-inducible intermediate stenoses.

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