Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
1. Cooper R, Cutler J, Desvigne-Nickens P, et al. Trends and disparities in coronary heart disease, stroke, and other cardiovascular diseases in the United States: findings of the national conference on cardiovascular disease prevention. *Circulation* 2000; 102(25):3137-3147.	Review/Other-Dx	N/A	Findings of the national conference on CVD prevention in the United States.	CHD mortality is still declining in the United States as a whole, although perhaps at a slower rate than in the 1980s; that stroke mortality rates have declined little, if at all, since 1990; and that there are striking differences in cardiovascular death rates by race/ethnicity, socioeconomic status, and geography. Trends in risk factors are consistent with a slowing of the decline in mortality; there has been little recent progress in risk factors such as smoking, physical inactivity, and hypertension control. There are increasing levels of obesity and type 2 diabetes, with major differences among subpopulations.	4
2. Greenland P, Alpert JS, Beller GA, et al. 2010 ACCF/AHA guideline for assessment of cardiovascular risk in asymptomatic adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2010; 56(25):e50-103.	Review/Other-Dx	N/A	AACF/AHA guideline for the assessment of cardiovascular risk in asymptomatic adults.	In analyzing the data and developing recommendations and supporting text, the writing committee used evidence-based methodologies developed by the Task Force that are described elsewhere.	4
3. Greenland P, Knoll MD, Stamler J, et al. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. *JAMA* 2003; 290(7):891-897.	Observational-Dx	347,978 men aged 35 to 57 years; and a population-based sample of 3,295 men and women from the Framingham study	To determine the frequency of exposure to major CHD risk factors.	For fatal CHD (n=20,995), exposure to at least 1 clinically elevated major risk factor ranged from 87% to 100%. Among those aged 40 to 59 years at baseline with fatal CHD (n=19,263), exposure to at least 1 major risk factor ranged from 87% to 94%. For nonfatal MI, prior exposure was documented in 92% (95% CI, 87%-96%) (n=167) of men aged 40 to 59 years at baseline and in 87% (95% CI, 80%-94%) (n=94) of women in this age group.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
4. Wilson SR, Lin FY, Min JK. Role of coronary artery calcium score and coronary CT angiography in the diagnosis and risk stratification of individuals with suspected coronary artery disease. *Curr Cardiol Rep* 2011; 13(4):271-279.	Review/Other-Dx	N/A	To review the role of CACS and CCTA in the diagnosis and risk stratification of individuals with suspected CAD.	The CACS has been found to be a marker of vascular injury that correlates closely with overall atherosclerotic burden, whereas CCTA permits detection of noncalcified plaque coronary artery stenosis severity. A growing body of literature has developed detailing the valuable prognostic utility of these tests in the management of patients and how they may one day be used to complement current risk prediction models.	4
5. Eggen DA, Strong JP, McGill HC, Jr. Coronary calcification. Relationship to clinically significant coronary lesions and race, sex, and topographic distribution. *Circulation* 1965; 32(6):948-955.	Observational-Dx	1,242 consecutive necropsies	To evaluate coronary calcification and the relationship to clinically significant coronary lesions and race, sex, and topographic distribution.	The data indicate an association between calcification of coronary arteries and clinically significant atherosclerotic lesions. This association is sufficiently strong that radiologic detection of calcification in the coronary arteries in the living should provide information of value in the differential diagnosis of advanced coronary atherosclerosis, especially in the young.	3
6. Frink RJ, Achor RW, Brown AL, Jr., Kincaid OW, Brandenburg RO. Significance of calcification of the coronary arteries. *Am J Cardiol* 1970; 26(3):241-247.	Observational-Dx	200 human hearts	To evaluate the significance of calcification of the coronary arteries.	The total calcification and the proximal calcification scores for the left anterior descending, left circumflex and right coronary arteries tended to parallel each other closely and were frequently equivalent.	4
7. Lieber A, Jorgens J. Cinefluorography of coronary artery calcification. Correlation with clinical arteriosclerotic heart disease and autopsy findings. *Am J Roentgenol Radium Ther Nucl Med* 1961; 86:1063-1072.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
8. Oliver MF. The diagnostic value of detecting coronary calcification. *Circulation* 1970; 42(6):981-982.	Review/Other-Dx	N/A	Editorial on the diagnostic value of detecting coronary calcification.	No results stated.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
9. Iribarren C, Sidney S, Sternfeld B, Browner WS. Calcification of the aortic arch: risk factors and association with coronary heart disease, stroke, and peripheral vascular disease. *JAMA* 2000; 283(21):2810-2815.	Observational-Dx	60,393 women and 55,916 men	To evaluate risk factors for aortic arch calcification and its long-term association with CVDs in a population-based sample.	After adjustment for age, educational attainment, race/ethnicity, cigarette smoking, alcohol consumption, body mass index, serum cholesterol level, hypertension, diabetes, and family history of MI, aortic arch calcification was associated with an increased risk of CHD (in men, RR, 1.27; 95% CI, 1.11-1.45; in women, RR, 1. 22; 95% CI, 1.07-1.38). Among women, it was also independently associated with a 1.46-fold increased risk of ischemic stroke (95% CI, 1.28-1.67).	2
10. McGuire J, Schneider HJ, Chou TC. Clinical significance of coronary artery calcification seen fluoroscopically with the image intensifier. *Circulation* 1968; 37(1):82-87.	Observational-Dx	544 consecutive patients	To determine the clinical significance of coronary artery calcification in a mixed group of patients as recognized fluoroscopically with the image intensifier, and its usefulness as a routine procedure in the evaluation of patients suspected of having ischemic heart disease.	The overall prevalence of coronary calcification was 20% and there was a definite increase in the prevalence of the finding with increasing age.	3
11. Loecker TH, Schwartz RS, Cotta CW, Hickman JR, Jr. Fluoroscopic coronary artery calcification and associated coronary disease in asymptomatic young men. *J Am Coll Cardiol* 1992; 19(6):1167-1172.	Observational-Dx	1,466 men	To compare the presence of fluoroscopically detected coronary artery calcification with angiographic CAD in asymptomatic male military aircrew undergoing noninvasive cardiac screening tests and coronary arteriography for occupational indications.	Overall sensitivity and specificity for coronary artery calcification detection of significant disease, based only on those subjects undergoing arteriography, were 66.3% and 77.6%, respectively. For measurable disease (mild plus significant), sensitivity was 60.6% and specificity 85.9%. PPVs and NPVs were 37.7% and 91.9%, respectively, for significant disease. For measurable disease, PPVs and NPVs were 68.9% and 80.9%, respectively. In these asymptomatic young men, a fluoroscopic examination negative for coronary artery calcification indicated a low risk of significant CAD, whereas a positive test result (calcification present) substantially increased the likelihood of angiographically significant CAD.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
12. Margolis JR, Chen JT, Kong Y, Peter RH, Behar VS, Kisslo JA. The diagnostic and prognostic significance of coronary artery calcification. A report of 800 cases. *Radiology* 1980; 137(3):609-616.	Observational-Dx	800 patients	To evaluate the diagnostic and prognostic significance of coronary artery calcification.	Patients with calcification demonstrated poorer survival at all follow-up intervals (from 6 months to 5 years); the 5-year survival rate was 87% for patients without calcification, compared to 58% for those with calcification. The prognostic significance of coronary artery calcification appears to be independent of information obtained by cardiac catheterization and angiocardiography.	3
13. Polonsky TS, McClelland RL, Jorgensen NW, et al. Coronary artery calcium score and risk classification for coronary heart disease prediction. *JAMA* 2010; 303(16):1610-1616.	Observational-Dx	6,914 patients	To determine whether adding CACS to a prediction model based on traditional risk factors improves classification of risk.	209 CHD events occurred, of which 122 were MI, death from CHD, or resuscitated cardiac arrest. Model 2 resulted in significant improvements in risk prediction compared with model 1 (net reclassification improvement = 0.25; 95% CI, 0.16-0.34; P<.001). In model 1, 69% of the cohort was classified in the highest or lowest risk categories compared with 77% in model 2. An additional 23% of those who experienced events were reclassified as high risk, and an additional 13% without events were reclassified as low risk using model 2.	3
14. Rumberger JA. Tomographic plaque imaging with CT: technical considerations and capabilities. *Prog Cardiovasc Dis* 2003; 46(2):123-134.	Review/Other-Dx	N/A	To review the technical considerations and capabilities of tomographic plaque imaging with CT.	Details on the methodological differences between types of CT scanners and precision of calcium scoring are a function of their individual technical capabilities and limitations.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
15. Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. *J Am Coll Cardiol* 2005; 46(1):158-165.	Observational-Dx	4,903 asymptomatic patients	To determine the prognostic accuracy of EBCT scanning of the coronary arteries and the relationship of coronary calcification to standard coronary disease risk factors and C-reactive protein in the prediction of atherosclerotic CVD events in apparently healthy middle-age persons.	Subjects with atherosclerotic CVD events had higher baseline coronary calcium scores (median [interquartile range], Agatston method) than those without events: 384 (127, 800) vs 10 (0, 86) (P<0.0001). For coronary calcium score threshold ≥100 vs <100, RR (95% CI) was 9.6 (6.7 to 13.9) for all atherosclerotic CVD events, 11.1 (7.3 to 16.7) for all CAD events, and 9.2 (4.9 to 17.3) for non-fatal MI and death. The coronary calcium score predicted CAD events independently of standard risk factors and C-reactive protein (P=0.004), was superior to the Framingham risk index in the prediction of events (AUC of 0.79 +/- 0.03 vs 0.69 +/- 0.03, P=0.0006), and enhanced stratification of those falling into the Framingham categories of low, intermediate, and high risk (P<0.0001).	3
16. Raggi P, Cooil B, Shaw LJ, et al. Progression of coronary calcium on serial electron beam tomographic scanning is greater in patients with future myocardial infarction. *Am J Cardiol* 2003; 92(7):827-829.	Observational-Dx	817 asymptomatic patients	To observe the occurrence of acute MI to CAC progression.	There were no significant differences between the groups except for a more frequent use of lipid-lowering agents among the patients.	4
17. Wayhs R, Zelinger A, Raggi P. High coronary artery calcium scores pose an extremely elevated risk for hard events. *J Am Coll Cardiol* 2002; 39(2):225-230.	Observational-Dx	98 subjects	To assess the natural history of a cohort of asymptomatic individuals with very high (≥1,000) calcium scores on a screening EBCT not submitted to further testing after the initial scan. We also compared the outcome of our prospective cohort with that of historical controls with severe abnormalities on MPI.	During the follow-up period, 35 patients (36%) suffered a hard coronary event. All events were recorded in the first 28 months of follow-up. Subjects with hard coronary events had higher initial calcium scores than subjects not suffering hard coronary events (1,561 +/- 270 vs 1,199 +/- 200, P<0.001). The annualized event rate in subjects with a calcium scores ≥1,000 was significantly greater than that of historical controls with severe perfusion abnormalities on MPI (25% vs 7.4%, respectively; P<0.0001).	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
18. Shaw LJ, Raggi P, Schisterman E, Berman DS, Callister TQ. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. *Radiology* 2003; 228(3):826-833.	Observational-Dx	10,377 asymptomatic patients	To develop risk-adjusted multivariable models that included risk factors and coronary calcium scores determined with EBCT in asymptomatic patients for the prediction of all-cause mortality.	During a mean follow-up of 5.0 years +/- 0.0086 (standard error of the mean), the death rate was 2.4%. In a risk-adjusted model (model chi2 = 388.2, P<.001), coronary calcium was an independent predictor of mortality (P<.001). Risk-adjusted RR values for coronary calcium were 1.64, 1.74, 2.54, and 4.03 for scores of 11-100, 101-400, 401-1,000, and greater than 1,000, respectively (P<.001 for all values), as compared with that for a score of 10 or less. 5-year risk-adjusted survival was 99.0% for a calcium score of 10 or less and 95.0% for a score of greater than 1,000 (P<.001). With a ROC curve, the concordance index increased from 0.72 for cardiac risk factors alone to 0.78 (P<.001) when the calcium score was added to a multivariable model for prediction of death.	3
19. Kondos GT, Hoff JA, Sevrukov A, et al. Electron-beam tomography coronary artery calcium and cardiac events: a 37-month follow-up of 5635 initially asymptomatic low- to intermediate-risk adults. *Circulation* 2003; 107(20):2571-2576.	Observational-Dx	8,855 patients	To examine the association between EBCT CAC and cardiac events in initially asymptomatic low- to intermediate-risk individuals, with adjustment for the presence of hypercholesterolemia, hypertension, diabetes, and a history of cigarette smoking.	Conventional CAD risk factors were elicited by use of a questionnaire. After 37 +/- 12 months, information on the occurrence of cardiac events was collected and confirmed by use of medical records and death certificates. In men, events (n=192) were associated with the presence of CAC (RR=10.5, P<0.001), diabetes (RR=1.98, P=0.008), and smoking (RR=1.4, P=0.025), whereas in women, events (n=32) were linked to the presence of CAC (RR=2.6, P=0.037) and not risk factors. The presence of CAC provided incremental prognostic information in addition to age and other risk factors.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
20. Budoff MJ, Shaw LJ, Liu ST, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J Am Coll Cardiol* 2007; 49(18):1860-1870.	Observational-Dx	25,253 consecutive symptomatic individuals	To develop risk-adjusted multivariable models that include risk factors and CACSs measured with EBCT in asymptomatic patients for the prediction of all-cause mortality.	The frequency of CACSs was 44%, 14%, 20%, 13%, 6%, and 4% for scores of 0, 1 to 10, 11 to 100, 101 to 400, 401 to 1,000, and >1,000, respectively. During a mean follow-up of 6.8 +/- 3 years, the death rate was 2% (510 deaths). The CAC was an independent predictor of mortality in a multivariable model controlling for age, gender, ethnicity, and cardiac risk factors (model chi-square = 2,017, P<0.0001). The addition of CAC to traditional risk factors increased the concordance index significantly (0.61 for risk factors vs 0.81 for the CACS, P<0.0001). Risk-adjusted RR ratios for CAC were 2.2-, 4.5-, 6.4-, 9.2-, 10.4-, and 12.5-fold for scores of 11 to 100, 101 to 299, 300 to 399, 400 to 699, 700 to 999, and >1,000, respectively (P<0.0001), when compared with a score of 0. 10-year survival (after adjustment for risk factors, including age) was 99.4% for a CACS of 0 and worsened to 87.8% for a score of >1,000 (P<0.0001).	3
21. Erbel R, Mohlenkamp S, Moebus S, et al. Coronary risk stratification, discrimination, and reclassification improvement based on quantification of subclinical coronary atherosclerosis: the Heinz Nixdorf Recall study. *J Am Coll Cardiol* 2010; 56(17):1397-1406.	Observational-Dx	4,129 patients	To determine net reclassification improvement and improved risk prediction based on CAC scoring in comparison with traditional risk factors.	After 5 years of follow-up, 93 coronary deaths and nonfatal MIs occurred (cumulative risk 2.3%; 95% CI: 1.8% to 2.8%). Reclassifying intermediate (defined as 10% to 20% and 6% to 20%) risk subjects with CAC <100 to the low-risk category and with CAC ≥400 to the high-risk category yielded a net reclassification improvement of 21.7% (P=0.0002) and 30.6% (P<0.0001) for the Framingham Risk Score, respectively. Integrated discrimination improvement using Framingham Risk Score variables and CAC was 1.52% (P<0.0001). Adding CACSs to the Framingham Risk Score and National Cholesterol Education Panel ATP III categories improved the area under the curve from 0.681 to 0.749 (P<0.003) and from 0.653 to 0.755 (P=0.0001), respectively.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
22. Ferket BS, Genders TS, Colkesen EB, et al. Systematic review of guidelines on imaging of asymptomatic coronary artery disease. *J Am Coll Cardiol* 2011; 57(15):1591-1600.	Review/Other-Dx	N/A	To critically appraise guidelines on imaging of asymptomatic CAD.	Of 2,415 titles identified, 14 guidelines met our inclusion criteria. 11/14 guidelines reported relationship with industry. The AGREE scores varied across guidelines from 21% to 93%. Two guidelines considered cost effectiveness. Eight guidelines recommended against or found insufficient evidence for testing of asymptomatic CAD. The other 6 guidelines recommended imaging patients at intermediate or high CAD risk based on the Framingham risk score, and 5 considered CT calcium scoring useful for this purpose.	4
23. Taylor AJ, Cerqueira M, Hodgson JM, et al. ACCF/SCCT/ACR/AHA/ASE/ASNC/NASCI/SCAI/SCMR 2010 appropriate use criteria for cardiac computed tomography. A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. *J Am Coll Cardiol* 2010; 56(22):1864-1894.	Review/Other-Dx	N/A	A report of the American College of Cardiology Foundation Appropriate Use Criteria Task Force, the Society of Cardiovascular Computed Tomography, the American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance.	N/A	4
24. Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. *Circulation* 2002; 106(25):3143-3421.	Review/Other-Dx	N/A	Report on detection, evaluation, and treatment of high blood cholesterol in adults.	A literature search to identify interventions proven to help persons follow prescription medications uncovered a total of 4,762 citations. Of these, just 19 met the criteria of a confounded randomized clinical trial. Their panel of experts that reviewed this data concluded that current methods of improving adherence with chronic health problems are not very effective.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
25. Budoff MJ, Achenbach S, Blumenthal RS, et al. Assessment of coronary artery disease by cardiac computed tomography: a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. *Circulation* 2006; 114(16):1761-1791.	Review/Other-Dx	N/A	Scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention.	EBCT has undergone a 20-year period of testing for reliability and validity and is now established as a useful technique in identifying individuals with or at risk for CHD. MDCT is a promising tool for coronary calcium scoring while additional studies evaluating progression, reproducibility, and outcomes are currently under way. Radiation doses, reproducibility, and validation studies must be taken into account when choosing a cardiac CT study.	4
26. Dennie CJ, Leipsic J, Brydie A. Canadian Association of Radiologists: Consensus Guidelines and Standards for Cardiac CT. *Can Assoc Radiol J* 2009; 60(1):19-34.	Review/Other-Dx	N/A	2009 guidelines and standards for Cardiac CT from the Canadian Association of Radiologists.	N/A	4
27. Greenland P, Bonow RO, Brundage BH, et al. ACCF/AHA 2007 clinical expert consensus document on coronary artery calcium scoring by computed tomography in global cardiovascular risk assessment and in evaluation of patients with chest pain: a report of the American College of Cardiology Foundation Clinical Expert Consensus Task Force (ACCF/AHA Writing Committee to Update the 2000 Expert Consensus Document on Electron Beam Computed Tomography) developed in collaboration with the Society of Atherosclerosis Imaging and Prevention and the Society of Cardiovascular Computed Tomography. *J Am Coll Cardiol* 2007; 49(3):378-402.	Review/Other-Dx	N/A	2007 guidelines on CAC scoring by CT.	The Expert Panel concluded that the majority of the research on CAC measurement in the past 5 years has focused on 2 areas of clinical interest: 1) Risk assessment in the asymptomatic patient, for the primary purpose of modifying and potentially improving selection of patients for risk reducing therapies, and 2) Use of CAC measurement in symptomatic patients as a means of selecting patients who might require subsequent hospitalization or additional diagnostic or invasive procedures.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
28. Grundy SM, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation* 2004; 110(2):227-239	Review/Other-Dx	N/A	To review the results of recent trials and assesses their implications for cholesterol management.	In high-risk persons, the recommended LDL-C goal is <100 mg/dL, but when risk is very high, an LDL-C goal of <70 mg/dL is a therapeutic option, ie, a reasonable clinical strategy, on the basis of available clinical trial evidence. This therapeutic option extends also to patients at very high risk who have a baseline LDL-C <100 mg/dL. Moreover, when a high-risk patient has high triglycerides or low HDL-C, consideration can be given to combining a fibrate or nicotinic acid with an LDL-lowering drug. For moderately high-risk persons (2+ risk factors and 10-year risk 10% to 20%), the recommended LDL-C goal is <130 mg/dL, but an LDL-C goal <100 mg/dL is a therapeutic option on the basis of recent trial evidence. The latter option extends also to moderately high-risk persons with a baseline LDL-C of 100 to 129 mg/dL. When LDL-lowering drug therapy is employed in high-risk or moderately high-risk persons, it is advised that intensity of therapy be sufficient to achieve at least a 30% to 40% reduction in LDL-C levels. Moreover, any person at high risk or moderately high risk who has lifestyle-related risk factors (eg, obesity, physical inactivity, elevated triglycerides, low HDL-C, or metabolic syndrome) is a candidate for TLC to modify these risk factors regardless of LDL-C level. Finally, for people in lower-risk categories, recent clinical trials do not modify the goals and cutpoints of therapy.	4
29. Chow BJ, Larose E, Bilodeau S, et al. The 'what, when, where, who and how?' of cardiac computed tomography in 2009: guidelines for the clinician. *Can J Cardiol* 2009; 25(3):135-139.	Review/Other-Dx	N/A	2009 guidelines for cardiac CT.	N/A	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
30. Ferencik M, Moselewski F, Ropers D, et al. Quantitative parameters of image quality in multidetector spiral computed tomographic coronary imaging with submillimeter collimation. *Am J Cardiol* 2003; 92(11):1257-1262.	Observational-Dx	30 patients	To quantitatively evaluate the image quality that can be obtained with the latest generation of MDCT scanners with submillimeter collimation and increased gantry rotation speed.	90% of the overall visualized length of the coronary arteries was visualized free of motion artifacts, with slightly better results for the left main and left anterior descending arteries compared with the left circumflex and right coronary arteries. Patients with heart rates ≤60 beats/min had better image quality and fewer motion artifacts than those with heart rates >60 beats/min. Similar observations were made by other investigators using 4-slice MDCT.	3
31. Flohr T, Bruder H, Stierstorfer K, Simon J, Schaller S, Ohnesorge B. New technical developments in multislice CT, part 2: sub-millimeter 16-slice scanning and increased gantry rotation speed for cardiac imaging. *Rofo* 2002; 174(8):1022-1027.	Review/Other-Dx	N/A	To describe the technical principles of cardiac scanning with a state-of-the-art 16-slice CT equipment and to discuss an extension of the Adaptive Cardio Volume reconstruction approach for ECG-gated multislice spiral CT. To also show the impact of reduced gantry rotation time (0.42 sec) on temporal resolution, and we demonstrate the influence of slice width on the visualization of stents and plaques.	The new generation of multislice CT systems offering simultaneous acquisition of up to 16 sub-millimeter slices and gantry rotation times shorter than 0.5 sec has the potential to overcome these limitations.	4
32. Budoff MJ, Dowe D, Jollis JG, et al. Diagnostic performance of 64-multidetector row coronary computed tomographic angiography for evaluation of coronary artery stenosis in individuals without known coronary artery disease: results from the prospective multicenter ACCURACY (Assessment by Coronary Computed Tomographic Angiography of Individuals Undergoing Invasive Coronary Angiography) trial. *J Am Coll Cardiol* 2008; 52(21):1724-1732.	Observational-Dx	230 patients	To evaluate the diagnostic accuracy of electrocardiographically gated 64-multidetector row CCTA in individuals without known CAD.	On a patient-based model, the sensitivity, specificity, and PPVs and NPVs to detect ≥50% or ≥70% stenosis were 95%, 83%, 64%, and 99%, respectively, and 94%, 83%, 48%, 99%, respectively. No differences in sensitivity and specificity were noted for non-obese compared with obese subjects or for heart rates ≤65 beats/min compared with >65 beats/min, whereas calcium scores >400 reduced specificity significantly.	1

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
33. Meijboom WB, Meijs MF, Schuijf JD, et al. Diagnostic accuracy of 64-slice computed tomography coronary angiography: a prospective, multicenter, multivendor study. *J Am Coll Cardiol* 2008; 52(25):2135-2144.	Observational-Dx	360 patients	To determine the diagnostic accuracy of 64-slice CCTA to detect or rule out significant CAD.	The prevalence among patients of having at least 1 significant stenosis was 68%. In a patient-based analysis, the sensitivity for detecting patients with significant CAD was 99% (95% CI: 98% to 100%), specificity was 64% (95% CI: 55% to 73%), PPV was 86% (95% CI: 82% to 90%), and NPV was 97% (95% CI: 94% to 100%). In a segment-based analysis, the sensitivity was 88% (95% CI: 85% to 91%), specificity was 90% (95% CI: 89% to 92%), PPV was 47% (95% CI: 44% to 51%), and NPV was 99% (95% CI: 98% to 99%).	3
34. Miller JM, Rochitte CE, Dewey M, et al. Diagnostic performance of coronary angiography by 64-row CT. *N Engl J Med* 2008; 359(22):2324-2336.	Observational-Dx	291 patients	To examine the accuracy of MDCT angiography involving 64 detectors.	The patient-based diagnostic accuracy of quantitative CT angiography for detecting or ruling out stenoses of 50% or more according to conventional angiography revealed an AUC of 0.93 (95% CI, 0.90 to 0.96), with a sensitivity of 85% (95% CI, 79 to 90), a specificity of 90% (95% CI, 83 to 94), a PPV of 91% (95% CI, 86 to 95), and a NPV of 83% (95% CI, 75 to 89). CT angiography was similar to conventional angiography in its ability to identify patients who subsequently underwent revascularization: the AUC was 0.84 (95% CI, 0.79 to 0.88) for MDCT angiography and 0.82 (95% CI, 0.77 to 0.86) for conventional angiography. A per-vessel analysis of 866 vessels yielded an AUC of 0.91 (95% CI, 0.88 to 0.93). Disease severity ascertained by CT and conventional angiography was well correlated (r=0.81; 95% CI, 0.76 to 0.84). Two patients had important reactions to contrast medium after CT angiography.	1

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
35. Bachar GN, Atar E, Fuchs S, Dror D, Kornowski R. Prevalence and clinical predictors of atherosclerotic coronary artery disease in asymptomatic patients undergoing coronary multidetector computed tomography. *Coron Artery Dis* 2007; 18(5):353-360.	Observational-Dx	244 consecutive patients	To examine the prevalence and clinical predictors of atherosclerotic CAD in asymptomatic patients undergoing MDCT.	MDCT identified significant obstructive CAD (>50% luminal stenosis) in 13 patients (4.9%), mild or moderate nonobstructive disease (<50% stenosis) in 124 patients (50.8%), and no atherosclerosis in 108 patients (44.3%). On multivariate logistic regression analysis, significant independent clinical predictors of CAD were male sex (OR, 1.6, P<0.0047), family history of CAD (OR, 1.4, P<0.0099), LDL-C >130 mg/dl (OR 1.3, P<0.027), hypertension (OR, 1.27, P<0.05), and noninsulin-dependent diabetes mellitus (OR, 1.6, P<0.006). On the basis of the MDCT results, pharmacological treatment was initiated or intensified in 40% of patients (statins in 31% and aspirin in 9%). 22 patients (9%) were referred for complementary exercise testing and 5 (2%) for catheterization.	3
36. Choi EK, Choi SI, Rivera JJ, et al. Coronary computed tomography angiography as a screening tool for the detection of occult coronary artery disease in asymptomatic individuals. *J Am Coll Cardiol* 2008; 52(5):357-365.	Observational-Dx	1,000 consecutive subjects	To evaluate the prevalence of occult CAD with CCTA to characterize plaque composition and to evaluate the potential of this new technology to impact risk stratification in asymptomatic middle-aged subjects.	52 (5%) subjects had significant ≥50%) diameter stenosis and 21 (2%) had severe (≥75%) stenosis. 13 (25%) and 30 (58%) subjects with significant stenosis were classified into National Cholesterol Education Program low-risk and mild coronary calcification (CACSs <100), respectively. Midterm follow-up (17 +/- 2 months) revealed 15 cardiac events only in those with CAD on CCTA: 1 unstable angina requiring hospital stay and 14 revascularization procedures. Most (87%) events occurred within 90 days of index CCTA.	2

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
37. Hwang Y, Kim Y, Chung IM, Ryu J, Park H. Coronary heart disease risk assessment and characterization of coronary artery disease using coronary CT angiography: comparison of asymptomatic and symptomatic groups. *Clin Radiol* 2010; 65(8):601-608.	Observational-Dx	390 consecutive patients	To evaluate the prevalence of CAD in relation to risk of CHD and assess plaque characteristics from CCTA in asymptomatic and symptomatic patients.	CAD was observed in 42% of the asymptomatic group and 62% of the symptomatic group. In the former, the prevalence of CAD in low-, moderate- and high-risk subgroups was 21.4%, 47.4% and 65%, respectively, and was 33.3%, 74.4%, and 72.4% in the symptomatic group. Framingham 10-year risks of coronary events were significantly higher in patients with CAD than in normal participants, and ROCs curves showed that discriminatory power was poor in the asymptomatic group and symptomatic men, and good in symptomatic women. Of the participants in the asymptomatic group, 12% exhibited only non-calcified plaques and of the symptomatic group, 7% exhibited only non-calcified plaques. The coronary calcium score was significantly higher for significant stenosis than for non-significant stenosis in both groups.	3
38. Rivera JJ, Nasir K, Choi EK, et al. Detection of occult coronary artery disease in asymptomatic individuals with diabetes mellitus using non-invasive cardiac angiography. *Atherosclerosis* 2009; 203(2):442-448.	Observational-Dx	217 patients	To describe the prevalence of occult CAD in a group of asymptomatic subjects with diabetes using non-invasive coronary angiography, as well as to investigate the predictive accuracy of current guidelines with regards to their recommended criteria for further cardiac diagnostic testing in this patient population.	Diabetes duration was 7 +/- 7 years, mean Framingham risk score was 13%, and mean hemoglobin A1C level was 7%. Of the 217 outpatients, 138 (64%) had occult CAD based on CCTA findings. 36 (36/138; 26%) had a significant stenosis on CCTA. Nearly half of the individuals (62/138; 45%) had a combination of non-calcified and calcified plaques. Only 5 out of 217 (2%) individuals with significant stenosis would have been missed using the American Diabetes Association (ADA) criteria for further cardiac testing.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
39. Romeo F, Leo R, Clementi F, et al. Multislice computed tomography in an asymptomatic high-risk population. *Am J Cardiol* 2007; 99(3):325-328.	Observational-Dx	168 subjects	To evaluate the value of multislice CT for early detection of significant CAD in high-risk asymptomatic subjects.	Multislice CT displayed single-vessel CAD in 16% of patients, 2-vessel CAD in 7%, and 3-vessel CAD in 4%. Selective coronary angiography confirmed the results of multislice CT in 99% of all patients. Sensitivity and specificity of multislice CT coronary angiography were 100% and 98%, respectively, with a PPV of 95% and a NPV of 100%. In conclusion, multislice CT coronary angiography is an excellent noninvasive technique for early identification of significant CAD in high-risk asymptomatic patients with inconclusive or unfeasible noninvasive stress test results.	3
40. Hadamitzky M, Meyer T, Hein F, et al. Prognostic value of coronary computed tomographic angiography in asymptomatic patients. *Am J Cardiol* 2010; 105(12):1746-1751.	Observational-Dx	451 consecutive patients	To assess the value of CCTA in the prediction of cardiac events in asymptomatic patients.	Patients with obstructive CAD had a significantly higher event rate than those without obstructive CAD (risk ratio 13.9, 95% CI 4.0 to 48.0). In 217 patients (48%), the clinically assessed cardiovascular risk could be reclassified by CCTA from intermediate or high to low risk. In conclusion, although the event rate was low in asymptomatic patients, CCTA could reliably predict further cardiac events and could reclassify 2/3 of patients regarding their cardiovascular risk.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
41. Russo V, Zavalloni A, Bacchi Reggiani ML, et al. Incremental prognostic value of coronary CT angiography in patients with suspected coronary artery disease. *Circ Cardiovasc Imaging* 2010; 3(4):351-359.	Observational-Dx	441 patients	To determine the prognostic value of multidetector CCTA in patients with suspected but undocumented CAD and, in particular, the incremental prognostic value as compared with clinical risk and calcium scoring.	CT calcium scoring showed a statistically significant incremental prognostic value as compared to a baseline clinical risk model (P=0.018), whereas multidetector CCTA provided an additional incremental prognostic value as compared with a baseline clinical risk model plus calcium scoring if considering both nonobstructive vs obstructive CAD (P=0.016) or, better, plaque composition (calcified vs noncalcified and/or mixed plaques, P=0.0001). During follow-up, an excellent prognosis was noted in patients with normal coronary arteries, with an annualized incidence rate of 0.88% if compared with those with mild CAD (3.89%) and with patients with significant coronary disease (8.09%). The presence of noncalcified or mixed plaques, regardless of lesion severity, was found to be the strongest predictor of events (P<0.0001) as a potential marker of plaque vulnerability.	2
42. Gerber TC, Kantor B, McCollough CH. Radiation dose and safety in cardiac computed tomography. *Cardiol Clin* 2009; 27(4):665-677.	Review/Other-Dx	N/A	Review existing data regarding biologic hazards of radiation exposure associated with medical diagnostic testing, the methodologies used to estimate radiation exposure and dose, and the measures that can be taken to effectively reduce that exposure. Article focuses on cardiac CT imaging in adults.	Cardiac CT should be ordered consistent with established appropriateness criteria and expert consensus.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
43. Earls JP, Berman EL, Urban BA, et al. Prospectively gated transverse coronary CT angiography versus retrospectively gated helical technique: improved image quality and reduced radiation dose. *Radiology* 2008; 246(3):742-753.	Observational-Dx	203 patients	To retrospectively compare image quality, radiation dose, and blood vessel assessability for coronary artery CT angiograms obtained with a PGT CT technique and a RGH CT technique.	The mean effective dose for the group with the PGT technique was 2.8 mSv; this represents an 83% reduction as compared with that for the group with the RGH technique (mean, 18.4 mSv; P<.001). The image quality score for each of the arteries, as well as the overall combined score, was significantly greater for images obtained with PGT technique than for images obtained with RGH technique. The combined mean image quality score was 4.791 for images obtained with PGT technique vs 4.514 for images obtained with RGH technique (proportional odds model OR, 2.8; 95% CI: 1.7, 4.8). The percentage of assessable coronary artery segments was 98.6% (1,196/1,213) for images obtained with PGT technique vs 97.9% (1,741/1,778) for images obtained with RGH technique (P=.83).	2
44. Husmann L, Valenta I, Gaemperli O, et al. Feasibility of low-dose coronary CT angiography: first experience with prospective ECG-gating. *Eur Heart J* 2008; 29(2):191-197.	Observational-Dx	41 consecutive patients	To determine the feasibility of prospective ECG-gating to achieve low-dose CCTA	Mean effective radiation dose was 2.1 +/- 0.6 mSv (range, 1.1-3.0 mSv). Image quality was inversely related to heart rate (57.3 +/- 6.2, range 39-66 b.p.m.; r = 0.58, P<0.001), vessel attenuation (346 +/- 104, range 110-780 HU; r = 0.56, P<0.001), and body mass index (26.1 +/- 4.0, range 19.1-36.3 kg/m(2); r = 0.45, P<0.001), but not to heart rate variability (1.5 +/- 1.0, range 0.2-5.1 b.p.m.; r = 0.28, P=0.069). Nondiagnostic CCTA image quality was found in 5.0% of coronary segments. However, below a HR of 63 b.p.m. (n=28), as determined by receiver operator characteristic curve, only 1.1% of coronary segments were nondiagnostic compared with 14.8% with heart rate of >63 b.p.m. (P<0.001).	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
45. Stolzmann P, Leschka S, Scheffel H, et al. Dual-source CT in step-and-shoot mode: noninvasive coronary angiography with low radiation dose. *Radiology* 2008; 249(1):71-80.	Observational-Dx	40 patients	To prospectively investigate CT image quality parameters by using different protocols and to calculate radiation dose estimates for noninvasive coronary angiography performed with dual-source CT in the step-and-shoot mode.	Mean image noise was similar with protocols A and B. Mean attenuation in the aorta and coronary arteries with protocol A (444 HU) was significantly (P<.001) higher than that with protocol B (358 HU). The reduced contrast material dose in protocol C yielded attenuation similar to that with protocol B. Diagnostic image quality was achieved with all protocols in 1,237 (97.9%) of 1,264 coronary segments. No significant differences in image quality between the 100- and 120-kV protocols were found. Mean heart rate had a significant effect on motion artifacts (area under receiver operating characteristic curve = 0.818; 95% CI: 0.723, 0.892; P<.001), whereas heart rate variability had a significant effect on stair-step artifacts (area under receiver operating characteristic curve = 0.79; 95% CI: 0.687, 0.865; P<.001). The mean estimated effective dose was 1.2 mSv +/- 0.2 for protocols A and C and 2.6 mSv +/- 0.5 for protocol B.	2

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
46. Leipsic J, Labounty TM, Heilbron B, et al. Estimated radiation dose reduction using adaptive statistical iterative reconstruction in coronary CT angiography: the ERASIR study. *AJR Am J Roentgenol.* 2010;195(3):655-660.	Observational-Dx	574 consecutive patients	Prospectively evaluate patients undergoing CCTA at 3 centers to assess the impact of Adaptive Statistical Iterative Reconstruction (ASIR) on radiation dose and study quality for CCTA. Comparisons were performed between consecutive groups initially using filtered back projection (n = 331) and subsequently ASIR (n = 243) with regard to patient and scan characteristics, radiation dose, and diagnostic study quality.	There was no difference between groups in the use of prospective gating, tube voltage, or scan length. The examinations performed using ASIR had a lower median tube current than those obtained using filtered back projection (median [interquartile range], 450 mA [350–600] vs 650 mA [531–750], respectively; P<0.001). There was a 44% reduction in the median radiation dose between the filtered back projection and ASIR cohorts (4.1 mSv [2.3–5.2] vs 2.3 mSv [1.9–3.5]; P<0.001). After adjustment for scan settings, ASIR was associated with a 27% reduction in radiation dose compared with filtered back projection (95% CI, 21%–32%; P<0.001). Despite the reduced current, ASIR was not associated with a difference in adjusted signal, noise, or signal-to-noise ratio (P=not significant). No differences existed between filtered back projection and ASIR for interpretability per coronary artery (98.5% vs 99.3%, respectively; P=0.12) or per patient (96.1% vs 97.1%, P=0.65). ASIR enabled reduced tube current and lower radiation dose in comparison with filtered back projection, with preserved signal, noise, and study interpretability, in a large multicenter cohort. ASIR represents a new technique to reduce radiation dose in CCTA studies.	3
47. Achenbach S, Marwan M, Ropers D, et al. Coronary computed tomography angiography with a consistent dose below 1 mSv using prospectively electrocardiogram-triggered high-pitch spiral acquisition. *Eur Heart J* 2010; 31(3):340-346.	Observational-Dx	50 consecutive patients	To evaluate the feasibility and image quality of a new scan mode for CCTA with an effective dose of <1 mSv.	In all 50 patients, imaging was successful. Mean duration of data acquisition was 258 +/- 20 ms. Mean dose-length product was 62 +/- 5 mGy cm, the effective dose was 0.87 +/- 0.07 mSv (0.78-0.99 mSv). Of the 742 coronary artery segments, 94% had an image quality score of 1, 5.0% a score of 2, 0.9% a score of 3, and 4 segments (0.5%) were 'uninterpretable'. In nonobese patients with a low and stable heart rate, prospectively ECG-triggered high-pitch spiral coronary CTA provides excellent image quality at a consistent dose below 1.0 mSv.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
48. Grothues F, Smith GC, Moon JC, et al. Comparison of interstudy reproducibility of cardiovascular magnetic resonance with two-dimensional echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy. *Am J Cardiol* 2002; 90(1):29-34.	Observational-Dx	60 total subjects	To compare the interstudy reproducibility of cardiovascular MR with 2D echocardiography in normal subjects and in patients with heart failure or left ventricular hypertrophy.	The interstudy reproducibility coefficient of variability was superior for cardiovascular MR in all groups for all parameters. Statistical significance was reached for end-systolic volume (4.4% to 9.2% vs 13.7% to 20.3%, P<0.001), ejection fraction (2.4% to 7.3% vs 8.6% to 19.4%, P<0.001), and mass (2.8% to 4.8% vs 11.6% to 15.7% P<0.001), with a trend for end-diastolic volume (2.9% to 4.9% vs 5.5% to 10.5%, P=0.17). The superior interstudy reproducibility resulted in considerably lower calculated sample sizes (reductions of 55% to 93%) required by cardiovascular MR compared with echocardiography to show clinically relevant changes in left ventricular dimensions and function. Thus, cardiovascular MR has excellent interstudy reproducibility in normal, dilated, and hypertrophic hearts, and is superior to 2D echocardiography.	1
49. Nagel E, Klein C, Paetsch I, et al. Magnetic resonance perfusion measurements for the noninvasive detection of coronary artery disease. *Circulation* 2003; 108(4):432-437.	Observational-Dx	84 patients	To assess the value of myocardial perfusion reserve for the noninvasive detection of CAD in patients with suspected CAD.	ROCs were performed for different criteria to differentiate ischemic and nonischemic segments. Prevalence of CAD was 51%. Best results were achieved when only the 3 inner slices were assessed and a threshold value of 1.1 was used for the second smallest value as a marker for significant CAD. This approach yielded a sensitivity of 88%, specificity of 90%, and accuracy of 89%.	1
50. Schwitter J, Nanz D, Kneifel S, et al. Assessment of myocardial perfusion in coronary artery disease by magnetic resonance: a comparison with positron emission tomography and coronary angiography. *Circulation* 2001; 103(18):2230-2235.	Observational-Dx	48 patients	To determine the quality of a multislice MR approach with respect to the detection and sizing of compromised myocardium and compare with PET and quantitative coronary angiography.	ROC analysis of subendocardial upslope data revealed a sensitivity and specificity of 91% and 94%, respectively, for the detection of CAD as defined by PET (mean coronary flow reserve minus 2SD of controls) and a sensitivity and specificity of 87% and 85%, respectively, in comparison with quantitative coronary angiography (diameter stenosis ≥50%). The number of pathological sectors per patient on PET and MR studies correlated linearly (slope, 0.94; r=0.76; P<0.0001).	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
51. Wolff SD, Schwitter J, Coulden R, et al. Myocardial first-pass perfusion magnetic resonance imaging: a multicenter dose-ranging study. *Circulation* 2004; 110(6):732-737.	Observational-Dx	99 patients	To determine the minimally efficacious dose of gadopentetate dimeglumine injection for detecting obstructive CAD.	ROC analysis showed that the AUC were 0.90, 0.72, and 0.83 for the low-, medium-, and high-contrast doses, respectively, compared with quantitative coronary angiography (diameter stenosis ≥70%). For the low-dose group, mean sensitivity was 93 +/- 0%, mean specificity was 75 +/- 7%, and mean accuracy was 85 +/- 3%.	1
52. Hundley WG, Morgan TM, Neagle CM, Hamilton CA, Rerkpattanapipat P, Link KM. Magnetic resonance imaging determination of cardiac prognosis. *Circulation* 2002; 106(18):2328-2333.	Observational-Dx	279 patients	To determine if the presence of inducible ischemia identified during MRI stress tests could be used to identify those at risk of sustaining a future cardiac event.	279 patients referred (because of poor left ventricular endocardial visualization with echocardiography) for dobutamine/atropine MRI for the detection of inducible ischemia were followed for an average of 20 months. After MRI stress testing, the occurrence of MI, cardiac death, death attributable to any cause, coronary arterial revascularization, and unstable angina or congestive heart failure requiring hospitalization was determined. In a multivariate analysis, the presence of inducible ischemia (HR 3.3, CI 1.1 to 9.7) or an left ventricular ejection fraction <40% (HR 4.2, CI 1.3 to 13.9) was associated with future MI or cardiac death independent of the presence of risk factors for coronary arteriosclerosis.	3
53. Korosoglou G, Elhmidi Y, Steen H, et al. Prognostic value of high-dose dobutamine stress magnetic resonance imaging in 1,493 consecutive patients: assessment of myocardial wall motion and perfusion. *J Am Coll Cardiol* 2010; 56(15):1225-1234.	Observational-Dx	1,493 consecutive patients	To determine the prognostic value of wall motion and perfusion assessment during high-dose dobutamine stress cardiac MRI in a large patient cohort.	53 hard events, including 14 cardiac deaths and 39 nonfatal infarctions, occurred during the follow-up period, whereas 85 patients underwent "late" revascularization. Using multivariable regression analysis, an abnormal result for wall motion or perfusion during stress yielded the strongest independent prognostic value for both hard events and late revascularization, clearly surpassing that of clinical and baseline MR parameters (for wall motion: adjusted HR of 5.9 [95% CI: 2.5 to 13.6] for hard events and of 3.1 [95% CI: 1.7 to 5.6] for late revascularization, and for perfusion: adjusted HR of 5.4 [95% CI: 2.3 to 12.9] for hard events and of 6.2 [95% CI: 3.3 to 11.3] for late revascularization, P<0.001 for all).	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
54. Kim RJ, Fieno DS, Parrish TB, et al. Relationship of MRI delayed contrast enhancement to irreversible injury, infarct age, and contractile function. *Circulation* 1999; 100(19):1992-2002.	Review/Other-Dx	18 dogs	To compare contrast enhancement in acute infarction, after severe but reversible ischemic injury, and in chronic infarction.	High-resolution (0.5 x 0.5 x 0.5 mm) ex vivo MRI demonstrated that the spatial extent of hyperenhancement was the same as the spatial extent of myocyte necrosis with and without reperfusion at 1 day (R = 0.99, P<0.001) and 3 days (R = 0.99, P<0.001) and collagenous scar at 8 weeks (R = 0.97, P<0.001).	4
55. Fayad ZA, Fuster V, Fallon JT, et al. Noninvasive in vivo human coronary artery lumen and wall imaging using black-blood magnetic resonance imaging. *Circulation* 2000; 102(5):506-510.	Observational-Dx	13 subjects	To evaluate noninvasive in vivo human coronary artery lumen and wall imaging using black-blood MRI.	The average coronary wall thickness for each cross-sectional image was 0.75 +/- 0.17 mm (range, 0.55 to 1.0 mm) in the normal subjects. MRI of coronary arteries in patients with ≥40% stenosis as assessed by x-ray angiography showed localized wall thickness of 4.38 +/- 0.71 mm (range, 3.30 to 5.73 mm). The difference in maximum wall thickness between the normal subjects and patients was statistically significant (P<0.0001).	3
56. Kim WY, Stuber M, Bornert P, Kissinger KV, Manning WJ, Botnar RM. Three-dimensional black-blood cardiac magnetic resonance coronary vessel wall imaging detects positive arterial remodeling in patients with nonsignificant coronary artery disease. *Circulation* 2002; 106(3):296-299.	Observational-Dx	12 subjects	To evaluate high-resolution black-blood 3D cardiovascular MRI for in vivo visualization of the proximal coronary artery vessel wall.	Both mean vessel wall thickness (1.7 +/- 0.3 vs 1.0 +/- 0.2 mm) and wall area (25.4 +/- 6.9 vs 11.5 +/- 5.2 mm(2)) were significantly increased in the patients compared with the healthy subjects (both P<0.01). The lumen diameter (3.6 +/- 0.7 vs 3.4 +/- 0.5 mm, P=0.47) and lumen area (8.9 +/- 3.4 vs 7.9 +/- 3.5 mm(2), P=0.47) were similar in both groups.	3
57. Miao C, Chen S, Macedo R, et al. Positive remodeling of the coronary arteries detected by magnetic resonance imaging in an asymptomatic population: MESA (Multi-Ethnic Study of Atherosclerosis). *J Am Coll Cardiol* 2009; 53(18):1708-1715.	Observational-Dx	179 patients	To assess coronary arterial remodeling as a marker of subclinical atherosclerosis using coronary wall MRI in an asymptomatic population-based cohort.	Overall, coronary vessel size increased 25.9 mm(2) increase in coronary wall thickness, whereas, lumen area increased only slightly at 3.1 mm(2) for every millimeter increase in wall thickness (difference in slopes, P<0.0001). Adjusting for age and sex, participants with an Agatston score >0 were more likely to have wall thickness >2.0 mm (OR: 2.0, 95% CI: 1.01 to 3.84).	1
58. Schelbert EB, Cao JJ, Sigurdsson S, et al. Prevalence and prognosis of unrecognized myocardial infarction determined by cardiac magnetic resonance in older adults. *JAMA* 2012; 308(9):890-896.	Observational-Dx	936 patients	To determine prevalence and mortality risk for unrecognized MI detected by cardiac MRI or ECG among older individuals.	In a community-based cohort of older individuals, the prevalence of unrecognized MI by cardiac MRI was higher than the prevalence of recognized MI and was associated with increased mortality risk. In contrast, unrecognized MI by ECG prevalence was lower than that of recognized MI and was not associated with increased mortality risk.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
59. Perrone-Filardi P, Costanzo P, Dellegrottaglie S, et al. Prognostic role of myocardial single photon emission computed tomography in the elderly. *J Nucl Cardiol* 2010; 17(2):310-315.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
60. Shaw LJ, Iskandrian AE. Prognostic value of gated myocardial perfusion SPECT. *J Nucl Cardiol* 2004; 11(2):171-185.	Review/Other-Dx	N/A	No abstract available.	No abstract available.	4
61. Fleg JL, Gerstenblith G, Zonderman AB, et al. Prevalence and prognostic significance of exercise-induced silent myocardial ischemia detected by thallium scintigraphy and electrocardiography in asymptomatic volunteers. *Circulation* 1990; 81(2):428-436.	Observational-Dx	459 total patients from Baltimore Longitundal Study on Aging	To examine whether detection of reduced regional perfusion by thallium scintigraphy improves the predictive value of exercise-induced ST segment depression.	The prevalence of exercise-induced silent ischemia, defined by concordant ST segment depression and a thallium perfusion defect, increased more than sevenfold from 2% in the fifth and sixth decades to 15% in the ninth decade. Over a mean follow-up period of 4.6 years, cardiac events developed in 9.8% of subjects and consisted of 20 cases of new angina pectoris, 13 MIs, and 7 deaths. Events occurred in 7% of individuals with both negative 201Tl and ECG, 8% of those with either test positive, and 48% of those in whom both tests were positive (P<0.001). By proportional hazards analysis, age, hypertension, exercise duration, and a concordant positive ECG and 201Tl result were independent predictors of coronary events. Furthermore, those with positive ECG and 201Tl had a 3.6-fold RR for subsequent coronary events, independent of conventional risk factors.	4
62. Khandaker MH, Miller TD, Chareonthaitawee P, Askew JW, Hodge DO, Gibbons RJ. Stress single photon emission computed tomography for detection of coronary artery disease and risk stratification of asymptomatic patients at moderate risk. *J Nucl Cardiol* 2009; 16(4):516-523.	Observational-Dx	260 asymptomatic patients	To assigns a rating to SPECT MPI for detection and risk assessment of CAD in asymptomatic patients at moderate risk.	Mean follow-up 9.9 +/- 3.0 years. Abnormal SPECT MPI scans were present in 142 patients (55%). By summed stress score categories, SPECT scans were low-risk in 67%, intermediate-risk in 20%, and high-risk in 13% of patients. Overall survival at 10 years was 79%, significantly better than the age- and gender-matched Minnesota general population (P<0.001). Survival was 60% for patients with high-risk scans (95% CI 45%-80%), 79% with intermediate-risk scans (95% CI 69%-91%), and 83% with low-risk scans (95% CI 77%-88%) (P=0.03), including 84% (95% CI 77%-91%) with normal scans.	4

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
63. Zellweger MJ, Hachamovitch R, Kang X, et al. Threshold, incidence, and predictors of prognostically high-risk silent ischemia in asymptomatic patients without prior diagnosis of coronary artery disease. *J Nucl Cardiol* 2009; 16(2):193-200.	Observational-Dx	3,664 consecutive patients	To study incidence, threshold, and predictors of prognostically relevant silent ischemia.	Overall, ≥7.5% myocardium ischemic was consistent with high risk. 21 and 6% of patients had ischemia and high-risk ischemia, respectively. Patients with high-risk ischemia had a worse prognosis than patients with less silent ischemia, event rate of 3.1% and 0.4%, respectively, (P=.0001). Sex, age, diabetes, hypertension, abnormal resting ECG, angina, peak heart rate, blood pressure during treadmill testing, ST-depression, and Duke treadmill score were independent predictors of relevant silent ischemia.	3
64. Berman DS, Kang X, Hayes SW, et al. Adenosine myocardial perfusion single-photon emission computed tomography in women compared with men. Impact of diabetes mellitus on incremental prognostic value and effect on patient management. *J Am Coll Cardiol* 2003; 41(7):1125-1133.	Observational-Dx	6,173 consecutive patients	To assess the incremental prognostic value of adenosine stress myocardial perfusion SPECT in women vs men, and to explore the prognostic impact of diabetes mellitus.	During 27.0 +/- 8.8 month follow-up, cardiac death rates were lower in women than men (2.0%/year vs 2.7%/year, respectively, P<0.05). Before and after risk adjustment, cardiac death risk increased significantly in both men and women as a function of myocardial perfusion SPECT results. Multivariable models revealed that myocardial perfusion SPECT results provided incremental prognostic value over pre-scan data for the prediction of cardiac death in both genders. Also, while comparative unadjusted rates of early (≤60 days post-test) coronary angiography (17% vs 23%) and revascularization (8% vs 12%) were significantly lower in women (P<0.05), after adjusting for myocardial perfusion SPECT, these rates were similar in men and women. Importantly, diabetic women had a significantly greater risk of cardiac death compared with other patients. Also, after risk adjustment, patients with insulin-dependent diabetes mellitus had higher risk of cardiac death for any myocardial perfusion SPECT result than patients with non-insulin-dependent diabetes mellitus.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
65. Wackers FJ, Young LH, Inzucchi SE, et al. Detection of silent myocardial ischemia in asymptomatic diabetic subjects: the DIAD study. *Diabetes Care* 2004; 27(8):1954-1961.	Experimental-Dx	1,123 patients	To assess the prevalence and clinical predictors of silent myocardial ischemia in asymptomatic patients with type 2 diabetes and to test the effectiveness of current American Diabetes Association screening guidelines.	Moderate or large perfusion defects were present in 33 patients. The strongest predictors for abnormal tests were abnormal Valsalva (OR 5.6), male sex (2.5), and diabetes duration (5.2). Other traditional cardiac risk factors or inflammatory and prothrombotic markers were not predictive. Ischemic adenosine-induced ST-segment depression with normal perfusion (n=21) was associated with women (OR 3.4). Selecting only patients who met American Diabetes Association guidelines would have failed to identify 41% of patients with silent ischemia.	2
66. Young LH, Wackers FJ, Chyun DA, et al. Cardiac outcomes after screening for asymptomatic coronary artery disease in patients with type 2 diabetes: the DIAD study: a randomized controlled trial. *JAMA* 2009; 301(15):1547-1555.	Experimental-Dx	1,123 patients	To assess whether routine screening for CAD identifies patients with type 2 diabetes as being at high cardiac risk and whether it affects their cardiac outcomes.	The cumulative cardiac event rate was 2.9% over a mean (SD) follow-up of 4.8 (0.9) years for an average of 0.6% per year. 7 nonfatal MIs and 8 cardiac deaths (2.7%) occurred among the screened group and 10 nonfatal MIs and 7 cardiac deaths (3.0%) among the not-screened group (HR, 0.88; 95% CI, 0.44-1.88; P=.73). Of those in the screened group, 409 participants with normal results and 50 with small MPI defects had lower event rates than the 33 with moderate or large MPI defects; 0.4% per year vs 2.4% per year (HR, 6.3; 95% CI, 1.9-20.1; P=.001). Nevertheless, the PPV of having moderate or large MPI defects was only 12%. The overall rate of coronary revascularization was low in both groups: 31 (5.5%) in the screened group and 44 (7.8%) in the unscreened group (HR, 0.71; 95% CI, 0.45-1.1; P=.14). During the course of study there was a significant and equivalent increase in primary medical prevention in both groups.	2

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
67. Gibbons RJ, Chatterjee K, Daley J, et al. ACC/AHA/ACP-ASIM guidelines for the management of patients with chronic stable angina: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients With Chronic Stable Angina). *J Am Coll Cardiol* 1999; 33(7):2092-2197.	Review/Other-Dx	N/A	Guidelines for the management of patients with chronic stable angina.	This report attempts to combine previous sets of similar and dissimilar recommendations into one set of final recommendations.	4
68. Voigt JU, Exner B, Schmiedehausen K, et al. Strain-rate imaging during dobutamine stress echocardiography provides objective evidence of inducible ischemia. *Circulation* 2003; 107(16):2120-2126.	Observational-Dx	44 patients	To investigate strain-rate imaging markers of stress-induced ischemia and analyzed their applicability in a clinical setting.	In nonischemic segments, peak systolic strain rate increased significantly with dobutamine stress (-1.6 +/- 0.6 s-1 vs -3.4 +/- 1.4 s-1, P<0.01), whereas strain during ejection time changed only minimally (-17 +/- 6% vs -16 +/- 9%, P<0.05). During dobutamine-atropine stress echocardiography, 47 myocardial segments in 19 patients developed scintigraphy-proven ischemia. Strain-rate increase (-1.6 +/- 0.8 s-1 vs -2.0 +/- 1.1 s-1, P<0.05) and strain (-16 +/- 7% vs -10 +/- 8%, P<0.05) were significantly reduced (both P<0.01 compared with nonischemic). Postsystolic shortening was found in all ischemic segments. The ratio of postsystolic shortening to maximal segmental deformation was the best quantitative parameter to identify stress-induced ischemia. Compared with conventional readings, strain-rate imaging curved M-mode assessment improved sensitivity/specificity from 81%/82% to 86%/90%.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
69. McCully RB, Roger VL, Mahoney DW, et al. Outcome after normal exercise echocardiography and predictors of subsequent cardiac events: follow-up of 1,325 patients. *J Am Coll Cardiol* 1998; 31(1):144-149.	Observational-Dx	1,325 patients	To analyze outcomes after normal exercise echocardiography and predictors of subsequent cardiac events.	Overall survival of the study group was significantly better than that of an age- and gender-matched group obtained from life tables (P<0.0001). The cardiac event-free survival rates at 1, 2 and 3 years were 99.2%, 97.8% and 97.4%, respectively. The cardiac event rate per person-year of follow-up was 0.9%. Subgroups with an intermediate or high pretest probability of having CAD also had low cardiac event rates. Multivariate predictors of subsequent cardiac events were angina during treadmill exercise testing (RR 4.1, 95% CI, 1.5 to 11.0), low work load (defined as <7 metabolic equivalents for men and <5 metabolic equivalents for women; RR 3.2, 95% CI, 1.4 to 7.6), echocardiographic left ventricular hypertrophy (RR 2.6, 95% CI, 1.1 to 6.3) and advancing age (RR 1.04/year, 95% CI, 1.0 to 1.1).	3
70. Poldermans D, Fioretti PM, Boersma E, et al. Long-term prognostic value of dobutamine-atropine stress echocardiography in 1737 patients with known or suspected coronary artery disease: A single-center experience. *Circulation* 1999; 99(6):757-762.	Observational-Dx	1,734 consecutive patients	To assess the long-term value of dobutamine-atropine stress echocardiography for prediction of late cardiac events in patients with proven or suspected CAD.	428 cardiac events occurred in 366, documented cardiac death in 108 (total death, 247), nonfatal infarction in 128, and late revascularization in 192 patients. In a multivariable Cox proportional-hazards model, the ratio of documented cardiac death or (re)infarction was increased in the presence of stress-induced ischemia (HR, 3.3; 95% CI, 2.4 to 4.4) and extensive rest wall motion abnormalities (HR, 1.9; 95% CI, 1.3 to 2.6). The number of ischemic segments was predictive for late cardiac events. A normal dobutamine-atropine stress echocardiography carried a relatively good prognosis, with an annual event rate of cardiac death or infarction of 1.3% over a 5-year period.	3

Asymptomatic Patient at Risk for Coronary Artery Disease
EVIDENCE TABLE

Reference	Study Type	Patients/ Events	Study Objective (Purpose of Study)	Study Results	Study Quality
71. Chelliah R, Anantharam B, Burden L, Alhajiri A, Senior R. Independent and incremental value of stress echocardiography over clinical and stress electrocardiographic parameters for the prediction of hard cardiac events in new-onset suspected angina with no history of coronary artery disease. *Eur J Echocardiogr* 2010; 11(10):875-882.	Observational-Dx	547 consecutive patients	To evaluate the independent and incremental value of stress echocardiography over clinical and stress electrocardiographic parameters for the prediction of hard cardiac events in new-onset suspected angina.	At a median follow-up period of 28 months, there were a total of 35 hard cardiac events (5 deaths and 30 non-fatal AMI). Among the prognostic clinical, resting/stress ECG, and standard error data, univariate predictors were the Framingham risk score (P=0.025), diabetes (P=0.06), hypercholesterolaemia (P=0.06), stress ECG ischaemia (P=0.044), stress heart rate (P = 0.019), and standard error-determined ischemic burden (stress-rest wall thickening score index; P<0.001). In a multivariate model, ischemic burden was the only independent predictor of events (P<0.001). Standard error also showed incremental prognostic value over and above clinical (Framingham's risk score) and stress ECG changes in a global $\chi(2)$ model. This was true also for patients undergoing only exercise standard error (n=347).	3

Evidence Table Key

Study Quality Category Definitions

- *Category 1* The study is well-designed and accounts for common biases.
- *Category 2* The study is moderately well-designed and accounts for most common biases.
- *Category 3* There are important study design limitations.
- *Category 4* The study is not useful as primary evidence. The article may not be a clinical study or the study design is invalid, or conclusions are based on expert consensus. For example:
  a) the study does not meet the criteria for or is not a hypothesis-based clinical study (e.g., a book chapter or case report or case series description);
  b) the study may synthesize and draw conclusions about several studies such as a literature review article or book chapter but is not primary evidence;
  c) the study is an expert opinion or consensus document.

Dx = Diagnostic

Tx = Treatment

Abbreviations Key

AUC = Area under the receiver operating characteristic curve

CACS = Coronary artery calcium score

CAD = Coronary artery disease

CCTA = Coronary computed tomographic angiography

CHD = Coronary heart disease

CI = Confidence interval

CT = Computed tomography

CVD = Cardiovascular disease

EBCT = Electron-beam computed tomography

ECG = Electrocardiogram

HDL-C = High-density lipoprotein cholesterol

HR = Hazard ratio

LDL-C = Low-density lipoprotein cholesterol

MDCT = Multidetector computed tomography

MI = Myocardial infarction

MPI = Myocardial perfusion imaging

MRI = Magnetic resonance imaging

NPV = Negative predictive value

OR = Odds ratio

PET = Positron emission tomography

PGT = Prospectively gated transverse

PPV = Positive predictive value

RGH = Retrospectively gated helical

ROC = Receiver-operator characteristic

RR = Relative risk

SD = Standard deviation

SPECT = Single-photon emission tomography