Bibliographic Cite	PMID Link	Literature Type	Level of Evidence	Purpose	Population	Intervention and Outcome Measures	Results/ Recommendations	Study Limitiations
Buckert D, Witzel S, Steinacker JM, et al. Comparing cardiac magnetic resonance-guided versus angiography-guided treatment of patients with stable coronary artery disease: Results from a prospective randomized controlled trial. JACC Cardiovasc Imaging. 2018; 11(7):987-996.	29976305	Prospective, single-center, multi-reader	moderate	The prospective and randomized evaluation of cardiovascular endpoints and quality of life in patients with stable coronary artery disease comparing a cardiac magnetic resonance (CMR)-based management strategy with a coronary angiography-based approach.	Patients presenting to the outpatient clinic of a single institution for the evaluation of symptoms indicating stable symptomatic CAD (e.g., exercise-related angina pectoris or dyspnea) were considered eligible and consecutively screened for enrollment. Patients had to be at intermediate to high CAD risk. Exclusion criteria were unstable angina pectoris, cardiac or respiratory instability, contraindication to CMR, age <18 years, and inability to give written informed consent.	Patients with symptomatic CAD were randomized to diagnostic coronary angiography (group 1) or adenosine stress CMR (group 2). The primary endpoint was the composite of cardiac death and nonfatal myocardial infarction. Quality of life was assessed using the Seattle Angina Questionnaire at baseline and during follow-up. All CMR images were analyzed by 2 readers in consensus. To avoid bias, readers were blinded to initial clinical assessment and the results of other examinations (e.g., treadmill testing).Follow-up information was gathered annually after enrollment by outpatient clinic visits and by telephone interviews of patients and their general practitioners.	Two hundred patients were enrolled. In group 1, 45 revascularizations (45.9%) were performed. In group 2, 27 patients (28.1%) were referred to revascularization because of ischemia on CMR. At 12-month follow-up, 7 primary events occurred: 3 in group 1 (event rate 3.1%) and 4 in group 2 (event rate 4.2%), with no statistically significant difference (p = 0.72). Within the next 2 years, 6 additional events could be observed, giving 4 events in group 1 and 9 events in group 2 (event rate 4.1% vs. 9.4%; p = 0.25). Group 2 showed significant quality-of-life improvement after 1 year in comparison to group 1. The authors conclude that a CMR-based management strategy for patients with stable coronary artery disease was safe, reduced revascularization procedures, and resulted in better quality of life at 12-month follow-up, though noninferiority could not be proved. Optimal timing for reassessment remains to be investigated.	There was a small but significant difference concerning physical limitation, treatment satisfaction, and quality of life in favor of the CMR group after 12 months of follow-up. This finding supports the appropriateness of stress perfusion CMR in patient management. Nevertheless, the differences in quality of life were not sustained during longer term follow-up. This finding might be consistent with the observation that more endpoints occurred and revascularization procedures were performed in this period. Further studies focusing on long-term management of patients with stable CAD on the basis of symptoms and already performed diagnostic and therapeutic interventions thus are warranted.
Budoff MJ, Li D, Kazerooni EA, et al. Diagnostic accuracy of noninvasive 64-row computed tomographic coronary angiography (CCTA) compared with myocardial perfusion imaging (MPI): The PICTURE study, a prospective multicenter trial. Acad Radiol. 2017; 24(1):22-29.	27771227	Prospective, multi-center, multi-reader	moderate	To evaluate the diagnostic accuracy of 64-row CCTA to detect obstructive coronary stenosis compared to myocardial perfusion imaging (MPI), using quantitative coronary angiography (QCA) as a reference standard.	Individuals were eligible for participation in the PICTURE trial if they were ≥18 years of age, experienced typical or atypical chest pain, and were being referred for nuclear testing for evaluation of their chest pain. Individuals were excluded from participation in the PICTURE trial for the following reasons: known allergy to iodinated contrast; baseline renal insufficiency (creatinine ≥1.7 mg/dL); irregular cardiac rhythm; resting heart rate >100 beats perminute; resting systolic blood pressure <100 mmHg; contraindication to beta blocker, calcium channel blocker, or nitroglycerin; pregnancy; or known history of CAD (prior myocardial infarction, percutaneous transluminal coronary angioplasty or intracoronary stent, or coronary artery bypass surgery). All patients had to undergo both MPI and CCTA prior to ICA to be enrolled.	Twelve sites prospectively enrolled 230 patients (49% male, 57.8 years) with chest pain. All patients underwent MPI and CCTA (Lightspeed VCT/Visipaque 320, GE Healthcare, Milwaukee, WI, USA) prior to invasive coronary angiography (ICA). All patients were evaluated, and those found to have either an abnormal MPI or CCTA were clinically referred for ICA. CCTAs were graded on a 15-segment American Heart Association model by three blinded readers for presence of obstructive stenosis (>50% or >70%); MPI was graded by two blinded readers using a 17 segment model for estimation of the % myocardium ischemic or with stress defects. ICAs were independently graded for % stenosis by QCA. The efficacies of MPI and CCTA were assessed including all vessel segments for per-patient and per-vessel analyses.	The prevalence of stenosis ≥50% by ICA was 52.1% (25 of 48). The sensitivity of CCTA was significantly higher than nuclear imaging (92.0% vs 54.5%, P < 0.001), with similar specificity (87.0% vs 78.3%) when obstructive disease was defined as ≥50%. CCTA provided superior sensitivity (92.6% vs 59.3%, P < 0.001) and similar specificity (88.9% vs 81.5%) using QCA stenosis ≥70%. For ≥50% stenosis, the computed tomographic angiography odds ratio for ICA disease was 51.75 (95% CI = 8.50–314.94, P < 0.001). For summed stress score ≥5%, the odds ratio for ICA CAD was 12.73 (95% CI = 2.43–66.55, P < 0.001). Using receiver operating characteristic curve analysis, CCTA was better at classifying obstructive coronary artery disease when compared to MPI (area = 0.85 vs 0.71, P < 0.0001). The authors conclude that this study represents one of the first prospective multicenter, controlled clinical trials comparing 64-row CCTA to MPI in the same patients, demonstrating superior diagnostic accuracy of CCTA over myocardial perfusion single photon emission computed tomography (MPS) to reliably detect >50% and >70% stenosis in stable chest pain patients.	The major limitation of the current study is the final number of patients who underwent invasive angiography. When the study was conceived, it was anticipated that 50% of participants would ultimately require invasive angiography, but only 21% required the said procedure, limiting the sample size to compare diagnostic accuracy, and introducing verification bias. A further limitation is the use of thallium/technetium increase the radiation dose and may affect diagnostic accuracy.
Danand I, Raijmakers PG, Driessen RS, et al. Comparison of coronary CT angiography, SPECT, PET, and hybrid imaging for diagnosis of ischemic heart disease determined by fractional flow reserve. JAMA Cardiol. 2017; 2(10):1100-1107.	28813561	Prospective, single-center, single-reader	low	To establish the diagnostic accuracy of CCTA, SPECT, and PET and explore the incremental value of hybrid imaging compared with fractional flow reserve.	A total of 1,598 patients were assessed for eligibility. Of these, 1,390 were excluded, primarily for previous revascularization (n = 925), workup for aortic valve replacement (n = 121), or previous cardiac imaging (n = 106). A total of 208 patients were included in the study.	This prospective clinical study included 208 patients with suspected CAD who underwent CCTA, technetium 99m/tetrofosmin–labeled SPECT, and [15O]H2O PET with examination of all coronary arteries by fractional flow reserve, and was performed from January 23, 2012, to October 25, 2014. Scans were interpreted by core laboratories on an intention-to-diagnose basis. Hybrid images were generated in case of abnormal noninvasive anatomical or functional test results. Main outcome was hemodynamically significant stenosis in at least 1 coronary artery as indicated by a fractional flow reserve of 0.80 or less and relative diagnostic accuracy of SPECT, PET, and CCTA in detecting hemodynamically significant CAD.	Of the 208 patients in the study (76 women and 132 men; mean [SD] age, 58 [9] years), 92 (44.2%) had significant CAD (fractional flow reserve 0.80). Sensitivity was 90% (95%CI, 82%-95%) for CCTA, 57% (95%CI, 46%-67%) for SPECT, and 87% (95%CI, 78%-93%) for PET, whereas specificity was 60% (95%CI, 51%-69%) for CCTA, 94% (95%CI, 88%-98%) for SPECT, and 84% (95%CI, 75%-89%) for PET. Single-photon emission tomography was found to be noninferior to PET in terms of specificity (P < .001) but not in terms of sensitivity (P > .99) using the predefined absolute margin of 10%. Diagnostic accuracy was highest for PET (85%; 95%CI, 80%-90%) compared with that of CCTA (74%; 95%CI, 67%-79%; P = .003) and SPECT (77%; 95%CI, 71%-83%; P = .02). Diagnostic accuracy was not enhanced by either hybrid SPECT and CCTA (76%; 95%CI, 70%-82%; P = .75) or by PET and CCTA (84%; 95%CI, 79%-89%; P = .82), but resulted in an increase in specificity (P = .004) at the cost of a decrease in sensitivity (P = .001). The authors conclude that this controlled clinical head-to-head comparative study revealed PET to exhibit the highest accuracy for diagnosis of myocardial ischemia. Furthermore, a combined anatomical and functional assessment does not add incremental diagnostic value but guides clinical decision-making in an unsalutary fashion.	This study was powered for noninferiority testing of SPECT comparedwith PET, whereas secondary end points of hybrid imaging should be interpreted with caution given the limited sample size. The prevalence of disease in this study was generally higher than reported in other trials of the diagnostic accuracy of noninvasive imaging to detect CAD; these results should be interpreted in the context of this particular patient population.

Dedic A, Kate GJ, Roos CJ, et al. Prognostic value of coronary computed tomography imaging in patients at high risk without symptoms of coronary artery disease. Am J Cardiol. 2016; 117(5):768-774.	26754124	Prospective / retrospective, multi-center, single-reader	low	To determine the prognostic value of coronary computed tomography (CT) angiography (CCTA) next to the coronary artery calcium score (CACS) in patients at high CVD risk without symptoms suspect for coronary artery disease (CAD).	Eligible patients (aged between 45 and 70 years) were those clinically referred to the outpatient clinics of 2 academic hospitals by general practitioners or other physicians for optimized cardiovascular management and primary prevention according to current guidelines. Exclusion criteria included a history of CAD, renal dysfunction (serum creatinine >120 mmol/L), contrast allergy, irregular heart rhythm, severe chronic obstructive pulmonary disease, or known pregnancy.	Image acquisition was performed on multidetector row CT scanners with 64 rows. Detection of coronary artery calcium was performed using an electrocardiogram-triggered axial scan and measured using the Agatston method. Patients were stratified in groups according to the extent of coronary artery calcification: 0, 1 to 100, 101 to 400, and >400 CACS. CCTA was performed during a single inspiration using an electrocardiogram-triggered axial scan with X-ray tube current modulation and tube voltage reduction when clinically feasible. Stenosis grade was visually classified either as <29%, 30–49%, 50–69%, ≥70% luminal narrowing or occluded. The primary outcome measure was a combination of adverse events including all-cause mortality, nonfatal myocardial infarction (MI), unstable angina, or coronary revascularization beyond 90 days after the index CCTA.	A total of 665 patients at high risk (mean age 56±9 years, 417 men), were included. During a median follow-up of 3.0 (interquartile range 1.3 to 4.1) years, adverse events occurred in 40 subjects (6.0%). By multivariate analysis, adjusted for age, gender, and CACS, obstructive CAD on CCTA (≥50% luminal stenosis) was a significant predictor of adverse events (hazard ratio 5.9 [CI 1.3 to 26.1]). Addition of CCTA to age, gender, plus CACS, increased the C statistic from 0.81 to 0.84 and resulted in a total net reclassification index of 0.19 (p<0.01). The authors conclude that CCTA has incremental prognostic value and risk reclassification benefit beyond CACS in patients without CAD symptoms but with high risk of developing CVD.	First, the rather low adverse event rate requires caution to the interpretation of the predictive power of CCTA. Larger study populations and/or longer follow-up times, expecting to yield higher incidences of adverse events, should provide more robust outcomes. The incorporation of late coronary revascularization in addition to all-cause mortality and nonfatal MI may be a limitation as late revascularization is a less hard outcome. However, by incorporating late coronary revascularization as part of our composite outcome, we attempted to investigate whether CCTA findings are associated with CAD that is prone to progress, causing symptoms and eventually the need for coronary revascularization. Also, late coronary revascularization was incorporated into the composite outcome, as is it is often included as an outcome of other comparable imaging studies focused on prognosis.
Dudum R, Dzaye O, Mirbolouk M et al. Coronary artery calcium scoring in low risk patients with family history of coronary heart disease: Validation of the SCCT guideline approach in the coronary artery calcium consortium. J Cardiovasc Comput Tomogr. 2019; 13(3):21-25.	30935842	Retrospective, multi-center, single-reader	low	To critically assess the unique 2017 Society of Cardiovascular Computed Tomography (SCCT) recommendation of considering coronary artery calcium (CAC) scoring in low risk individuals (< 5%) with a family history (FH) of CHD using the largest multi-center observational cohort study of CAC scoring yet assembled, the CAC Consortium.	Included were asymptomatic participants with a self-reported FH of CHD and ASCVD risk <5% as defined using the 2013 ACC/AHA Pooled Cohort Equation (N=14,169). Patients were referred for CAC scoring by a physician.	The CAC Consortium is a multi-center observational cohort study from four clinical centers linked to long-term follow-up for cause-specific mortality. FH of CHD was generally reported as the presence of a first-degree relative with a history of CHD. Hypertension, dyslipidemia, and diabetes were considered present if a patient reported a prior diagnosis and/or was on therapy with anti-hypertensives, lipid-lowering medications, or oral hypoglycemics or insulin. Smoking status was characterized as “never, former, or current smoker	This cohort had a mean age of 48.1 (SD 7.4), was 91.3% white, 47.4% female, had an average ASCVD score of 2.3% (SD 1.3), and 59.4% had a CAC=0. The event rate for all-cause mortality was 1.2 per 1,000 person-years, 0.3 per 1,000 person-years for CVD-specific mortality, and 0.2 per 1,000 person-years for CHD-specific mortality. In multivariable Cox proportional hazard models, those with CAC>100 had a 2.2 (95% CI 1.5–3.3) higher risk of all-cause mortality, 4.3 (95% CI 1.9–9.5) times higher risk of CVD-specific mortality, and a 10.4 (95% CI 3.2–33.7) times higher risk of CHD-specific mortality compared to individuals with CAC=0. The NNS to detect CAC >100 in this sample was 9. The authors conclude that, in otherwise low risk patients with FH of CHD, CAC>100 were associated with increased risk of all-cause and CHD mortality with event rates in a range that may benefit with preventive pharmacotherapy. These data strongly support new SCCT recommendations regarding testing of patients with a family history of CHD.	This study is an observational, retrospective cohort study of patients referred for clinical CAC scanning, and as such, results may not be generalizable to all patients with FH of CHD because of potential referral bias. Second, the population is predominantly white (91.3%), which limits its generalizability to other ethnic groups. Additionally, the effect of our study is likely to be underestimated as both patients and clinicians were informed about the results of the CAC scan, which may have led to altered treatment decisions and risk factor modification in those with the highest CAC scores.
Heitner JF, Kim RJ, Kim HW, et al. Prognostic value of vasodilator stress cardiac magnetic resonance imaging: A multicenter study with 48,000 patient-years of follow-up. JAMA Cardiol. 2019; 4(3):256-264.	30735566	Retrospective, multi-center, single-reader	low	To determine whether stress cardiac magnetic resonance imaging (CMR) is associated with patient mortality.	Across the 7 participating centers, all consecutive patients undergoing stress CMR with a clinical indication to evaluate myocardial ischemia were included. Of the 9,454 consecutive patients undergoing their first CMR stress test, 303 were missing data for 1 or more cardiac risk factors and were therefore excluded from the primary analysis.Accordingly, the study population consisted of a total of 9151 patients. The 303 excluded patients had a similar incidence of positive / negative stress test results compared with the 9,151 included patients.	This was a multicenter study of patients undergoing clinical evaluation of myocardial ischemia. Patients with known or suspected coronary artery disease (CAD) underwent clinical vasodilator stress CMR at 7 different hospitals. An automated process collected data from the finalized clinical reports, deidentified and aggregated the data, and assessed mortality using the US Social Security Death Index. Main outcome was all-cause patient mortality.	The median (interquartile range) patient age was 63 (51-70) years, and 55% were men. There was a total 48,615 patient-years of follow-up. Of these patients, 4,408 had a normal stress CMR exam, 4,743 had an abnormal exam, and 1,517 died during a median follow-up time of 5.0 years. Using multivariable analysis, addition of stress CMR improved prediction of mortality in 2 different risk models (model 1 hazard ratio [HR], 1.83; 95%CI, 1.63-2.06; P < .001; model 2: HR, 1.80; 95%CI, 1.60-2.03; P < .001) and also improved risk reclassification (net improvement: 11.4%; 95%CI, 7.3-13.6; P < .001). After adjustment for patient age, sex, and cardiac risk factors, Kaplan-Meier survival analysis showed a strong association between an abnormal stress CMR and mortality in all patients (HR, 1.883; 95%CI, 1.680-2.112; P < .001), patients with (HR, 1.955; 95%CI, 1.712-2.233; P < .001) and without (HR, 1.578; 95%CI, 1.235-2.2018; P < .001) a history of CAD, and patients with normal (HR, 1.385; 95%CI, 1.194-1.606; P < .001) and abnormal left ventricular ejection fraction (HR, 1.836; 95%CI, 1.299-2.594; P < .001). The authors conclude that clinical vasodilator stress CMR is associated with patient mortality in a large, diverse population of patients with known or suspected CAD as well as in multiple subpopulations defined by history of CAD and left ventricular ejection fraction.	Several limitations are noted by the authors. Baseline demographics were obtained by local site investigators at the time of the clinical study and were limited to the prespecified variables presented in this article, which do not represent a comprehensive list of all possible prognostic markers and do not account for changes in these variables during the follow-up period. Secondly, information regarding specific cardiovascular outcomes, such as myocardial infarction, sudden death, implantable defibrillator placement, transplantation, or hospitalization, were not available. Follow-up data in this study were limited to the primary end point of all-cause death, and the cause of death was not known. Thus, not all deaths were necessarily owing to cardiac causes. Finally,in this study, authors were unable to determine whether patients were revascularized after the CMR stress test.

Hoffman U, Ferencik M, Udelson JE, et al. Prognostic value of noninvasive cardiovascular testing in patients with stable chest pain: Insights from the PROMISE Trial (prospective multicenter imaging study for evaluation of chest pain). Circulation. 2017; 135(24):2320-2332.	28389572	Prespecified secondary analysis of a prospective randomized trial	moderate	To perform a prespecified secondary analysis of the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain), comparing the prognostic value of an anatomic versus a functional testing strategy in stable symptomatic patients with suspected CAD.	For this analysis, authors included patients who received the initial diagnostic test as randomly assigned. They excluded subjects who received other tests as their first test, did not undergo any diagnostic test, or received noncontrast CTA only. In addition, we excluded patients whose test results could not be assigned to prespecified test strata because of indeterminate test results, including patients who underwent functional testing with exercise but achieved <75% of maximum predicted heart rate.	In the PROMISE trial (Prospective Multicenter Imaging Study for Evaluation of Chest Pain), patients with stable chest pain and intermediate pretest probability for obstructive coronary artery disease (CAD) were randomly assigned to functional testing (exercise electrocardiography, nuclear stress, or stress echocardiography) or coronary computed tomography angiography (CTA). Site-based diagnostic test reports were classified as normal or mildly, moderately, or severely abnormal. The primary end point was death, myocardial infarction, or unstable angina hospitalizations over a median follow-up of 26.1 months.	Both prevalence of normal test results and incidence rate of events in patients were significantly lower among 4,500 patients randomly assigned to CTA in comparison with 4,602 patients randomly assigned to functional testing (33.4% vs 78.0%, and 0.9% vs 2.1%, respectively; both P<0.001). In CTA, 54.0% of events (n=74/137) occurred in patients with nonobstructive CAD (1%–69% stenosis). Prevalence of obstructive CAD and myocardial ischemia was low (11.9% versus 12.7%, respectively), with both findings having similar prognostic value (hazard ratio, 3.74; 95% confidence interval [CI], 2.60–5.39; and 3.47; 95% CI, 2.42–4.99). When test findings were stratified as mildly, moderately, or severely abnormal, hazard ratios for events in comparison with normal tests increased proportionally for CTA (2.94; 7.67–10.13; all P<0.001) but not for corresponding functional testing categories (0.94 [P=0.87], 2.65 [P=0.001], 3.88 [P<0.001]). The discriminatory ability of CTA in predicting events was significantly better than functional testing (c-index, 0.72; 95% CI, 0.68–0.76 versus 0.64; 95% CI, 0.59–0.69; P=0.04). If 2714 patients with at least an intermediate Framingham Risk Score (>10%) who had a normal functional test were reclassified as being mildly abnormal, the discriminatory capacity improved to 0.69 (95% CI, 0.64–0.74).	Although the PROMISE trial was designed to compare 2 fundamentally different approaches to the management of patients with stable chest pain, anatomic versus functional testing, authors acknowledge that the sensitivities, specificities, predictive values, and prognostic values can vary between different functional testing modalities and by age, sex, and other patient characteristics (eg, body mass index). They further acknowledge that the choice of functional test was dictated by physician preferences and patient presentation, and thus will vary by individual clinician choices. It is further important to note that treatments based on imaging results were not accounted for in the analysis, but may have affected the cardiovascular outcomes assessed. The study had a relatively small number of events and a short median follow-up of 26 months. Further, the study excluded patients with abnormal left ventricular function or a history of myocardial infarction, and hence the prognostic value of diagnostic hallmarks of functional testing such as left ventricular function or fixed perfusion defects could not be assessed.
Houssany-Pissot S, Rosencher J, et al. Screening coronary artery disease with computed tomography angiogram should limit normal invasive coronary angiogram, regardless of pretest probability. Am Heart J. 2020; 223:113-119.	32087878	Retrospective, multi-center, single-reader	low	To evaluate, in a real-life setting, the rate of strictly normal invasive coronary angiogram (ICA) following a positive non-invasive test (either functional testing (FT) or computed tomography angiogram (CCTA)).	Included were all patients who underwent an ICA with a prior positive FT or CCTA. A total of 2,513 patients who have had neither functional testing nor CCTA prior to ICA were excluded. This left a final sample of 4,952 patients who underwent ICA following either a positive functional test (3,276) or a positive CCTA (1,676).	Patients were categorized in 5 subgroups, according to pretest probability (PTP) of having a coronary artery disease (CAD). Main results of ICA were defined as normal ICA, non-obstructive CAD (nonoCAD) and obstructive CAD (oCAD). Positive functional testing was defined by ischemia findings during stress or recovery, like patient chest pain, ECG modifications, left ventricle ejection fraction decrease, abnormal cinetic wall motion, and abnormal myocardial perfusion. CCTA findings were deemed positive if coronary artery stenosis ≥ 50% was reported, if the stenosis calcification was classified as severe, or if the coronary artery calcium score considering the Agatston method was too high (i.e. above 400). Based on guidelines recommendations, patients were categorized in one of the 5 PTP following groups: (1) low risk [PTP <15%], (2) lower intermediate risk [PTP 15 to 35%], (3) higher intermediate risk [PTP 35 to 50%], (4) high-risk [PTP 50% to 65%] and (5) very high-risk [PTP > 65%].	For 4952 patients who underwent ICA following either a positive FT (3276, 66.2%) or CCTA (1676, 33.8%), the PTP was: (1) low [< 15%; n=968,19.5%], (2) lower intermediate [15 to 35%; n=1336,27.0%], (3) higher intermediate [35 to 50%; n=806,16.3%], (4) high [50% to 65%; n=806,17.7%], and (5) very high [> 65%; n=965, 19.5%]. ICA showed no CAD (819 patients, 16.5%), non-oCAD (1193 patients, 24.1%) or oCAD (2940 patients, 59.4%). Without considering the PTP values, CCTA compared to FT showed less frequently normal ICA (7% vs. 16.5%), and more frequently CAD (non-oCAD 27.9% vs. 22.2%; oCAD 65.1% vs. 56.4%)(all p<0.0001). When authors considered the different PTP values, CCTA always showed lower rates of normal ICA than the FT. In low and lower intermediate-risk patients, CCTA detected more frequently oCAD compared to FT (p<0.001). The authors conclude that CCTA is a better alternative than FT to limit unnecessary ICA regardless of PTP value, without missing abnormal ICA.	This was a retrospective study. So the comparison between anatomical and functional testing was not based on randomized inclusion. Second, as the study was not randomized, the proportions of each non-invasive functional testing were not equal. However, because the functional testing group were higher risk, the authors note it is even more surprising that CTCA managed to have lower rates of normal angiograms.
Lee H, Yoon YE, Lee W, et al. Prognosis of anatomic coronary artery disease without myocardial ischemia: Coronary computed tomography angiography detects high-risk patients even in cases of negative single-photon emission computed tomography findings. J Cardiol. 2018; 72(2):162-169.	29525542	Retrospective, multi-center, multi-reader	low	To suggest a new risk stratification strategy using CCTA in patients with anatomic CAD but without myocardial ischemia on SPECT.	Consecutive patients (n = 798) with CAD on CCTA who underwent SPECT for evaluation of myocardial ischemia were retrospectively evaluated. The inclusion criteria were as follows: (1) patients with coronary atherosclerotic plaque on CCTA and (2) patients who underwent SPECT for evaluation of the hemodynamic significance of CAD within 90 days from CCTA. Patients were excluded from the study if any of the following was present: (1) prior history of CAD or (2) uninterpretable CCTA images. Consequently, 798 patients were included in the analysis.	The primary outcome was the occurrence of adverse cardiac events, including cardiac death, nonfatal myocardial infarction, unstable angina, and late revascularization. CCTA images were acquired using either a retrospectively electrocardiogram (ECG) gated or prospectively ECG-triggered protocol using a 64-detector row CT scanner. The coronary artery calcium score (CACS) was measured using the Agatston scoring system (in units), and graded as follows: 0, 1–399, and 400. Myocardial SPECT was performed with pharmacologic stress, using technetium-99m tetrofosmin or sestamibi as the radiotracer. Follow-up information was obtained by either clinical visits or telephone interview.	Of the enrolled patients, 542 (68%) showed no perfusion defect (PD) on SPECT. During the follow-up (median, 22.6 months), adverse cardiac events occurred in 23 patients without PD (4.6%). Presence of plaque in ≥ 4 coronary segments, plaque in the left main or proximal left anterior descending coronary artery, and partially calcified plaque presence were independent predictors of adverse events. When authors defined the CCTA score based on these 3 predictors (0–3 points), the annualized event rates increased with increasing CCTA scores. Patients with a CCTA score of 3 were associated with a 23-fold risk increase (adjusted HR 23.18; p = 0.003) and showed unfavorable event-free survival, comparable to those with PD on SPECT (p = 0.191). The authors conclude that anatomic CAD patients without evidence of myocardial ischemia on SPECT but with high risk characteristics on CCTA showed unfavorable outcomes, comparable to those with PD. CCTA allows further risk stratification even in patients with negative SPECT findings.	The subsequent diagnostic tests or therapeutic procedures were not guided by a specific protocol, and might have been influenced by the CCTA results. Secondly, plaque composition was simply classified as non-calcified, partially calcified, or calcified plaque and the plaque characteristics that were known as the rupture-prone plaque – positive remodeling, low attenuation plaque, spotty calcification, or napkin-ring sign – were not included in the study analysis. Lastly, although this is the largest study evaluating prognostic value of CCTA exclusively in patients with anatomic CAD, the effect of aggressive medical treatment in each risk group could not be evaluated, because of the limited number of patients.

Nagel E, Greenwood JP, McCann GP, et al. Magnetic resonance perfusion or fractional flow reserve in coronary disease. N Engl J Med. 2019; 380(25):2418-2428.	31216398	Prospective, multi-center, single-reader	low	To determine whether an initial management strategy to guide revascularization based on myocardial-perfusion cardiovascular MRI would be noninferior to a strategy guided by invasive angiography and FFR in terms of major adverse cardiac events.	Total of 918 patients were enrolled at 16 sites in the United Kingdom, Portugal, Germany, and Australia. Patients ≥ 18 years with typical angina symptoms and either two or more cardiovascular risk factors (smoking, diabetes, hypertension, hyperlipidemia, or a family history of coronary artery disease) or a positive exercise treadmill test were included. Exclusion criteria were contraindications to adenosine myocardial-perfusion cardiovascular MRI, cardiac arrhythmias, a known left ventricular ejection fraction < 30%, class III or IV heart failure, previous CABG, PCI within 6 months, or an estimated glomerular filtration rate of < 30 ml per minute per 1.73 m2 of body surface area.	This was an unblinded, multicenter, clinical effectiveness trial that randomly assigned 918 patients with typical angina and either two or more cardiovascular risk factors or a positive exercise treadmill test to a cardiovascular MRI–based strategy or an FFR-based strategy. Revascularization was recommended for patients in the cardiovascular-MRI group with ischemia in at least 6% of the myocardium or in the FFR group with an FFR of 0.8 or less. The composite primary outcome was death, nonfatal myocardial infarction, or target-vessel revascularization within 1 year. The noninferiority margin was a risk difference of 6 percentage points.	A total of 184 of 454 patients (40.5%) in the cardiovascular-MRI group and 213 of 464 patients (45.9%) in the FFR group met criteria to recommend revascularization (P = 0.11). Fewer patients in the cardiovascular-MRI group than in the FFR group underwent index revascularization (162 [35.7%] vs. 209 [45.0%], P = 0.005). The primary outcome occurred in 15 of 421 patients (3.6%) in the cardiovascular-MRI group and 16 of 430 patients (3.7%) in the FFR group (risk difference, −0.2 percentage points; 95% confidence interval, −2.7 to 2.4), findings that met the noninferiority threshold. The percentage of patients free from angina at 12 months did not differ significantly between the two groups (49.2% in the cardiovascular-MRI group and 43.8% in the FFR group, P = 0.21). The authors conclude that, among patients with stable angina and risk factors for coronary artery disease, myocardial-perfusion cardiovascular MRI was associated with a lower incidence of coronary revascularization than FFR and was noninferior to FFR with respect to major adverse cardiac events.	The most important limitation of the trial is that the incidences of outcome events at 1 year were lower than expected on the basis of data from the FAME trial (which enrolled only patients with documented multivessel disease). As a result, the noninferiority margin was large relative to the incidence of major adverse cardiac events. Thus, noninferiority of cardiovascular MRI would have been shown even if the incidence was twice as high as that in the FFR group. The actual incidences in the two groups, however, were similar. Systematic maximization of antianginal therapy was not performed before screening for enrollment, so patients who might have been asymptomatic after medication adjustment may have been enrolled in the trial. The follow-up period of 1 year may mask some longer-term differences between the strategies. The patient population was primarily male and white. The results cannot be extrapolated to other tests for myocardial ischemia or the functional significance of a coronary artery stenosis because of differences in diagnostic performance as compared with myocardial perfusion cardiovascular MRI.
Patel KK, Badarin F, Chan PS, et al. Randomized comparison of clinical effectiveness of pharmacologic SPECT and PET MPI in symptomatic CAD patients. JACC Cardiovasc Imaging. 2019; 12(9):1821-1831.	31326480	Prospective, single-center, multi-reader	low	To compare the clinical effectiveness of pharmacologic stress myocardial perfusion imaging (MPI) plus positron emission tomography (PET) with single-photon emission computed tomography (SPECT) in patients with known coronary artery disease (CAD) presenting with symptoms suggestive of ischemia.	Patients had a history of CAD and presented with new or worsening symptoms, for whom an MPI test was ordered by the referring physicians and who required pharmacologic stress MPI. Exclusion criteria included renal dysfunction (serum creatinine concentration >2.5 mg/dl), myocardial infarction or coronary revascularization within past 6 months, significant valvular disease, prior transplantation, morbid obesity (body mass index of ≥38 kg/m2), left ventricular ejection fraction (LVEF) <40%, pregnant patients, and patients who were unwilling to undergo angiography if indicated.	Patients with known CAD and suspected ischemia were randomized to undergo PET or attenuation-corrected SPECT MPI between June 2009 and September 2013. Post-test management was at the discretion of the referring physician, and patients were followed for 12 months. The primary endpoint was diagnostic failure, defined as unnecessary angiography (absence of ≥50% stenosis in ≥1 vessel) or additional noninvasive testing within 60 days of the MPI. Secondary endpoints were post-test escalation of antianginal therapy, referral for angiography, coronary revascularization, and health status at 3, 6, and 12 months.	A total of 322 patients with an evaluable MPI were randomized (n = 161 in each group). At baseline, 88.8% of patients were receiving aspirin therapy, 76.7% were taking beta-blockers, and 77.3% were taking statin therapy. Diagnostic failure within 60 days occurred in only 7 patients (2.2%) (3 [1.9%] in the PET group and 4 [2.5%] in the SPECT group; p = 0.70). There were no significant differences between the 2 groups in subsequent rates of coronary angiography, coronary revascularization, or health status at 3, 6, and 12 months of follow-up (all p values ≥0.20); however, when subjects were stratified by findings on MPI in a post hoc analysis, those with high-risk MPI on PET testing had higher rates of angiography and revascularization on follow-up than those who had SPECT MPI, whereas those undergoing low-risk PET studies had lower rates of both procedures than those undergoing SPECT (interaction between randomized modality *high-risk MPI for 12-month catheterization [p = 0.001] and 12-month revascularization [p = 0.09]). The authors conclude that in this cohort of symptomatic CAD patients, there were no discernible differences in rates of diagnostic failure at 60 days, subsequent coronary angiography, revascularization, or patient health status at 1 year between patients evaluated by pharmacologic PET compared with those evaluated by SPECT MPI.	This was a single-center randomized trial conducted at a tertiary referral center with expertise in nuclear cardiology. The quality of MPI studies as well as clinical decision making patterns after MPI testing may be different in other settings. The authors were unable to determine the appropriateness of downstream testing ordered by the referring physicians. Finally, the study appears to be underpowered for the primary endpoint of diagnostic failure as well as secondary endpoints for follow-up catheterization and revascularization rates.
Pontone G, Andreini D, Guaricci AI, et al. The STRATEGY study (stress cardiac magnetic resonance versus computed tomography coronary angiography for the management of symptomatic revascularized patients): Resources and outcomes impact. Circ Cardiovasc Imaging. 2016; 9(10):e005171.	27894070	Prospective, single-center, multi-reader	low	To compare an anatomic (computed tomography coronary angiography; cTCA) versus a functional (stress-CMR) strategy in symptomatic patients with previous myocardiial revascularization procedures.	600 symptomatic patients with a previous history of revascularization by PCI or CABG referred to a single hospital between January 2011 and December 2013 to be evaluated by clinically indicated cTCA or stress-CMR were enrolled. Exclusion criteria were unstable angina; cardiac diseases different from CAD, such as heart failure, infiltrative or hypertrophic cardiomyopathy, and myocarditis; estimated glomerular filtration rate ≤30 mL/min; hypersensitivity to iodinecontrast agent; inability to sustain a breath hold; pregnancy; cardiac arrhythmias; body mass index >35 kg/m2; claustrophobia; presence of a pacemaker or implantable cardioverter device; and contraindication to dipyridamole and gadolinium intravenous administration.	Patients with chest pain and previous revascularization included in a prospective observational registry and evaluated by clinically indicated cTCA (n=300, mean age 68.2±9.7 years, male 255) or stress-CMR (n=300, mean age 67.6±9.7 years, male 263) were enrolled and followed-up in terms of subsequent noninvasive tests, invasive coronary angiography, revascularization procedures, cumulative effective radiation dose, major adverse cardiac events, defined as a composite end point of nonfatal myocardial infarction and cardiac death, and medical costs.	The mean follow-up for cTCA and stress-CMR groups was similar (773.6±345 versus 752.8±291 days; P=0.21). Compared with stress-CMR, cTCA was associated with a higher rate of subsequent noninvasive tests (28% versus 17%; P=0.0009), invasive coronary angiography (31% versus 20%; P=0.0009), and revascularization procedures (24% versus 16%; P=0.007). Stress-CMR strategy was associated with a significant reduction of radiation exposure and cumulative costs (59% and 24%, respectively; P<0.001). Finally, patients undergoing stress-CMR showed a lower rate of major adverse cardiac events (5% versus 10%; P<0.010) and cost-effectiveness ratio (119.98±250.92 versus 218.12±298.45 Euro/y; P<0.001). The authors conclude that, compared with cTCA, stress-CMR is more cost-effective in symptomatic revascularized patients.	The major limitation is that this is an observational study, and therefore, its results are subject to potential selection biases in comparison to the results from randomized controlled trials. Second, this is a single-center study from an Institute with extensive experience in performing cTCA and stress-CMR examinations. Therefore, findings could not be directly transferred to the real clinical world. The study also did not compare the index tests at baseline with a reference standard technique.

Rudzinski PN, Kruk M, Kepka C, et al. The value of coronary artery computed tomography as the first-line anatomical test for stable patients with indications for invasive angiography due to suspected coronary artery disease: CAT-CAD randomized trial. J Cardiovasc Comput Tomogr. 2018; 12(6):472-479.	30201310	Prospective, single-center, multi-reader	low	To evaluate whether the use of coronary computed tomography angiography (CCTA) as the first-line anatomical test in patients with suspected significant coronary artery disease (CAD) may reduce the number of coronary invasive angiographies (ICA), and expand the use of CCTA in patients currently diagnosed invasively.	Study included stable patients with suspected CAD. Patients were excluded if they had: a diagnosis of acute coronary syndrome, high likelihood of in-stent restenosis (evaluated as a recurrence of typical angina symptoms within one year of their last PCI), contraindications to ICA, estimated glomerular filtration rate<60 ml/min/1.73m2, significant arrhythmia, or body mass index (BMI) > 35 kg/m2.	120 patients (age:60.6 ± 7.9 years, 35% female) with indications to ICA were randomized 1:1 to undergo CCTA versus direct ICA. Outcomes were evaluated during the diagnostic and therapeutic periods. In order to define the type of angina, the traditional clinical classification of chest pain was used initially (typical angina, atypical angina, non-anginal chest pain). Basing on the criteria of age, sex and anginal symptoms, the PTP value was estimated. Finally, it enabled the proper selection of individuals with indications for elective ICA. Those were patients with the left ventricle ejection fraction <50% with typical angina symptoms, patients with PTP 50–85% with positive/intermediate (unclear) functional test, or patients with PTP>85%.	The number of invasively examined patients was reduced by 64.4% in the CCTA group as compared to the direct ICA group (21vs59,p < 0.0001). The number of patients with ICAs not followed by coronary intervention was reduced by 88.1% with the CCTA strategy (5vs42,p < 0.0001). Over the diagnostic and therapeutic course there were no significant differences regarding the median volume of contrast (CCTA 80.3 ml [65.0–165.0] vs ICA 90.0 ml[55.0–100.0], p=0.099), while a non-significant trend towards higher radiation dose in the CCTA group was observed (9.9 mSv[7.0–22.1] vs 9.4 mSv[5.2–14.0], p=0.05). There were no acute cardiovascular events. The authors conclude that CCTA may hypothetically act as an effective 'gatekeeper' to the catheterization laboratory in the diagnosis of stable patients with current indications for ICA. This strategy may result in non-invasive, outpatient-based triage of two thirds of individuals without actionable CAD, obviating unnecessary invasive examinations. However, the longer follow-up is indispensable.	First, this was an open-label study and individual decisions for treatment options may have been influenced by the initial diagnostic modality employed. Second, the study group was relatively small, which did not allow for a robust evaluation of clinical complications associated with either strategy, except for the number of hospitalizations. Third, authors excluded patients with decreased renal function for the purpose of this investigation. Fourth, the primary outcome measures aimed to explore the impact of CCTA during the early diagnostic-therapeutic period in patients with suspected CAD, with regards to a definitive diagnosis and subsequent clinical management decisions. Fifth, the study was performed in an experienced center with a high volume CCTA program, which may not reflect the factual clinical situation in the majority of institutions. Sixth, due to high prevalence of patients with advanced atherosclerosis, results hardly can be referred to application of basic, 64 slice CT scanner for the tested clinical scenario.
SCOT-HEART Investigators; Newby DE, Adamson PD, Berry C, et al. Coronary CT angiography and 5-year risk of myocardial infarction. N Engl J Med. 2018; 379(10):924-933.	30145934	Open-label, multi-center, parallel-group trial	high	Both the SCOT-HEART and PROMISE trials followed patients for a relatively short time (20-22 months), and the longer-term effects on coronary heart disease events are unknown. The authors now report the 5-year clinical outcomes of the SCOT-HEART trial to determin the effect of CTA on longer-term investigations, treatments, and clinical events.	Inclusion criteria were age >18 and ≤75 years and attendance at the outpatient cardiology clinic with chest pain (Rapid Access Chest Pain Clinic). Exclusion criteria were inability or unwilling to undergo computed tomography scanning, known severe renal failure (serum creatinine >2.26 mg/dL or estimated glomerular filtration rate <30 mL/min/1.73 m2), previous recruitment to the trial, major allergy to iodinated contrast agent, unable to give informed consent, known pregnancy and acute coronary syndrome within 3 months.	In an open-label, multicenter, parallel-group trial, authors randomly assigned 4,146 patients with stable chest pain who had been referred to a cardiology clinic for evaluation to standard care plus CTA (2,073 patients) or to standard care alone (2,073 patients). Investigations, treatments, and clinical outcomes were assessed over 3 to 7 years of follow-up. The primary end point was death from coronary heart disease or nonfatal myocardial infarction at 5 years.	Median duration of follow-up was 4.8 years, which yielded 20,254 patient years of follow-up. The 5-year rate of the primary end point was lower in the CTA group than in the standard-care group (2.3% [48 patients] vs. 3.9% [81 patients]; hazard ratio, 0.59; 95% confidence interval [CI], 0.41 to 0.84; P = 0.004). Although the rates of invasive coronary angiography and coronary revascularization were higher in the CTA group than in the standard-care group in the first few months of follow-up, overall rates were similar at 5 years: invasive coronary angiography was performed in 491 patients in the CTA group and in 502 patients in the standard-care group (hazard ratio, 1.00; 95% CI, 0.88 to 1.13), and coronary revascularization was performed in 279 patients in the CTA group and in 267 in the standard-care group (hazard ratio, 1.07; 95% CI, 0.91 to 1.27). However, more preventive therapies were initiated in patients in the CTA group (odds ratio, 1.40; 95% CI, 1.19 to 1.65), as were more antianginal therapies (odds ratio, 1.27; 95% CI, 1.05 to 1.54). There were no significant between-group differences in the rates of cardiovascular or noncardiovascular deaths or deaths from any cause. Authors conclude that use of CTA in addition to standard care resulted in significantly lower rate of death at 5 years than standard care alone, without resulting in higher rate of coronary angiography or revascularization.	First, this was an open-label trial, and ascertainment bias is inherent to the trial design. Because event adjudication was not blinded and clinical diagnoses were coded with knowledge of the assigned trial group, the risk of ascertainment bias is probably higher. This risk may have been mitigated, however, by the fact that the primary long-term end point was composed of hard clinical events. Second, authors do not have data on lifestyle alterations during follow-up and can only speculate that these may have been greater in the CTA group than in the standard-care group. Third, cardiovascular-risk thresholds for the initiation of preventive therapies have fallen since the trial was completed, and it is unclear whether the benefits of CTA will be maintained with these lower thresholds. Finally, the benefit of CTA with respect to the rate of death from coronary heart disease and nonfatal myocardial infarction (1.6 percentage points lower than the rate with standard therapy) may be considered modest, but this absolute benefit is similar to, if not greater than, the benefits achieved in recent pharmaceutical interventional trials involving patients with established coronary heart disease.