Diagnostic Flowcharts

21

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In patients with known or suspected coronary artery disease, diagnosis and risk stratification can be aided by noninvasive tests for myocardial ischemia. Guidelines for choosing among the different stress testing approaches have been published [1–5], but the use of these tests by physicians varies widely according to diagnostic yields, cost, and convenience. Some general principles should be considered. First, no single test or strategy has been proven to be overall superior [5]. Second, all published research consistently demonstrates that stress testing with radionuclide scintigraphy and echocardiography provides more information than exercise electrocardiography alone [1–4].

However, the fact that a test provides more information does not mean that it is the most appropriate test. Other important issues are whether the additional information is sufficient to change patient care in ways that would be expected to improve outcomes [5]. Third, regardless of which test is used, a normal test result should never be considered a guarantee that the patient does not have coronary artery disease or has no risk of cardiovascular events [3]. The rational diagnostic approach can be divided into four successive steps, progressing from the clinical picture to exercise electrocardiography, then to the imaging stress test. In highly selected cases, testing for coronary vasospasm can be considered.

21.1 Step 1: Clinical Picture

Simple ECG and resting echocardiography can integrate the clinical picture sufficiently to identify patients with a higher probability of severe disease, warranting coronary angiography. In such patients, the good cardiologist needs hardly any help to place the patient on the fast-track of coronary angiography. Early after myocardial infarction associated with ischemic, mechanical, or arrhythmic complications, patients with unstable angina that is not alleviated by maximal therapy, or patients with malignant arrhythmias associated with spontaneous episodes, should be referred directly for coronary angiography (Table 21.1). The guidelines from the American College of Cardiology and of the American Heart Association consistently indicate exercise electrocardiography as the appropriate first test

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Table 21.1 Indications for the use of stress imaging rather than exercise electrocardiography[a]

Coronary angiography first	EET first	Stress imaging first (rather than exercise electrocardiography)
Complicated myocardial infarction	After uncomplicated myocardial infarction	Complete LBBB
Unstable coronary syndromes after maximal therapy	Stable chest pain syndrome	Electronically paced ventricular rhythm
Aborted sudden death, etc.	Capability to exercise	More than 1 mm ST-segment depression on resting ECG
	No contraindications to exercise testing	Unable to exercise
	Interpretable ECG	Poor left ventricular function if viability is critical

EET exercise electrocardiography, *ECG* electrocardiography, *LBBB* left bundle branch block
[a] Modified and adapted from the guidelines developed by the American College of Cardiology, the American Heart Association, the American College of Physicians, and the American Society of Internal Medicine [1–5]

[1–4] in the initial assessment of a patient with known or suspected stable coronary artery disease, who is capable of exercising and has an interpretable baseline ECG. Exercise electrocardiography is of little diagnostic value in patients with particular electrocardiographic abnormalities at rest, including left bundle branch block, electronically paced ventricular rhythm, and ST-segment depression greater than 1 mm (Table 21.1). In such patients, and in patients who are unable to exercise, and/or with poor left ventricular function if viability is critical, noninvasive testing with some forms of imaging is indicated by default [5].

21.2 Step 2: Exercise Electrocardiography Stress Test

The high feasibility, excellent safety record, ease of application, and low cost make exercise electrocardiography a first-line tool for screening patients with known or suspected coronary artery disease. The rate of acute myocardial infarction or death for this test is about 1 in 2,500 [6]. Compared to stress echocardiography and stress single photon emission computed tomography, the cost of exercise electrocardiography is at least two to five times lower, respectively. In addition, the exercise test provides information not only on the coronary reserve, but also on cardiovascular efficiency (i.e., the way in which coronary reserve can be translated into external work). Both these variables (coronary reserve and cardiovascular efficiency) concur in determining exercise tolerance and, therefore, quality of life in the individual patient [7, 8]. A negative exercise electrocardiography test result is associated with 99.3% survival at 5-year follow-up in patients with normal resting function [9]. Survival is only slightly lower in patients with previous myocardial infarction. It is hard to believe that one can improve on this extraordinarily good prognosis with any form of intervention. Therefore, in a patient capable of adequate physical effort and with

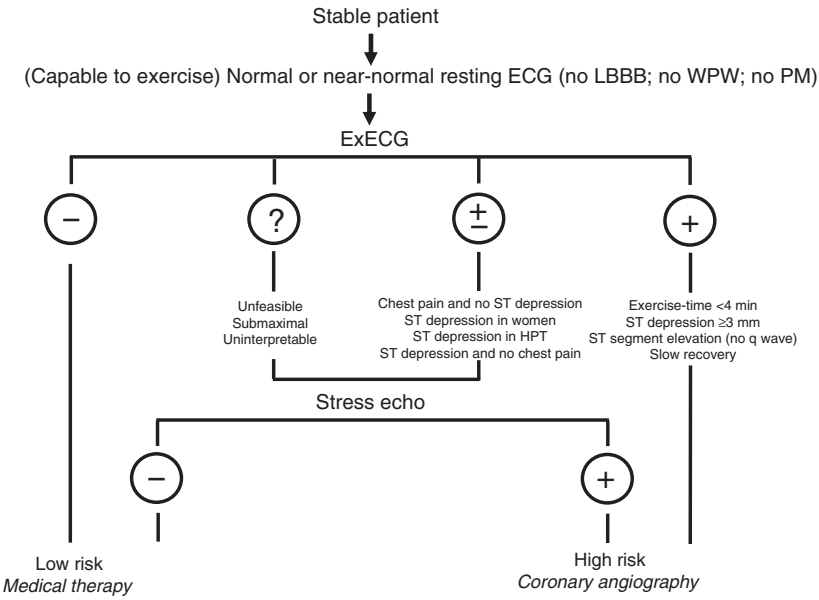

Fig. 21.1 In stable patients with known or suspected coronary artery disease and normal or near-normal resting ECG, the diagnostic algorithm should start with the exercise electrocardiography test. This remains the first noninvasive test to be done and often the last one: a maximal negative test result is associated with an extremely good prognosis; at the other end of the spectrum, a response of severe ischemia warrants coronary angiography without further investigations. In patients with ambiguous or uninterpretable results during exercise electrocardiography or patients in whom exercise is submaximal or contraindicated, stress echocardiography is an excellent choice. A normal stress echocardiogram identifies a low-risk group. A positive finding on a stress echocardiogram warrants a more aggressive therapeutic approach. HPT, hypertensives; LBBB, left bundle branch block; PM, pacemaker; WPW, Wolff-Parkinson-White

interpretable ECG, exercise electrocardiography should be the first step in the diagnostic sequence and, in case of negativity for both electrocardiographic criteria and chest pain at a maximal load, should also be the last (Fig. 21.1). The exercise electrocardiography test can also show a high-risk response (Fig. 21.1), including at least one of the following signs [10]:

1. Early positivity (with an exercise time of less than 4 min)
2. Prolonged positivity with slow recovery (>8 min)
3. Marked positivity (>3 mm of ST-segment depression or ST-segment elevation in the absence of resting Q waves)
4. Global ST-segment changes
5. Associated hypotension, which may indicate either left main or advanced triple-vessel coronary artery disease over underlying left ventricular dysfunction
6. Reproducible malignant arrhythmias

In patients with these or other markers of adverse prognosis, angiography is warranted without any further imaging testing (Fig. 21.1).

21.3 Step 3: Stress Imaging Testing

Exercise electrocardiography positivity at an intermediate to high load, as well as negativity at a submaximal workload, or negativity in the presence of chest pain, warrants a stress echocardiography test. The latter should establish the diagnosis of ischemia with a higher reliability and should define its extent and severity. Stress echocardiography test negativity makes the presence of a prognostically important organic coronary disease unlikely. The excellent outcome associated with this response does not support the decision to proceed with coronary angiography.

Stress echocardiography test positivity identifies a group of patients at higher risk in whom coronary angiography is warranted (Fig. 21.1). However, as discussed in Chap. 17, stress echocardiography positivity should be titrated, since the associated risk may range anywhere between 2 and 20% mortality per year, depending on the time, space, extent, severity, recovery of inducible wall motion abnormalities, and concomitant therapy at the time of testing (Table 21.2).

In the choice of an imaging technique (as detailed elsewhere; see Chaps. 1 and 36) stress echocardiography has to be preferred for logistic and economic reasons. However, nuclear perfusion imaging can still be a viable alternative in four basic situations, which can be related to the institution, the patient, or the stress used. These situations can be minimized, but not totally abolished, and therefore access to a high-quality nuclear laboratory remains an important resource for the clinical cardiologist. The situations in which nuclear perfusion imaging can be performed are the following: no stress echocardiography activity, stress echocardiography activities but semi-random results, patients with a poor acoustic window, and ambiguous stress echocardiography results, which can occur even in technically satisfactory studies (Chap. 36). In all these conditions, perfusion imaging can help considerably in patient work-up. In institutions with cardiac magnetic resonance facilities, this is the imaging test of choice as an alternative to stress echocardiography (Chap. 35).

Table 21.2 Stress echocardiography risk titration

Risk	Low (2% year)	High (20% year)
Dose/workload	High	Low
Resting EF	>50%	<40%
Antiischemic therapy	Off	On
Coronary territory	LCx/RCA	LAD
Peak WMSI	Low	High
Recovery	Fast	Slow
Positivity on baseline dyssynergy	Homozonal	Heterozonal
ESV increase at peak stress	No	Yes

EF ejection fraction, *WMSI* wall motion score index, *ESV* end-systolic volume, *LCx* left circumflex, *RCA* right coronary artery, *LAD* left anterior descending

Table 21.3 Stress echocardiography: which test for which patient

Patient characteristics	Exercise	Dipyridamole	Dobutamine
Inability to exercise	3	1	1
Contraindication to exercise	3	1	1
Positive EET at ≤6 min of exercise in hypertensives, women, baselne ECG changes	1	2	2
Asthmatic patient	2	3	1
Under theophylline therapy	1	3	1
Severe hypertension	3	1	3
Well-controlled hypertension	2	1	2
Relative hypotension	1	3	3
Malignant ventricular ectopy	1	1	3
2nd- to 3rd-degree AV block	1	3	2
Suboptimal acoustic window	3	1	2
Evaluation of antiischemic therapy efficacy	1	1	2
Unstable carotid disease	2	2	2
Permanent pacemaker	Pacemaker stress echocardiography		

1, Especially indicated; 2, relatively contraindicated; 3, contraindicated
EET exercise electrocardiography, *ECG* electrocardiography, *AV* atrioventricular

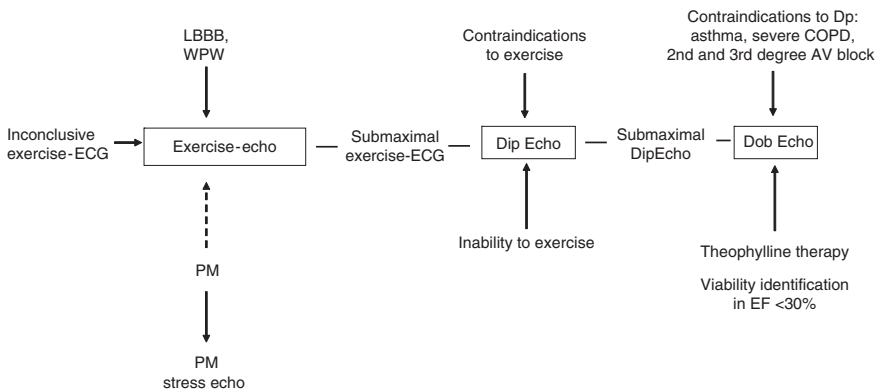

Fig. 21.2 The right type of stress echocardiography (exercise, dipyridamole, dobutamine, or pacemaker stress echocardiography) can be chosen according to several clinical, resting electrocardiography, resting echocardiography, and exercise electrocardiography test variables

It is important to choose the right stress echocardiography test for the right patient. Table 21.3 and Fig. 21.2 summarize the relative indications and contraindications to each of the major stresses according to the evidence more extensively discussed on Chap. 18.

Exercise echocardiography can, and should, be the first-line test, skipping the exercise electrocardiography test in patients with conditions making ECG uninterpretable, such as left bundle branch block or Wolff-Parkinson-White syndrome or baseline ST-segment abnormalities [1–4] (Fig. 21.2). Instead of pharmacological stress echocardiography, it may also be wise to choose exercise echocardiography in patients with an ambiguous positive result during an exercise electrocardiographic test at a workload of 6 min or less. This kind of patient (typically, a middle-aged hypertensive woman with ST-segment depression at a peak rate pressure product below 20,000) can have either angiographically normal or severely diseased coronary arteries. Exercise has the advantage of being the safest test and also being highly feasible and less technically demanding for low levels of exercise.

21.4 Step 4: Testing for Vasospasm

The possibility of testing for coronary vasospasm should be considered after complete negativity of maximal exercise stress testing or imaging stress at the end of the diagnostic evaluation (Fig. 15.4 in Chap. 15). Vasospasm testing is the last resort if chest pain is present and a coronary origin is sought. Before angiography, coronary vasospasm can be suspected in patients with angina at rest, particularly at night or in the early morning, and good or extremely variable effort tolerance. After angiography, the suspicion of spasm should be raised if coronary arteries are normal or mildly diseased, paradoxically in conflict with severe ischemia (Fig. 21.3). Clinically, the suspicion of vasospasm is also high

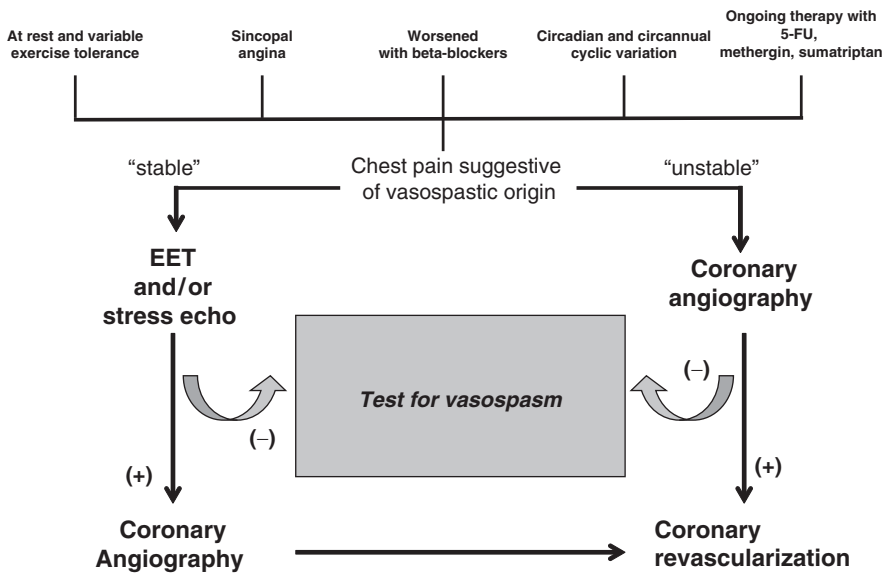

Fig. 21.3 The indication for coronary vasospasm testing in Pisa echocardiography laboratory. EET, exercise-electrocardiography testing; 5-FU, 5-fluorouracil

in patients with syncopal angina [11–14] or aborted sudden death [15, 16]. In susceptible patients, coronary vasospasm can be triggered by noncardiological medications such as the chemotherapeutic agent 5-fluorouracil in patients with cancer [17–19], sumatriptan in migraine sufferers [20, 21], or ergometrine given to young mothers in the puerperium phase [22–24] to reduce uterine blood loss through arterial vasoconstriction [23, 24], or bromocriptine, which is also given in obstetric clinics for milk suppression [25, 26]. In all these conditions, the diagnosis and treatment are easy and potentially life-saving only if one thinks of it in clinical scenarios far from the classic cardiological stage.

In properly selected patients, vasospasm testing (either with ergometrine or hyperventilation) can be performed safely and practically outside the cardiac catheterization laboratory. Testing for vasospasm is the only way to make a diagnosis that can be missed by conventional testing, imaging stress, and even coronary angiography. After all, according to Maseri [20], the single most important factor affecting the frequency with which variant angina is recognized depends on the physician's awareness of its existence.

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