3 Noninvasive Imaging Assessment of Coronary Heart Disease

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About Us The Robert Bosch Hospital is a charitable hospital in Stuttgart, Germany. It was founded by Robert Bosch in 1936. The hospital is supported by the Robert Bosch Foundation. The Department of Cardiology is part of the Center of Cardiovascular Medicine, which also includes the Department of Cardiac and Vascular Surgery. Noninvasive imaging is an essential aspect of managing cardiac patients and nuclear medicine examinations, echocardiography, magnetic resonance imaging, and computed tomography are performed frequently in the department. Treatment of stable and unstable coronary heart disease is frequently performed (800 PCI and more than 900 bypass operations per year). Indications for revascularization in stable patients with coronary heart disease are based on the results of ischemia testing.

Why Noninvasive Imaging in Coronary Heart Disease?

- Coronary heart disease (CHD) continues to be the most frequent cause of death in Western countries and attempts at reducing the death toll lead to high expenses for healthcare systems.
- Testing including noninvasive imaging is frequently performed in order to detect the presence of stenotic atherosclerotic disease of the coronary arteries which is thought to be the harbinger of doom. Early noninvasive detection is felt to be the optimal way of selecting patients who might benefit from subsequent coronary angiography.
- Ultimately, the aim is early intervention in the form of coronary revascularization in addition to medical therapy, with the expectation of relieving suffering and improving prognosis. Current European and US guidelines support this approach [1–3].

Do All Patients with Angina Have to Undergo Some Form of Preselection Testing Before Invasive Coronary Angiography?

- Some form of preselection testing in patients with stable coronary artery disease before invasive coronary angiography (ICA) makes sense in order to keep the number of normal coronary angiograms low.
- However, patients with severe angina and a high clinical likelihood of severe disease (clustering of risk factors, reduced ejection fraction) may and should undergo invasive coronary angiography without hesitation. This is certainly also true for patients with known coronary artery disease and such clinical features [1, 2].

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A. Myat et al. (eds.), *The Interventional Cardiology Training Manual*,
https://doi.org/10.1007/978-3-319-71635-0_3

- Patients with angina who have acute coronary syndromes (ACS) are usually sent for ICA based on current guidelines [4, 5]. However, stress imaging is also recommended before ICA in low-risk ACS patients (no troponin, no ECG changes) in order to confirm the diagnosis and perform risk stratification. In such patients stress imaging is preferred over stress ECG due to its better diagnostic performance. High-risk patients are sent to ICA [4].

Is the Stress ECG Completely Useless?

- In many situations the stress ECG is still an easy, cheap, and appropriate way of excluding relevant CHD. The following requirements need to be fulfilled:
  - Pretest probability for the presence of stenotic CHD should be reasonably low (below 50–60%). This excludes male patients and female patients older than 60 years with typical (retrosternal, elicited by exercise, stopped by rest or nitroglycerin) angina (see Table 3.1).
  - The 12-lead resting ECG should be interpretable (no ST-segment depression ≥1 mm, no bundle branch block, no pacemaker ECG).
  - Patients should be able to exercise adequately and reach 85% of target heart rate during exercise (i.e., 220 – age).
- These points pertain only to the diagnostic qualities of the exercise ECG not to its prognostic capabilities: irrespective of pretest probability and findings on the resting ECG, prognosis is generally good in a patient who is able to exercise to a high level of metabolic equivalents of task (METs) without angina (Duke treadmill score [6]).

Table 3.1 Clinical pretest probabilities in patients with stable chest pain symptoms

	Typical angina		Atypical angina		Non-anginal pain	
Age	Men	Women	Men	Women	Men	Women
30–39	59	28	29	10	18	5
40–49	69	37	38	14	25	8
50–59	77	47	49	20	34	12
60–69	84	58	59	28	44	17
70–79	89	68	69	37	54	24
>80	93	76	78	47	65	32

ECG electrocardiogram, *PTP* pretest probability, *SCAD* stable coronary artery disease

- Probabilities of obstructive coronary disease shown reflect the estimates for patients aged 35, 45, 55, 65, 75, and 85 years
- Groups in white boxes have a PTP <15% and hence can be managed without further testing
- Groups in blue boxes have a PTP of 15–65%. They could have an exercise ECG if feasible as the initial test. However, if local expertise and availability permit a noninvasive imaging-based test for ischemia this would be preferable given the superior diagnostic capabilities of such tests. In young patients radiation issues should be considered
- Groups in light red boxes have PTPs between 66 and 85% and hence should have a noninvasive imaging functional test for making a diagnosis of SCAD
- In groups in dark red boxes the PTP is >85% and one can assume that SCAD is present. They need risk stratification only
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How to Select Patients for Noninvasive Stress Imaging?

- Irrespective of pretest probability, stress imaging has a higher diagnostic accuracy than the stress ECG. The main difference is the higher sensitivity of stress imaging.
- However, there is one caveat: the low sensitivity of the stress ECG was reported in studies compensating for referral bias (this is the effect of preferentially including patients with abnormal stress ECGs into angiographic verification studies and underrepresentation of patients with normal stress ECGs in such studies which leads to overestimation of sensitivity and underestimation of specificity) [7].
- In contrast to the stress ECG, some stress imaging studies may not be entirely free from referral bias (at least it is often not mentioned that referral bias was systematically excluded), which would also lead to overestimation of sensitivity of these tests at the cost of specificity.
- However, a recent cardiac magnetic resonance (CMR) study in which all patients irrespective of the result of CMR were rigorously also studied by coronary angiography (exclusion of referral bias) confirmed the high sensitivity of this imaging technique while specificity was maintained above 80% [8].
- Single-photon-emission computed tomography (SPECT) perfusion imaging which was used for comparison in this study showed a sensitivity of only 67% (still above the sensitivity of the stress ECG) but specificity was at 83% similar to CMR. The low sensitivity of SPECT in this study without referral bias would support the argument that some of the stress imaging studies reported somewhat too high sensitivity values.
- The higher sensitivity of stress imaging is the argument for selecting one of these diagnostic procedures in patients who have an intermediate to high pretest probability [1, 2]. If the probability of having a flow-limiting coronary stenosis is already high based on sex, age, and angina typicality a low-sensitivity technique would miss many patients who might profit from an invasive procedure.
- Other advantages of stress imaging as compared to the exercise ECG are the ability to quantify and localize areas of ischemia and the ability to provide diagnostic information even in the presence of resting ECG abnormalities.
- Another important clinical reason for selecting stress imaging is the high diagnostic accuracy of pharmacologic stress testing. This makes this form of stress imaging ideally suited for patients who are too old or physically incapable of performing physical stress up to an adequate level.
- However, exercise testing better reflects the physical capacities of the patient and higher levels of stress can be achieved in many patients when exercise is used to provoke ischemia. One also gets a better impression about the level of exercise that provokes angina in daily life plus additional information from the ECG that is always registered simultaneously.
- Therefore, exercise stress testing in combination with imaging is preferred (if possible) over pharmacological stress testing alone although the reported sensitivities and specificities are similar.
- Finally, stress imaging is the first choice in patients with previous percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG), who often have preexisting ECG abnormalities and in whom the diagnosis of CAD is already known.
- On a more general note, the superior ability of stress imaging, compared with the exercise ECG, to localize and quantify ischemia also translates into more effective risk stratification, thus avoiding unnecessary invasive procedures [9]. This is why the 2013 ESC guidelines on the management of patients with stable coronary artery disease [1] recommend stress imaging as the first-line technique and the stress ECG only if imaging techniques are not available or too expensive.
- Stress imaging is also ideally suited to confirm or exclude ischemia in the perfusion bed of

angiographically seen intermediate coronary lesions (if fractional flow reserve—FFR—was not performed immediately). Ischemia associated with such lesions may be predictive of future events whereas the absence of ischemia can be used to define—and reassure—patients with a low cardiac risk [10].

Stress Imaging Versus Anatomic Imaging

- Noninvasive anatomic imaging of the coronary arteries has now become possible using advanced computed tomography (CT) technology [11]. The main advantages of coronary CT angiography are the following:
  - It has a superb capability of ruling out relevant CAD (sensitivity 98–99% [12]).
  - It can be quickly performed.
  - It provides additional information on the presence of coronary plaques which provides the indication for starting preventive medication [13].
- There are also downsides to the use of coronary CT angiography:
  - Specificity is not perfect and becomes rather low in patients who have a high pretest probability of disease [1]. The reason for this is that such patients frequently harbor coronary calcifications and these may lead to the false impression that the lumen is obstructed [14] (Fig. 3.1).
  - Coronary CT angiography exposes the patient to radiation and contrast media, which may be a problem in young patients, in the elderly, and those with renal dysfunction overall.
  - Coronary CT angiography does not provide adequate image quality in obese patients, those with irregular heart rhythms, or patients at a high heart rate (unless relatively high doses of radiation are applied). Table 3.2 lists factors to be considered when selecting patients for coronary CT angiography.
- Current guidelines still favor stress testing [2] (stress imaging [1]) over coronary CT angiography but this may soon change with the advent of the 2017 National Institute for Health and Care Excellence (NICE) guidelines on stable angina. Recent randomized data prove that outcomes are similar irrespective of whether functional or anatomic testing is the initial test in the workup of intermediate-risk patients with stable CHD [15]. However, patients in the CT arm had ICA more often and more revascularization procedures in this study [14].

Is CT Calcium Scoring Useful in Symptomatic Patients?

- The use of calcium scoring by CT in symptomatic patients has been intensely debated. A recent study in 868 patients with low- to intermediate-risk stable angina and a calcium score of zero showed ischemia in only 3% [16]. None of these patients had obstructive disease at angiography.
- This suggests that state-of-the-art calcium scoring which can be done at a very low radiation dose of 0.2 mSV should be performed before coronary CT angiography.
- This would allow skipping subsequent coronary CT angiography in 25% of patients and saving additional radiation [16].

Which Kind of Stress Imaging?

- There is no ideal stress imaging techniques suitable for all patients. Table 3.3 lists the advantages and disadvantages of the available techniques and Table 3.4 gives the values for sensitivity and specificity of these techniques as listed in the 2013 ESC guidelines on the management of stable coronary artery disease.
- The references on which the values in Table 3.4 are based can be found in the full text of the

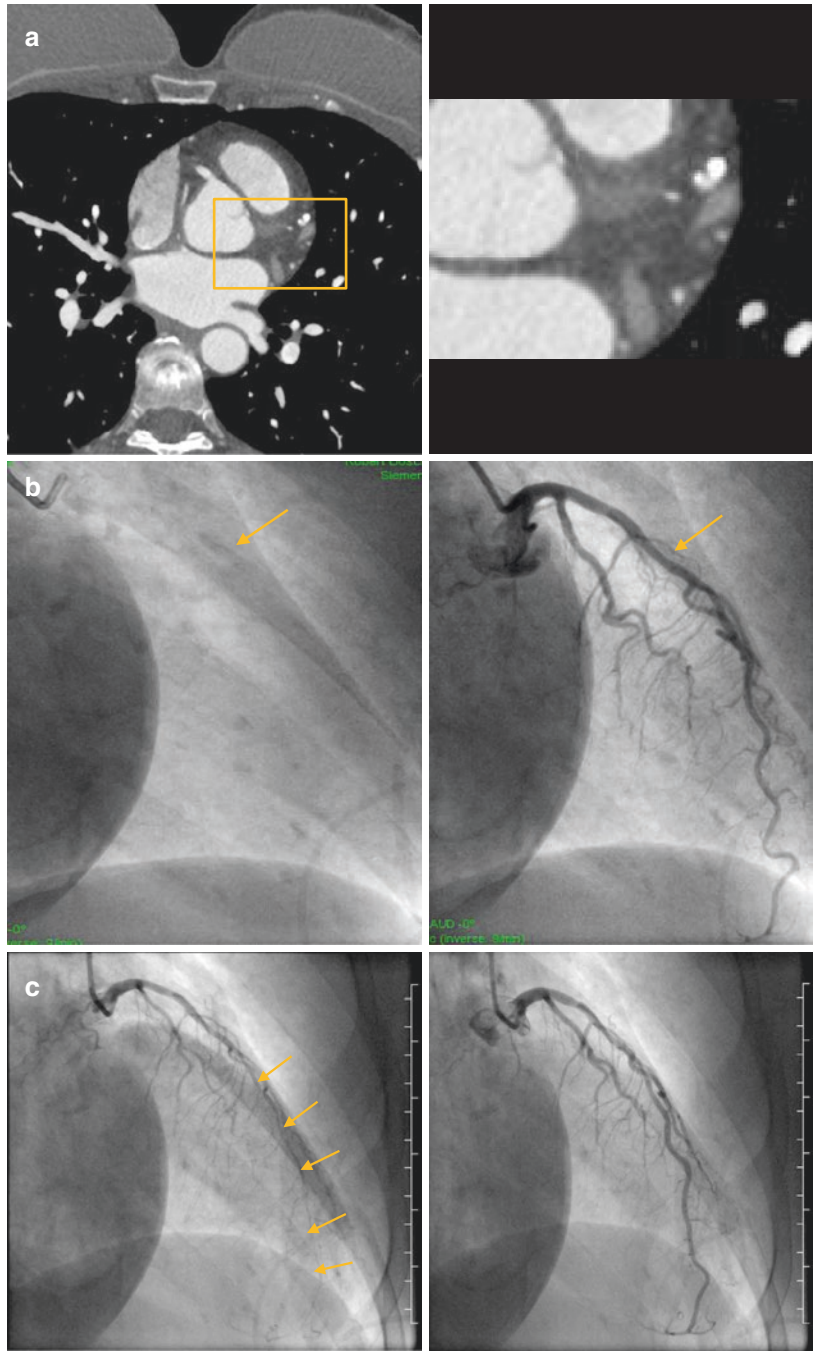

Fig. 3.1 Effect of a focal calcified plaque on the interpretation of coronary CT angiography examination. This 57-year-old woman had dyspnea when climbing three flights of stairs. She also had occasional mild resting chest pain. An exercise stress ECG was mildly abnormal (0.1 mV ST-segment depression). Her 64-line coronary CT angiogram showed focal calcification in the left anterior descending (LAD) coronary artery (Panel A with magnification inset) and was read as diagnostic of a significant stenosis in the LAD. Invasive coronary angiography was advised (Panel B). The grey shadow of linear calcification next to the LAD (yellow arrow) can be seen on the X-ray image without application of intracoronary contrast material (Panel B, left). It is evident that there is no LAD stenosis when contrast is injected (Panel B, right). Intracoronary acetylcholine testing (Panel C) demonstrated diffuse distal occlusive LAD spasm (left) associated with her usual chest oppression which, however, was now more intense. This indicates an enhanced reaction to the substance, which is often associated with clinical symptoms of microvascular dysfunction. LAD after intracoronary nitroglycerine is shown on the right (Panel C). Reproduced from Sechtem U et al. - Testing in patients with stable coronary artery disease – the debate continues. Circ J 2016;80:802–810 with permission of the publisher

Table 3.2 Patient factors considered important for optimal image quality of coronary CT angiography

No known CHD
Intermediate pretest probability up to 50%
Age <70 years
Regular heart rhythm
Low heart rate (e.g., <65 bpm), in some patients only after administration of beta-blockers
BMI <40 kg/m^2
Creatinine clearance >30 mL/kg/1.73 m^2
No known contrast allergy

BMI body mass index, *CHD* coronary heart disease, *CT* computed tomography

Table 3.3 Advantages and disadvantages of stress imaging techniques and coronary CT angiography

Technique	Advantages	Disadvantages
Echocardiography	Wide access	Echo contrast needed in patients with poor ultrasound windows
	Portability	
	No radiation	Dependent on operator skills
	Low cost	
SPECT	Wide access	Radiation
	Extensive data	
PET	Flow quantitation	Radiation
		Limited access
		High cost
CMR	High soft-tissue contrast including precise imaging of myocardial scar	Limited access in cardiology
		Contraindications
	No radiation	Functional analysis limited in arrhythmias
		Limited 3D quantification of ischemia
		High cost
Coronary CTA	High NPV in pts. with low PTP	Limited availability
		Radiation
		Assessment limited with extensive coronary calcification or previous stent implantation
		Image quality limited with arrhythmias and high heart rates that cannot be lowered beyond 60–65/min
		Low NPV in patients with high PTP

3D three-dimensional, *CMR*, cardiac magnetic resonance, *CTA* computed tomography angiography, *NPV* negative predictive value, *PET* positron-emission tomography, *PTP* pretest probability, *pts*. patients, *SPECT* single-photon-emission computed tomography

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ESC guideline (in Table 12 of the guideline). It is obvious that the range of these values is very similar between stress echocardiography, stress SPECT, and stress CMR. Stress PET plays a minor role because this technique is even less broadly available than stress CMR. The major players worldwide are stress echocardiography and stress SPECT.

- Stress echocardiography is the obvious choice for patients with adequate anatomy, as well as

Table 3.4 Characteristics of tests commonly used to diagnose the presence of coronary heart disease

	Diagnosis of CAD	
	Sensitivity (%)	Specificity (%)
Exercise ECG[a]	45–50	85–90
Exercise stress echocardiography	80–85	80–88
Exercise stress SPECT	73–92	63–87
Dobutamine stress echocardiography	79–83	82–86
Dobutamine stress MRI[b]	79–88	81–91
Vasodilator stress echocardiography	72–79	92–95
Vasodilator stress SPECT	90–91	75–84
Vasodilator stress MRI[b]	67–94	61–85
Coronary CTA[c]	95–99	64–83
Vasodilator stress PET	81–97	74–91

CAD coronary artery disease, *CTA* computed tomography angiography, *ECG* electrocardiogram, *MRI* magnetic resonance imaging, *PET* positron-emission tomography, *SPECT* single-photon-emission computed tomography

[a]Results without/with minimal referral bias

[b]Results obtained in populations with medium-to-high prevalence of disease without compensation for referral bias

[c]Results obtained in populations with low-to-medium prevalence of disease

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due to the availability of an experienced echocardiographer and sufficient space and manpower to perform this complex procedure in larger numbers of patients. This technique is cheap, does not expose the patient to ionizing radiation, and can be performed in many patients as an exercise stress test.

- However, interpretation of stress-induced wall motion abnormalities can be difficult, especially in the presence of preexisting wall motion abnormalities. Therefore, the use of contrast agents is advised when two or more contiguous segments in the 17 segment LV model are not well visualized at rest [17].
- The use of contrast during stress echocardiography not only enhances image quality, but also improves reader confidence and enhances accuracy for the detection of CHD.
- Myocardial perfusion scintigraphy (SPECT) is most commonly used in conjunction with technetium-99m radiopharmaceuticals as tracers. Symptom-limited physical exercise is the stress of choice.
- New SPECT cameras reduce radiation and/or acquisition times significantly [18]. In the US SPECT perfusion imaging is the most commonly used stress imaging modality whereas stress echocardiography is more prevalent in Europe. In the hands of experienced examiners both techniques yield similar results.
- Myocardial perfusion imaging using positron-emission tomography (PET) is superior to SPECT imaging for the detection of stable CHD in terms of image quality, interpretative certainty, and diagnostic accuracy [19]. It also has the unique ability to quantify blood flow in mL/min/g of myocardium, which allows detection of microvascular disease [20]. Nevertheless, PET scanners and especially cyclotron-produced radiotracers are more expensive than SPECT equipment, which limits their use in daily clinical practice.
- Stress CMR imaging is not performed with physical exercise but with pharmacological stress. If dobutamine is used as a stressor induction of wall motion abnormalities is the target. If adenosine is the stressor imbalances of perfusion are sought for.
- Stress CMR is an alternative to stress echocardiography in patients with suboptimal acoustic windows [21] or an alternative to stress SPECT for patients in whom radiation should be avoided [21].
- In a head-to-head comparison with SPECT, adenosine CMR was found to have a significantly better sensitivity in diagnosing obstructive coronary artery disease in women but specificities were similar for both techniques (both >80%) [22].

How Should Imaging Be Employed in a Patient with Suspected Stable Coronary Artery Disease?

- The guidelines of the ESC [1], the AHA guidelines [2], and the NICE guidelines [23] differ in their recommendations on the use of stress imaging in such patients. All three recommend stress testing in patients who have an intermediate pretest probability of obstructive disease.
- However, intermediate is defined in the NICE guidelines on "chest pain of recent onset" [23] as 10–90%, the ESC feel that the appropriate level is 15–85%, and the US guidelines set the level from 20 to 70%.
- All three guidelines recommend omitting testing in patients with a pretest probability below these levels. The reason is that the imperfect test characteristics of the main test employed (stress ECG, stress echocardiogram, stress SPECT) lead to a higher number of false positives than true positives at this low level of pretest probability.
- Guidelines differ in their recommendations on what to do with patients who have a pretest probability above the intermediate level. Whereas the ESC and the NICE guidelines consider the diagnosis of obstructive CHD is based just on the high pretest probability, further testing is recommended in the US guidelines. However, testing at such high pretest probabilities with the characteristics of the imperfect tests available may lead to more false negatives than true negatives with the obvious problem of underestimation of disease.
- Stress imaging is the preferred test mode in the ESC guidelines and the only recommended ischemia test in patients in the higher intermediate range of pretest probabilities. No differential recommendations are made with respect to the use of specific imaging techniques.
- In contrast to the ESC guidelines, the US guidelines restrict the use of stress imaging to patients whose resting ECG is not interpretable and those with a high pretest probability of obstructive CHD. They also favor stress echocardiography and stress SPECT over stress CMR.
- The US guidelines feel that coronary CT angiography is appropriate in patients with intermediate to high pretest probabilities.
- In contrast, the ESC guidelines advise specifically against the use of coronary CTA in patients with a pretest probability above 50% due to the frequent presence of severe calcifications.
- The only other patients in whom the US guidelines recommend coronary CT angiography are those who have contraindications to stress testing.
- In contrast, the ESC guidelines suggest coronary CT angiography as a second-line choice behind stress testing in patients with a pretest probability in the lower intermediate range. The ESC guidelines specifically add that coronary CT scans showing high global or focal calcifications should be read as "not interpretable" with respect to lesion quantification.
- The NICE guidelines chose to use cardiac CT calcium scoring as a first-line investigation in patients with a low pretest probability between 10 and 30%. In these patients, the NICE guideline advises that the absence of calcium makes obstructive CHD likely not the reason for the patient's symptoms.
- Intermediate calcium scores in these low pretest probability patients between 1 and 400 are recommended to be followed by coronary CT angiography whereas patients with high calcium scores (>400) are recommended to undergo ICA.
- Thus, the largest disparities among the three guidelines with respect to imaging for testing for the presence of obstructive CAD are in their recommendations pertaining to coronary CT.
- The flowchart of testing in patients with intermediate pretest probability as described in the ESC guidelines is shown in Fig. 3.2.

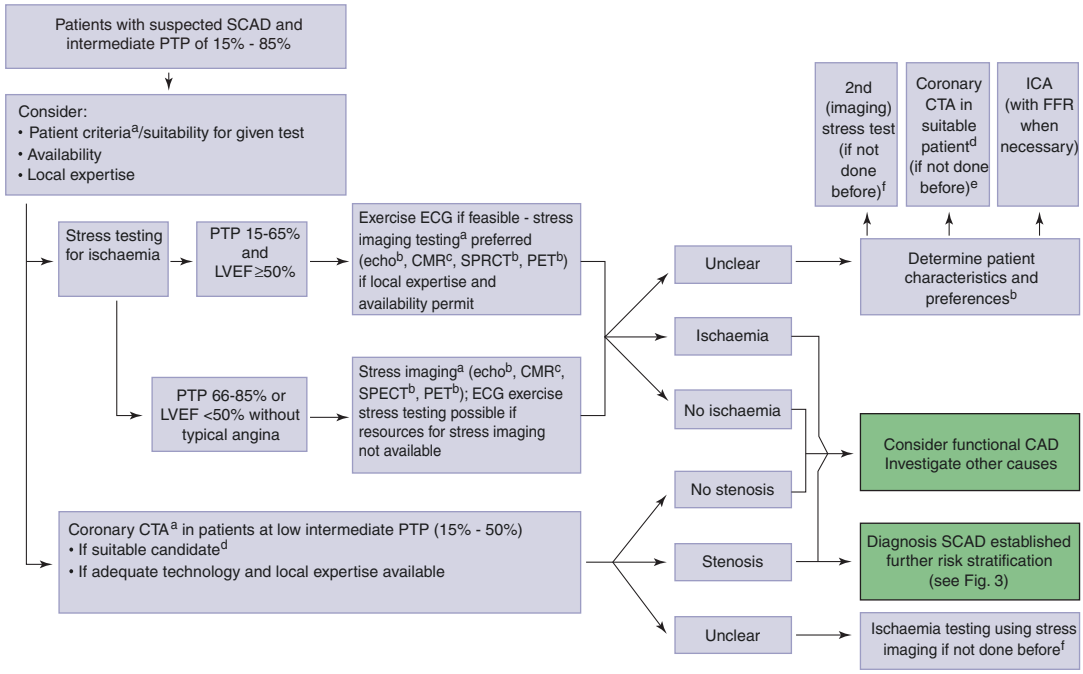

Fig. 3.2 Noninvasive testing in patients with suspected stable coronary artery disease (SCAD) and an intermediate pretest probability. *CAD* coronary artery disease, *CTA* computed tomography angiography, *CMR* cardiac magnetic resonance, *ECG* electrocardiogram, *ICA* invasive coronary angiography, *LVEF* left ventricular ejection fraction, *PET* positron-emission tomography, *PTP* pretest probability, *SCAD* stable coronary artery disease, *SPECT* single-photon-emission computed tomography. (1) Consider the age of patient versus radiation exposure. (2) In patients unable to exercise use echo or SPECT/PET with pharmacologic stress instead. (3) CMR is only performed using pharmacologic stress. (4) Patient characteristics should make a fully diagnostic coronary CTA scan highly probable. Consider result to be unclear in patients with severe diffuse or focal calcification. (5) Proceed as in lower left coronary CTA box. (6) Proceed as in stress testing for ischemia box. (7) It is not uncommon that the clinician could consider a stress test indeterminate or unclear as seen in the upper right-hand corner. In such a circumstance there are three possibilities and the decision on how to proceed further should be made together with the patient: it is justified to push for a diagnosis by using ICA but one needs to be careful to not fall victim to the oculostenotic reflex and perform PCI on any lesion of questionable significance but instead employ FFR measurements and only place a stent if this measurement is clearly abnormal. One may also switch from stress testing to coronary CT angiography in suitable patients. (8) Finally it is also a possibility to perform a second imaging stress test although this is conceptually the least attractive choice. On the other hand if the patient had coronary CT angiography as the first test and calcifications obscure the image to a degree that no judgement can be made to the degree of stenosis at this position then stress imaging is a valid potential second test (see lower right-hand corner). Reproduced from Montalescot G et al. - 2013 ESC guidelines on the management of stable coronary artery disease. Eur Heart J. 2013;34:2949–3003 with permission of the publisher

What to Do with the Result of Noninvasive Imaging Assessment?

- Improving symptoms in patients with obstructive coronary disease can be achieved by medication and/or coronary revascularization. The latter produces the desired result immediately. However, in the long term (3 years) both forms of therapy achieve similar symptomatic results (although there is approximately one-third of patients crossing over from the initially chosen medical arm to the revascularization arm) [24].

Table 3.5 Definitions of risk for various test modalities

Exercise stress ECG[a]	High risk	CV mortality >3%/year
	Intermediate risk	CV mortality between 1 and 3%/year
	Low risk	CV mortality <1%/year
Ischemia imaging	High risk	Area of ischemia >10% (>10% for SPECT; limited quantitative data for CMR—probably ≥2/16 segments with new perfusion defects or ≥3 dobutamine-induced dysfunctional segments; ≥3 segments of LV by stress echo)
	Intermediate risk	Area of ischemia between 1 and 10% or any ischemia less than high risk by CMR or stress echo
	Low risk	No ischemia
Coronary CTA[b]	High risk	Significant lesions of high-risk category (three-vessel disease with proximal stenoses, LM, and proximal anterior descending CAD)
	Intermediate rick	Significant lesion(s) in large and proximal coronary artery(ies) but not high-risk category
	Low risk	Normal coronary artery or plaques only

CAD coronary artery disease, *CMR* cardiac magnetic resonance, *CTA* computed tomography angiography, *CV* cardiovascular, *ECG* electrocardiogram, *ICA* invasive coronary angiography, *LM* left main, *PTP* pretest probability, *SPECT* single-photon-emission computed tomography

[a] From nomogram (see web addenda of the 2013 ESC guidelines on the management of stable coronary artery disease, Figure W1) or http://www.cardiology.org/tools/medcalc/duke/

[b] See Fig. 3.2; consider possible overestimation of the presence of significant multivessel disease by coronary CTA in patients with high intermediate PTP (≥50%) and/or severe diffuse or focal coronary calcifications and consider performing additional stress testing in patients without severe symptoms before ICA

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- Thus, it is largely the choice of the patient and the physician whether to choose drugs or revascularization when it comes to improvement of symptoms.
- The matter is more complicated when it comes to improvement of prognosis. However, in the absence of randomized data results from registries indicate that larger extents of ischemia or severe proximal coronary obstructions are required functionally or anatomically in order to demonstrate positive prognostic effects of revascularization [25, 26]. Death rates in patients with such large areas of ischemia or such severe proximal coronary obstructions, receiving previously suboptimal medical treatment in the 1980s and 1990s, were more than 3% annually. Only in these patients it could be shown that revascularization may improve prognosis [25, 26].
- The ESC guidelines indicate how the results of stress testing and coronary CT angiography can be translated into risk groups with different annual mortalities (Table 3.5). Consequently, they recommend revascularization for prognostic purposes only in those in the highest risk group but an invasive strategy can be chosen by the patient and the physician in patients in the intermediate-risk group (Fig. 3.3).

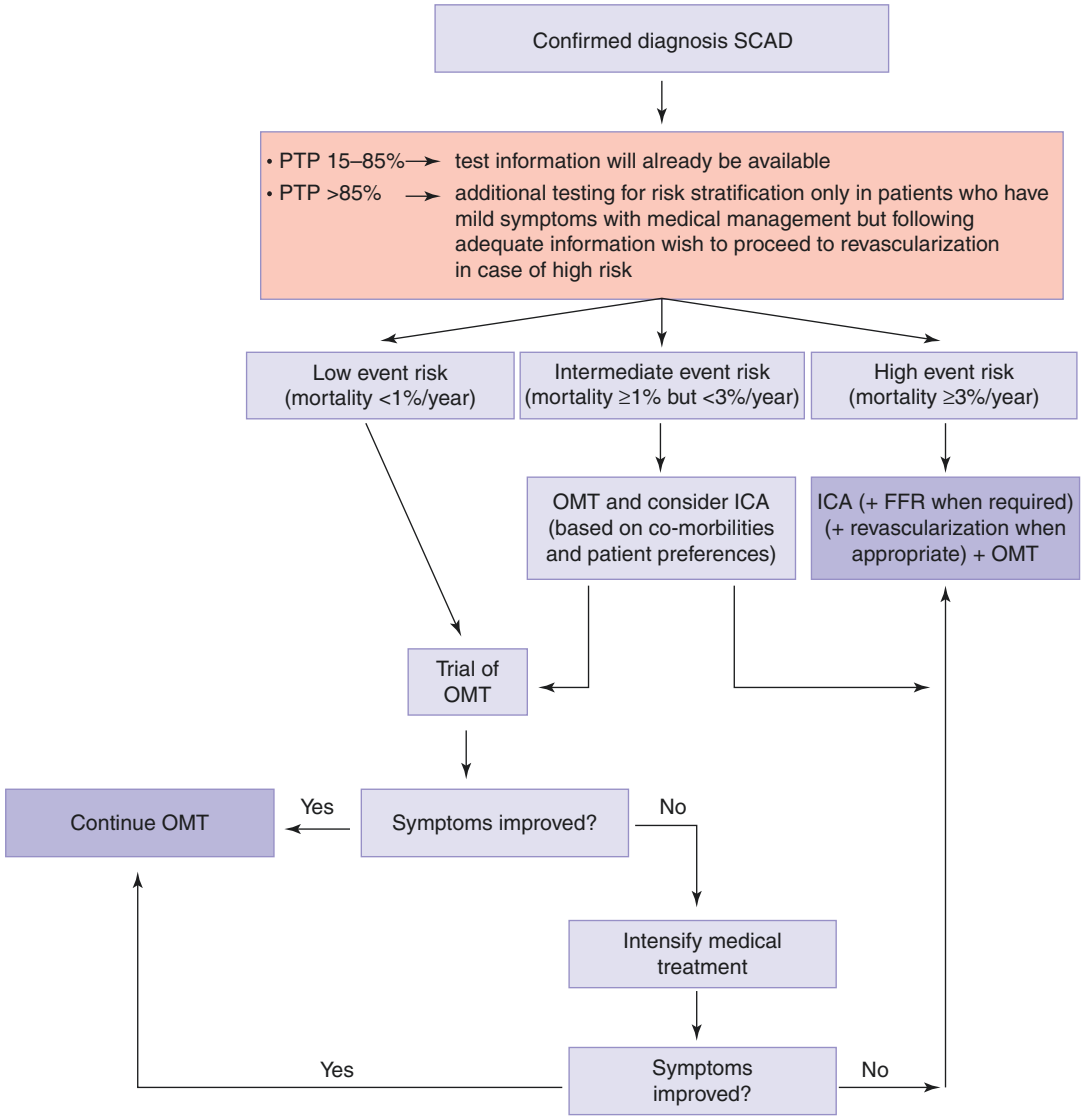

Fig. 3.3 Management based on risk determination for prognosis in patients with chest pain and suspected SCAD (for choice of test see Fig. 3.2, for definitions of event risk see Table 3.5). *ICA* invasive coronary angiography, *OMT* optimal medical therapy, *PTP* pretest probability, *SCAD* stable coronary artery disease. Reproduced from Montalescot G et al. - 2013 ESC guidelines on the management of stable coronary artery disease. Eur Heart J 2013;34:2949–3003 with permission of the publisher

Critique of Imaging in Patients with Suspected CHD

- The recent PROMISE trial randomized patients with an intermediate mean pretest probability of 50% (according to the Diamond-Forrester tables) to stress imaging or coronary CT angiography [15]. In both arms pathology was only found in about 10% of patients despite the expectation (based on pretest probability) that 50% of those should have either ischemia or anatomic stenosis. Moreover, only about 2% of these patients in both arms experienced hard events (death or myocardial infarction) during a follow-up of 2 years.
- Other findings of a similar kind [27] led to concerns about over-testing in patients with chest pain especially with respect to inappropriate use and overuse of imaging techniques [28].
- Patients who are unlikely to have high-risk CAD, clinical events, or revascularization will derive minimal benefit and value from noninvasive testing. Efforts are made to design clinical tools in order to identify such minimal risk patients for whom deferred testing may be considered [29].

Conclusion

- Preselection of patients with chest pain who are likely to derive any benefit from an invasive management strategy is highly desirable in order to avoid even more invasive coronary angiograms showing the absence of stenoses.
- The purpose of excluding relevant CHD is most elegantly served by coronary CT angiography but this approach might also lead to some overuse of imaging (if employed in patients with very low pretest probabilities).
- Stress imaging techniques are most useful in patients with known diffuse CAD in whom a normal stress test confers a good prognosis.
- In patients with an abnormal stress test who are sent to invasive coronary angiography, the angiographer has some important clues as to where to direct special attention.

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References

1. Task Force M, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, Bugiardini R, Crea F, Cuisset T, Di Mario C, Ferreira JR, Gersh BJ, Gitt AK, Hulot JS, Marx N, Opie LH, Pfisterer M, Prescott E, Ruschitzka F, Sabate M, Senior R, Taggart DP, van der Wall EE, Vrints CJ, Guidelines ESCCP, Zamorano JL, Achenbach S, Baumgartner H, Bax JJ, Bueno H, Dean V, Deaton C, Erol C, Fagard R, Ferrari R, Hasdai D, Hoes AW, Kirchhof P, Knuuti J, Kolh P, Lancellotti P, Linhart A, Nihoyannopoulos P, Piepoli MF, Ponikowski P, Sirnes PA, Tamargo JL, Tendera M, Torbicki A, Wijns W, Windecker S, Document R, Knuuti J, Valgimigli M, Bueno H, Claeys MJ, Donner-Banzhoff N, Erol C, Frank H, Funck-Brentano C, Gaemperli O, Gonzalez-Juanatey JR, Hamilos M, Hasdai D, Husted S, James SK, Kervinen K, Kolh P, Kristensen SD, Lancellotti P, Maggioni AP, Piepoli MF, Pries AR, Romeo F, Ryden L, Simoons ML, Sirnes PA, Steg PG, Timmis A, Wijns W, Windecker S, Yildirir A, Zamorano JL. ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34:2949–3003.
2. Fihn SD, Gardin JM, Abrams J, Berra K, Blankenship JC, Dallas AP, Douglas PS, Foody JM, Gerber TC, Hinderliter AL, King SB 3rd, Kligfield PD, Krumholz HM, Kwong RY, Lim MJ, Linderbaum JA, Mack MJ, Munger MA, Prager RL, Sabik JF, Shaw LJ, Sikkema JD, Smith CR, Jr SSC Jr, Spertus JA, Williams SV, American College of Cardiology F, American Heart Association Task Force on Practice G, American College of P, American Association for Thoracic S, Preventive Cardiovascular Nurses A, Society for Cardiovascular A, Interventions, Society of Thoracic S. 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, and the American College of Physicians, American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2012;60:e44–e164.
3. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, Fonarow GC, Lange RA,

Levine GN, Maddox TM, Naidu SS, Ohman EM, Smith PK. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. J Am Coll Cardiol. 2014;64:1929–49.

4. Roffi M, Patrono C, Collet JP, Mueller C, Valgimigli M, Andreotti F, Bax JJ, Borger MA, Brotons C, Chew DP, Gencer B, Hasenfuss G, Kjeldsen K, Lancellotti P, Landmesser U, Mehilli J, Mukherjee D, Storey RF, Windecker S, Baumgartner H, Gaemperli O, Achenbach S, Agewall S, Badimon L, Baigent C, Bueno H, Bugiardini R, Carerj S, Casselman F, Cuisset T, Erol C, Fitzsimons D, Halle M, Hamm C, Hildick-Smith D, Huber K, Iliodromitis E, James S, Lewis BS, Lip GY, Piepoli MF, Richter D, Rosemann T, Sechtem U, Steg PG, Vrints C, Luis Zamorano J. 2015 ESC guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). Eur Heart J. 2016;37:267–315.
5. Amsterdam EA, Wenger NK, Brindis RG, Casey DE, Jr GTG, Holmes DR, Jr JAS, Jneid H, Kelly RF, Kontos MC, Levine GN, Liebson PR, Mukherjee D, Peterson ED, Sabatine MS, Smalling RW, Zieman SJ, American College of C, American Heart Association Task Force on Practice G, Society for Cardiovascular A, Interventions, Society of Thoracic S, American Association for Clinical C. 2014 AHA/ACC Guideline for the Management of Patients with Non-ST-Elevation Acute Coronary Syndromes: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;64:e139–228.
6. Mark DB, Shaw L, Harrell FE Jr, Hlatky MA, Lee KL, Bengtson JR, McCants CB, Califf RM, Pryor DB. Prognostic value of a treadmill exercise score in outpatients with suspected coronary artery disease. N Engl J Med. 1991;325:849–53.
7. Ladapo JA, Blecker S, Elashoff MR, Federspiel JJ, Vieira DL, Sharma G, Monane M, Rosenberg S, Phelps CE, Douglas PS. Clinical implications of referral bias in the diagnostic performance of exercise testing for coronary artery disease. J Am Heart Assoc. 2013;2:e000505.
8. Greenwood JP, Maredia N, Younger JF, Brown JM, Nixon J, Everett CC, Bijsterveld P, Ridgway JP, Radjenovic A, Dickinson CJ, Ball SG, Plein S. Cardiovascular magnetic resonance and single-photon emission computed tomography for diagnosis of coronary heart disease (CE-MARC): a prospective trial. Lancet. 2012;379:453–60.
9. 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;11:875–82.
10. Hachamovitch R, Rozanski A, Shaw LJ, Stone GW, Thomson LE, Friedman JD, Hayes SW, Cohen I, Germano G, Berman DS. Impact of ischaemia and scar on the therapeutic benefit derived from myocardial revascularization vs. medical therapy among patients undergoing stress-rest myocardial perfusion scintigraphy. Eur Heart J. 2011;32:1012–24.
11. Bittencourt MS, Hulten EA, Veeranna V, Blankstein R. Coronary computed tomography angiography in the evaluation of chest pain of suspected cardiac origin. Circulation. 2016;133:1963–8.
12. Nielsen LH, Ortner N, Norgaard BL, Achenbach S, Leipsic J, Abdulla J. The diagnostic accuracy and outcomes after coronary computed tomography angiography vs. conventional functional testing in patients with stable angina pectoris: a systematic review and meta-analysis. Eur Heart J Cardiovasc Imaging. 2014;15:961–71.
13. Piepoli MF, Hoes AW, Agewall S, Albus C, Brotons C, Catapano AL, Cooney MT, Corra U, Cosyns B, Deaton C, Graham I, Hall MS, Hobbs FD, Lochen ML, Lollgen H, Marques-Vidal P, Perk J, Prescott E, Redon J, Richter DJ, Sattar N, Smulders Y, Tiberi M, van der Worp HB, van Dis I, Verschuren WM, Authors/Task Force M. European guidelines on cardiovascular disease prevention in clinical practice: The Sixth Joint Task Force of the European Society of Cardiology and Other Societies on Cardiovascular Disease Prevention in Clinical Practice (constituted by representatives of 10 societies and by invited experts) Developed with the special contribution of the European Association for Cardiovascular Prevention & Rehabilitation (EACPR). Eur Heart J. 2016;37:2315–81.
14. Schmidt T, Maag R, Foy AJ. Overdiagnosis of coronary artery disease detected by coronary computed tomography angiography: a teachable moment. JAMA Intern Med. 2016;176:1747–8.
15. Douglas PS, Hoffmann U, Patel MR, Mark DB, Al-Khalidi HR, Cavanaugh B, Cole J, Dolor RJ, Fordyce CB, Huang M, Khan MA, Kosinski AS, Krucoff MW, Malhotra V, Picard MH, Udelson JE, Velazquez EJ, Yow E, Cooper LS, Lee KL, Investigators P. Outcomes of anatomical versus functional testing for coronary artery disease. N Engl J Med. 2015;372:1291–300.
16. Mouden M, Timmer JR, Reiffers S, Oostdijk AH, Knollema S, Ottervanger JP, Jager PL. Coronary artery calcium scoring to exclude flow-limiting coronary artery disease in symptomatic stable patients at low or intermediate risk. Radiology. 2013;269:77–83.
17. Senior R, Becher H, Monaghan M, Agati L, Zamorano J, Vanoverschelde JL, Nihoyannopoulos P. Contrast echocardiography: evidence-based recommendations

by European Association of Echocardiography. Eur J Echocardiogr. 2009;10:194–212.
18. Imbert L, Poussier S, Franken PR, Songy B, Verger A, Morel O, Wolf D, Noel A, Karcher G, Marie PY. Compared performance of high-sensitivity cameras dedicated to myocardial perfusion SPECT: a comprehensive analysis of phantom and human images. J Nucl Med. 2012;53:1897–903.
19. Bateman TM, Heller GV, McGhie AI, Friedman JD, Case JA, Bryngelson JR, Hertenstein GK, Moutray KL, Reid K, Cullom SJ. Diagnostic accuracy of rest/stress ECG-gated Rb-82 myocardial perfusion PET: comparison with ECG-gated Tc-99m sestamibi SPECT. J Nucl Cardiol. 2006;13:24–33.
20. Taqueti VR, Shaw LJ, Cook NR, Murthy VL, Shah NR, Foster CR, Hainer J, Blankstein R, Dorbala S, Di Carli MF. Excess cardiovascular risk in women relative to men referred for coronary angiography is associated with severely impaired coronary flow reserve, not obstructive disease. Circulation. 2017;135(6):566–77.
21. Al Sayari S, Kopp S, Bremerich J. Stress cardiac MR imaging: the role of stress functional assessment and perfusion imaging in the evaluation of ischemic heart disease. Radiol Clin North Am. 2015;53:355–67.
22. Greenwood JP, Motwani M, Maredia N, Brown JM, Everett CC, Nixon J, Bijsterveld P, Dickinson CJ, Ball SG, Plein S. Comparison of cardiovascular magnetic resonance and single-photon emission computed tomography in women with suspected coronary artery disease from the clinical evaluation of magnetic resonance imaging in coronary heart disease (CE-MARC) trial. Circulation. 2014;129:1129–38.
23. National Institute for Health and Clinical Excellence. Chest pain of recent onset. (Clinical guideline 95). http://guidance.nice.org.uk/CG95 and http://www.nice.org.uk/guidance/CG95. 2010.
24. Weintraub WS, Spertus JA, Kolm P, Maron DJ, Zhang Z, Jurkovitz C, Zhang W, Hartigan PM, Lewis C, Veledar E, Bowen J, Dunbar SB, Deaton C, Kaufman S, O'Rourke RA, Goeree R, Barnett PG, Teo KK, Boden WE, Group CTR, Mancini GB. Effect of PCI on quality of life in patients with stable coronary disease. N Engl J Med. 2008;359:677–87.
25. Hachamovitch R, Hayes SW, Friedman JD, Cohen I, Berman DS. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation. 2003;107:2900–7.
26. Mark DB, Nelson CL, Califf RM, Harrell FE Jr, Lee KL, Jones RH, Fortin DF, Stack RS, Glower DD, Smith LR, et al. Continuing evolution of therapy for coronary artery disease. Initial results from the era of coronary angioplasty. Circulation. 1994;89:2015–25.
27. Rozanski A, Gransar H, Hayes SW, Min J, Friedman JD, Thomson LE, Berman DS. Temporal trends in the frequency of inducible myocardial ischemia during cardiac stress testing: 1991 to 2009. J Am Coll Cardiol. 2013;61:1054–65.
28. Ladapo JA, Blecker S, Douglas PS. Physician decision making and trends in the use of cardiac stress testing in the United States: an analysis of repeated cross-sectional data. Ann Intern Med. 2014;161:482–90.
29. Fordyce CB, Douglas PS, Roberts RS, Hoffmann U, Al-Khalidi HR, Patel MR, Granger CB, Kostis J, Mark DB, Lee KL, Udelson JE, Prospective Multicenter Imaging Study for Evaluation of Chest Pain I. Identification of patients with stable chest pain deriving minimal value from noninvasive testing: the PROMISE minimal-risk tool, a secondary analysis of a randomized clinical trial. JAMA Cardiol. 2017;2(4):400–8.