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ORIGINAL PAPER

Incremental value of stress echocardiography and computed tomography coronary calcium scoring for the diagnosis of coronary artery disease

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Abstract

Computed tomography coronary angiography (CTCA) has a higher negative predictive value (NPV) for coronary artery disease (CAD) than stress echocardiography (SE). CT calcium scoring (CTCS) allows detection and quantification of coronary artery calcification (CAC). The NPV of combined SE and CTCS for CAD is not well defined. Consecutive patients from the executive screening program who underwent exercise SE and concomitant CTCA were retrospectively identified between January 2010 and December 2014. Patients with normal SE and CAC score of zero were determined, and the presence or absence of any CAD (obstructive or non-obstructive plaques) on CTCA was confirmed. The NPV of combined SE and CTCS was then re-tested using a validation cohort of subsequent consecutive patients enrolled between January 2015 and July 2018. The initial cohort consisted of 173 patients (19% age > 65 years, 19% diabetic); 40% had normal CTCA, 48% with non-obstructive CTCA (77 with CAC score > 0), and 12% with obstructive CTCA (all with CAC score > 0). There were 16 (9.2%) patients with inducible ischemia on SE. A normal SE had a 93% NPV to exclude obstructive CAD but only 42% NPV to exclude any CAD. A combined normal SE and CTCS had a 100% NPV for obstructive CAD, and 92% for any CAD. In a validation cohort of 111 patients, a normal SE and CAC score of zero had NPV of 100% for obstructive CAD and 92% for any CAD. The combined cohort consisted of predominately low Framingham risk patients; more than 40% (70/181) had CAC score > 0 and 5/70 had obstructive CAD, with the remaining non-obstructive. A concomitant normal SE and CAC score of zero excluded obstructive CAD (NPV 100%) and any CAD in 92% of the testing and validation cohorts. CTCS seems to add incremental risk stratification, particularly for patients with low Framingham score.

Keywords Stress echocardiography · Computed tomography coronary angiography · Coronary artery disease · Coronary artery calcium score

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Abbreviations

CAC	Coronary artery calcification/calcium
CAD	Coronary artery disease

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CTCA Computed tomography coronary angiography
CTCS Computed tomography calcium scoring
ECG Electrocardiogram
FRS Framingham risk score
HR Heart rate
MACE Major adverse cardiovascular events
NPV Negative predictive value
PPV Positive predictive value
SE Stress echocardiography

Introduction

Stress echocardiography (SE) has become a standard routine non-invasive imaging technique for evaluation of coronary artery disease (CAD) [1, 2]. Computed tomography coronary angiography (CTCA), however, is superior to SE in excluding CAD, with a higher negative predictive value (NPV) and ability to detect non-obstructive disease [3]. It allows visualization of calcified and non-calcified plaques as well as quantification of luminal obstruction. However, it requires administration of intravenous contrast, heart rate preparation and radiation exposure. Non-contrast CT calcium scoring (CTCS) allows detection and quantification of coronary artery calcification (CAC) and does not require contrast administration or preparation [1, 4]. There are limited data however using combined SE and CTCS for diagnosis of CAD. Our study aimed at assessing the added value of both techniques in comparison with CTCA to exclude CAD.

Methods

Study population

From the SE database at Clemenceau Medical Center, Beirut, Lebanon, we retrospectively identified all consecutive patients undergoing executive screening program between January 2010 and December 2014. All patients had SE and same day CTCA. All patients were younger than 75 years, had normal resting left ventricular ejection fraction, no prior history of significant valvular disease, arrhythmia, left bundle branch block, congenital heart disease, pericarditis of any etiology, myocarditis, previous cardiac surgery or myocardial infarction within the last 6 months. While many patients had risk factors and wanted to be checked out, several patients had non-specific or atypical symptoms.

A validation cohort was also identified and included consecutive executive patients enrolled between January 2015 and July 2018. Demographics and comorbidities were prospectively entered at the time of testing and were subsequently retrieved for analysis. Framingham 10-year risk score for coronary heart disease was calculated and patients were stratified as low (< 10%), intermediate (10–20%) or high risk (> 20%) [5–7].

This research study was approved by the Institutional Review Board committee and complied with the Declaration of Helsinki [8].

Hemodynamics

Resting and peak stress heart rate (HR) and blood pressure measurements were recorded prospectively at the time of stress testing and subsequently retrieved from the database.

Resting and stress echocardiography

The SE study consisted of performing a full resting transthoracic echocardiogram followed by exercise stress and then reacquiring images at peak stress. The resting transthoracic echocardiogram was performed with the patient in the left lateral decubitus position using the commercially available machines GE, Vivid E9 Vingmed Ultrasound, Horten, Norway (for the initial cohort) and GE Healthcare Vivid E95 (for the validation cohort), with the M5Sc-D probe. The images were recorded and saved on the machines, and offline analyses were performed using EchoPAC software (GE Medical Systems, Model BT10, Horten, Norway).

Five views were obtained during image acquisition: parasternal long axis, parasternal short axis, apical four chamber, apical two chamber, and apical three chamber. The whole echocardiographic study was performed by the same physician and in the same echocardiography laboratory.

Left ventricular ejection fraction was assessed in semi-quantitative manner using the biplane Simpson method (for most patients) or Teichholz's method (for those with suboptimal images) in case of regional wall motion abnormalities (WMAs) as previously described [9].

After obtaining rest images, exercise testing was performed according to a multistage, variable load, upright bicycle ergometer starting by a workload of 25 W and increasing by an increment of 25 W for every 2 min as previously published [10]. Duke treadmill score was calculated using minutes of exercise, ST changes and angina score, and classified as low (≥ 5), intermediate (> − 10 but < 4), or high (< − 10) [11, 12]. The echocardiographic images were acquired at peak stress within 1 min with standardized views according to the published guidelines [10].

SE was considered normal (no inducible ischemia) or abnormal if new exercise-induced WMAs were detected at peak stress in one or more segments or there was early termination of the study as a result of ST-segment changes consistent with ischemia, fatigue, chest pain, any arrhythmia, or hypotension. Images were interpreted independently and by a level III trained echocardiography-certified cardiologist (EC) who was blinded to the results of the CTCA. In case of a discrepancy, the images were reviewed by a second cardiologist.

Computed tomography coronary angiography and coronary artery calcium scoring

CTCA was performed as a standard test on all patients for the diagnosis of CAD, using 64-slice GE Discovery 750 HD GSI scanner according to CMC protocol and as previously published [13]. All coronary scans were performed after the SE, during the same day. The CTCA study included a calcium score assessment followed by intravenous contrast administration for the coronary angiogram. The CTCS and CTCA were read by a level III trained cardiologist (WJ) who was blinded to the results of the SE.

Patient preparation and premedication

Resting HR was measured for all patients who underwent CTCA before the procedure with a target HR ≤ 60 bpm for optimal images. Accordingly, patients were prepared and often required the administration of beta blockers with or without ivabradine.

Image acquisition and electrocardiogram gating

The CTCA scan was performed using an electrocardiogram (ECG)-gated retrospective study similar to a previously published protocol [13, 14]. Images were reconstructed using continuous acquisition of CTCA data throughout the cardiac cycle. The use of retrospective ECG-gated reconstruction allowed image reconstruction at different points of the R-R interval, allowing to choose the optimal cycle for image reconstruction. CTCA was considered normal, non-obstructive CAD, or obstructive CAD (plaque with ≥ 70% stenosis in a major epicardial vessel or ≥ 50% stenosis in the left main coronary artery).

The CTCS was an ECG-gated prospective study performed similar to a previously published protocol [13]. Standard Agatston's method was used to calculate the degree of CAC [15]. Image slices were typically triggered between 65% and 80% of the R-R interval. Threshold for calcific lesions was set a priori at a density of ≥ 130 Hounsfield units with a minimal area of 1 mm^2, as previously published [15].

Statistical analysis

Continuous data were expressed as mean ± standard deviation and compared using the two-tailed Student's t-test for normally distributed data, and the Wilcoxon test for skewed data. Categorical data were displayed as frequencies and percentages, and compared using Pearson Chi square test. Two by two factorial tables were performed to compare reported and actual presence of CAD, and determine NPV of the tests. All tests were two-tailed, and a P-value < 0.05 (set a priori) was considered statistically significant. All statistical analyses were carried out with SPSS Statistics version 22 (IBM, Inc., Armonk, NY).

Results

Baseline characteristics

There were 173 patients (mean age 53 years, 19% older than 65 years, 83% male, and 19% diabetic) who had concomitant SE and CTCA (initial testing cohort). Patients with obstructive CTCA had more cardiovascular risk factors and co-morbidities (Table 1).

Combined SE and CTCS stratified by CTCA

There were 69 (40%) patients with normal CTCA, 83 (48%) with non-obstructive CTCA (77 with CAC score > 0, median CAC score 40, IQR 5-238), and 21 (12%) with obstructive CTCA (all with CAC score > 0, median CAC score 238, IQR 238–488). There were 16 (9.2%) patients with inducible ischemia on SE (3 with normal CTCA, 3 with non-obstructive CTCA, and 10 with obstructive CTCA, P-value < 0.0001) (Table 2).

A normal SE had a 93% NPV to exclude obstructive CAD but only 42% NPV to exclude any CAD (non-obstructive and obstructive). There were 72 patients with no ischemia and CAC score of zero; 66 (96%) had normal CTCA, 6 (7%) had non-obstructive CAD, and none with obstructive CAD (Table 2). A combined normal SE and CTCS had a 100% NPV for obstructive CAD, and 92% for any CAD (non-obstructive or obstructive).

Validation cohort

When repeating the same analysis in a validation cohort of 111 patients (mean age 54 years, 17% elderly, 82% male, 14% diabetic), there were 53 patients with no ischemia and CAC score of zero (49 with normal CTCA, 4 with non-obstructive CAD and none with obstructive CAD). Combined normal SE and CTCS had a corresponding NPV of 100% for obstructive CAD and 92% for any CAD. Figure 1 summarizes the findings of the combined cohort.

Framingham risk score

The combined cohort consisted of 284 patients, the majority of which having low Framingham risk score (FRS) (181/284), with 70 and 33 having intermediate and high scores, respectively (Fig. 2). While the majority of patients

Table 1 Baseline characteristics stratified by computed tomography coronary angiography results of the initial cohort

Variable	All patients (N = 173)	Normal CTCA (N = 69)	Non-obstructive CTCA (N = 83)	Obstructive CTCA (N = 21)	P-value
Age, years	53 ± 12	46 ± 11	55 ± 9	68 ± 8	< 0.0001
Age > 65 years	33 (19%)	5 (7.2%)	12 (15%)	16 (76%)	< 0.0001
Male gender	114 (83%)	49 (79%)	78 (94%)	17 (81%)	0.001
BMI, Kg/m^2	29 ± 5	28 ± 4	30 ± 5	31 ± 6	0.032
Resting SBP, mmHg	118 ± 12	114 ± 10	120 ± 12	124 ± 15	0.01
Resting HR, bpm	69 ± 10	69 ± 8	69 ± 10	72 ± 15	0.36
Cerebrovascular disease	23 (13%)	2 (2.9%)	8 (9.6%)	13 (61.9%)	< 0.0001
Diabetes mellitus	32 (19%)	5 (72%)	20 (24%)	7 (33%)	0.005
Hypertension	55 (32%)	9 (13%)	32 (39%)	14 (67%)	< 0.0001
Dyslipidemia	64 (37%)	15 (22%)	34 (41%)	15 (71%)	< 0.0001
Smoking history	112 (65%)	41 (59%)	57 (69%)	14 (67%)	0.48
Ejection fraction (%)	65 ± 8	69 ± 8	69 ± 10	62 ± 10	0.22

BMI Body Mass Index, *bpm* beats per minute, *CTCA* computed tomography coronary angiography, *HR* heart rate, *SBP* systolic blood pressure

Table 2 Coronary artery calcium score and stress echocardiogram results stratified by computed tomography coronary angiography results of the initial cohort

Variable	All patients (N = 173)	Normal CTCA (N = 69)	Non-obstructive CTCA (N = 83)	Obstructive CTCA (N = 21)	P-value
CAC present	98 (57%)	0 (0%)	77 (93%)	21 (100%)	< 0.0001
CAC score (median, IQR)	3 (0; 184)	0 (0; 0)	40 (5; 238)	238 (238;488)	< 0.0001
Ischemia	16 (9.2%)	3 (4.3%)	3 (3.6%)	10 (48%)	< 0.0001
Ischemia and CAC score					< 0.0001
No ischemia and CAC = 0	72 (42%)	66 (96%)	6 (7%)	0 (0%)	
Ischemia and CAC = 0	3 (1.7%)	3 (4%)	0 (0%)	0 (0%)	
No ischemia and CAC > 0	85 (49%)	0 (0%)	74 (89%)	11 (52%)	
Ischemia and CAC > 0	13 (7.5%)	0 (0%)	3 (4%)	10 (48%)	
Poor image quality on SE	41 (24%)	17 (25%)	19 (23%)	5 (24%)	0.48

bpm beats per minute, *CAC* coronary artery calcium, *CTCA* computed tomography coronary angiography, *IQR* interquartile range, *SE* stress echocardiography

with intermediate and high FRS had CAC score > 0 (74% and 91%, respectively), more than 40% of patients with low FRS had CAC score > 0 with 69/74 and 5/74 having non-obstructive and obstructive CTCA, respectively (Fig. 2). Hence, among patients with low FRS who were predominately asymptomatic and coming for an executive check-up, only half (99/181) had a normal CTCA.

Discussion

In this retrospective single center study, 284 patients with predominately low-intermediate FRS and mainly asymptomatic (executive check-up), were evaluated to assess the combined role of SE and CTCS in excluding CAD. The main findings of this study were: (1) almost half of patients with no inducible ischemia on SE had CAC score of zero (2) CAC score of zero increased the NPV of normal SE for exclusion of obstructive CAD from 93 to 100%; (3) concomitant normal SE and CTCS had a NPV of 92% compared to 42% for normal SE alone for any CAD; (4) 40% of patients with low FRS have CAC score > 0 with 7% (5/74) having obstructive CAD; and (5) only half of predominately asymptomatic patients with low FRS have normal CCTA.

While SE demonstrates high specificity for obstructive CAD [16] as also seen in our study (specificity 77%, 16 patients by SE vs. 21 patients by CTCA), it is relatively insensitive for small areas of subendocardial or microvascular ischemia in patients who were free of chest pain at the time of peak stress or those with poor image quality or off-axis imaging (Table 2). Nevertheless, it cannot exclude non-obstructive plaques (majority have CAC score > 0) as most of them are not hemodynamically flow limiting. Still, these patients are at higher risk for future major adverse

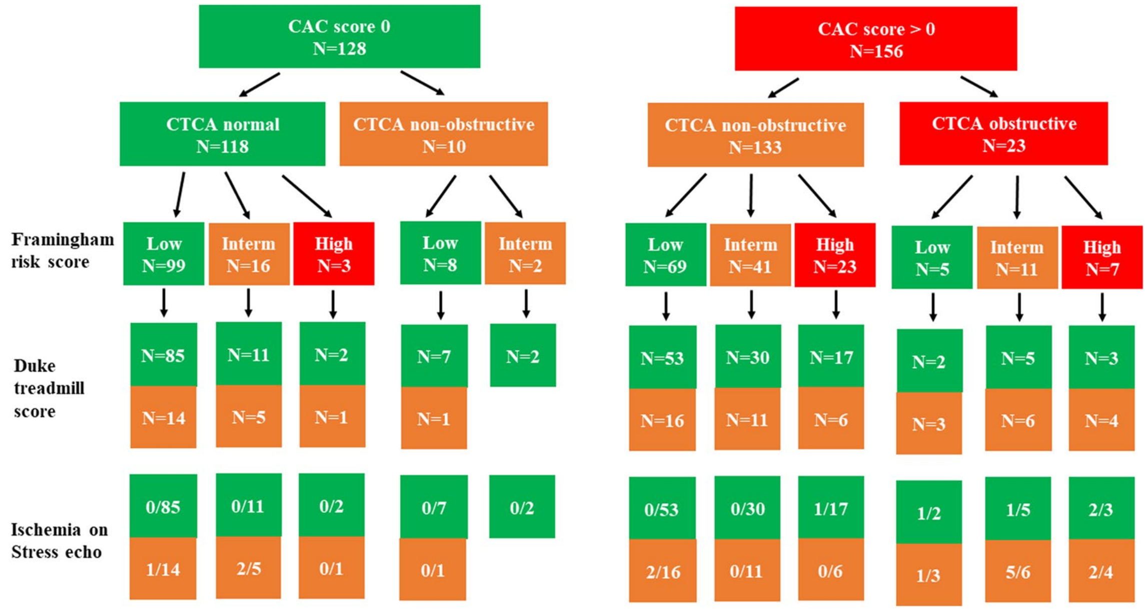

Fig. 1 Color-coded diagram of the combined cohort showing patients divided according to their calcium score and further classified according to their Framingham risk score, Duke treadmill score and ischemia on stress echocardiography. *CAC* coronary artery calcium, *CTCA* computed tomography coronary angiography, *Interm* intermediate. Green: low risk, orange: intermediate risk; red: high risk

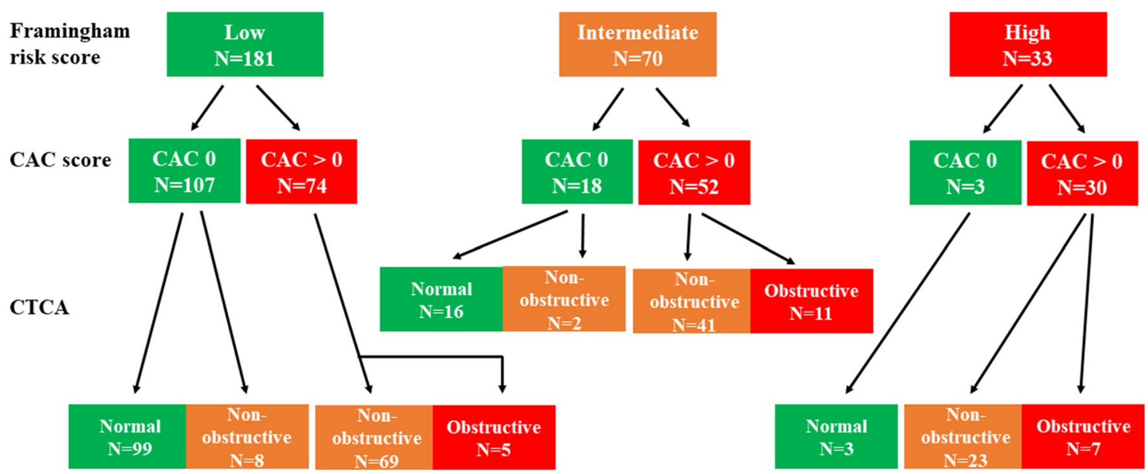

Fig. 2 Color-coded diagram of the combined cohort showing patients divided according to their Framingham risk score and further classified according to their calcium score and CT coronary angiogram findings. *CAC* coronary artery calcium, *CTCA* computed tomography coronary angiography

cardiovascular events (MACE) as compared to those with CAC score of zero [1]. In a large multicenter cohort conducted on greater than 8800 patients with stable ischemic heart disease [1], CTCS was compared to functional testing; while functional testing carried a high specificity for the diagnosis of obstructive CAD, a CAC score of zero excluded future MACE [1]. This was also seen in a more recent study where CAC score of zero had 100% NPV for predicting MACE [17].

While pharmacological stress cardiac magnetic resonance (CMR) myocardial perfusion imaging (MPI) is effective in diagnosing CAD and risk-stratifying patients with suspected myocardial ischemia as recommended by the recent guidelines [16], it is indicated for patients at intermediate to high pretest probability of ischemic heart disease and its availability is often limited to highly specialized centers.

Compared to CTCA, CTCS has lower diagnostic accuracy [18]. However, when CAC score is added to single-photon emission computed tomography and positron emission tomography MPI using hybrid scanners [19, 20], it adds to the diagnostic accuracy of the study. Indeed, Berman et al. [20] showed that ischemia was rarely seen on perfusion imaging with a CAC score < 100. Also, while CAC score, CTCA and MPI are individually predictors of MACE, CTCA does not provide incremental prognostic information after combining CAC score and MPI findings with clinical data [17].

Our findings underline the added value of CTCS to the SE study, which is not well defined, as most studies included CTCS with MPI. In fact, concomitant SE and CTCS had a 100% NPV for excluding obstructive CAD, similar to CTCA. Thus, the combined technique could screen for subclinical obstructive CAD, further reclassify patients, change treatment, prognosis, and enhance follow-up in order to have important implications for patients' health-related quality of life, and therefore affecting clinical-decision making and outcome [19].

In a review comparing the cost-effectiveness of non-invasive imaging modalities for evaluation of low-intermediate risk patients with chronic stable chest pain [18], CTCA has been proven to be a cost-effective and accurate test. Although CTCA provides better understanding of the coronary anatomy, CTCS is much cheaper and does not require administration of intravenous contrast [1, 4, 19]. In addition, it has a significantly lower radiation burden as compared to CTCA [1, 4]. When examining the role of this diagnostic test, consideration must be placed not only on the accuracy of the results, but also its impact on patient care and outcomes. This is further implicated in the health status of low-income countries and patient population. Consistent with the changing patterns of diagnosis and follow-up, the use of CTCA was associated with increased recommendations for preventive therapies [3, 21].

The current guidelines recommend against screening with CAC score of asymptomatic patients at low FRS [7]. However, such guidelines are not strictly enforced in clinical practice. In a large multi-ethnic study conducted on women at low FRS, 30% of them had prevalent CAC. The authors found that the presence of CAC was an independent predictor of coronary heart disease and cardiovascular disease on 3.75 years follow-up [22]. Indeed, CAC score is routinely performed at our institution for patients presenting for an executive check-up. Of patients with low FRS, 40% had CAC score > 0 with 7% (5/74) having obstructive CAD. This subgroup of patients who would have not had a CTCS if strict guidelines were implemented, is at higher risk for MACE and would benefit from secondary prevention using statins for example. Whether indeed such risk stratification by CAC score of this low risk score would impact outcomes and whether it is cost-effective is worth further evaluation. While the current results of our study do not imply that we should disregard the current guideline recommendation and perform CAC score on all asymptomatic patients with low FRS, further evaluation, validation from larger multicenter registries is warranted, particularly that CAC score is routinely available, relatively cheap and easy to perform.

Strengths and limitations

To the best of our knowledge, this is the first study to assess patients with low-intermediate risk using concomitant SE and CTCS for diagnosis of CAD, and to validate it in a large cohort. Furthermore, SE and CTCS/CTCA results were interpreted independently and blindly by two readers/experienced cardiologists. Also, the study provides relevant information on low risk predominately asymptomatic patients undergoing non-invasive imaging. However, we recognize several limitations. First, data were collected from the same executive screening program; patients were at low-intermediate risk for MACE with minimal symptoms or presenting for check-up, and do not reflect other group of patients presenting to clinic and daily practice. Second, the majority of patients enrolled were men. Since non-invasive diagnostic testing for CAD may be less accurate in women than in men (because of the higher prevalence of atypical chest pain among women) [23], our results cannot be generalized to the whole population. Third, our data lacked family history for dyslipidemia and atherosclerotic disease, particularly for patients at low FRS. In addition, it is not clear whether the use of concomitant SE and CTCS instead of CTCA affects outcome or not. Finally, we used CTCA as a gold standard to identify obstructive CAD rather than invasive coronary angiography or fractional flow reserve.

Conclusions

In this retrospective single center study of low-intermediate risk patients undergoing exercise SE and CTCA, a concomitant negative SE for ischemia and CAC score of zero excluded obstructive CAD (NPV 100%), and excluded non-obstructive soft plaques in 92% of patients and in the validation cohort as well. Hence, CTCS can further risk stratify patients undergoing SE, exclude CAD and obviate the need for further more expensive testing such as CTCA and/or invasive coronary angiography. While the current results of our study do not imply that we should disregard the current guideline recommendation and perform CAC score on all asymptomatic patients with low FRS, further evaluation, validation from larger multicenter registries is warranted. This is particularly true since CAC score > 0 which is well known to be an independent predictor of outcomes is very common in this cohort.

Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

References

1. Budoff MJ, Mayrhofer T, Ferencik M, Bittner D, Lee KL, Lu MT et al (2017) Prognostic value of coronary artery calcium in the PROMISE study (prospective multicenter imaging study for evaluation of chest pain). Circulation 136(21):1993–2005
2. Neglia D, Rovai D, Caselli C, Pietila M, Teresinska A, Aguade-Bruix S et al (2015) Detection of significant coronary artery disease by noninvasive anatomical and functional imaging. Circ Cardiovasc Imaging 8:e002179
3. Doris M, Newby DE (2016) How should CT coronary angiography be integrated into the management of patients with chest pain and how does this affect outcomes? Eur Heart J Qual Care Clin Outcomes 2(2):72–80
4. Budoff MJ, Shaw LJ, Liu ST, Weinstein SR, Mosler TP, Tseng PH et al (2007) Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol 49:1860–1870
5. Wilson PW, D'Agostino RB, Levy D, Belanger AM, Silbershatz H, Kannel WB (1998) Prediction of coronary heart disease using risk factor categories. Circulation 97:1837–1847
6. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB, Gibbons R Sr et al (2014) 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol 63:2935–2959 ;(25 Pt B)
7. Greenland P, Alpert JS, Beller GA, Benjamin EJ, Budoff MJ, Fayad ZA et al (2010) 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 56(25):e50–e103
8. Mansour MJ, Aljaroudi W, Mroueh A, Hamoui O, Honeine W, Khoury N et al (2017) Stress-induced worsening of left ventricular diastolic function as a marker of myocardial ischemia. J Cardiovasc Echogr 27:45–51
9. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al (2015) Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 16:233–237
10. Pellikka PA, Nagueh SF, Elhendy AA, Kuehl CA, Sawada SG, American Society of Echocardiography et al (2007) American society of echocardiography recommendations for performance, interpretation, and application of stress echocardiography. J Am Soc Echocardiogr 20:1021–1041
11. Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR et al (1991) Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med 325(12):849–853
12. Gibbons RJ, Balady GJ, Beasley JW, Bricker JT, Duvernoy WF, Froelicher VF et al (1997) ACC/AHA guidelines for exercise testing: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Exercise Testing). Circulation 96(1):345–354
13. Abbara S, Blanke P, Maroules CD, Cheezum M, Choi AD, Han BK (2016) SCCT guidelines for the performance and acquisition of coronary computed tomographic angiography: A report of the society of Cardiovascular Computed Tomography Guidelines Committee: Endorsed by the North American Society for Cardiovascular Imaging (NASCI). J Cardiovasc Comput Tomogr 10(6):435–449
14. Schroeder S, Achenbach S, Bengel F, Burgstahler C, Cademartiri F, de Feyter P et al (2008) Cardiac computed tomography: indications, applications, limitations, and training requirements: report of a writing group deployed by the Working Group Nuclear Cardiology and Cardiac CT of the European Society of Cardiology and the European Council of Nuclear Cardiology. Eur Heart J 29:531–556
15. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R et al (1990) Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol 15(4):827–832
16. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP et al (2012) 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol 60(24):e44
17. Nappi C, Nicolai E, Daniele S, Acampa W, Gaudieri V, Assante R et al (2018) Long-term prognostic value of coronary artery calcium scanning, coronary computed tomographic angiography and stress myocardial perfusion imaging in patients with suspected coronary artery disease. J Nucl Cardiol 25:833–841
18. van Waardhuizen CN, Khanji MY, Genders TSS, Ferket BS, Fleischmann KE, Hunink MGM et al (2016) Comparative cost-effectiveness of non-invasive imaging tests in patients presenting with chronic stable chest pain with suspected coronary artery disease: a systematic review. Eur Heart J Qual Care Clin Outcomes 2(4):245–260
19. Greenland P, Blaha MJ, Budoff MJ, Erbel R, Watson KE (2018) Coronary calcium score and cardiovascular risk. J Am Coll Cardiol 72(4):434–447
20. Berman DS, Wong ND, Gransar H et al (2004) Relationship between stress-induced myocardial ischemia and atherosclerosis measured by coronary calcium tomography. J Am Coll Cardiol 44:923–930
21. Newby DE (2015) The SCOT-HEART investigators. CT coronary angiography in patients with suspected angina due to coronary heart disease (SCOT-HEART): an open label, parallel-group, multicenter trial. Lancet 385:2383–2391
22. Lakoski SG, Greenland P, Wong ND, Schreiner PJ, Herrington DM, Kronmal RA et al (2007) Coronary artery calcium scores and risk for cardiovascular events in women classified as "low risk" based on Framingham risk score: the multi-ethnic study of atherosclerosis (MESA). Arch Intern Med 167(22):2437–2442
23. Nasir K, Redberg RF, Budoff MJ, Hui E, Post WS, Blumenthal RS (2004) Utility of stress testing and coronary calcification measurement for detection of coronary artery disease in women. Arch Intern Med 164(15):1610–1620