

Guidelines for Diagnosis and Risk Assessment in Subjects with Suspected or Known Coronary Artery Disease

Script and main responsibility: Michel Romanens, MD
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Material (Guidelines)

Stress Testing Guidelines, AHA/ACC 2000
Circulation 2000;102:1726 / 1010009.pdf

Guidelines for the Management of Patients with chronic stable Angina
Circulation 1999;99:2829 / 0106995.pdf

Guidelines for the Management of Patients with chronic stable Angina
EHJ 1997;18:394 / AP-ESC.pdf

Background

Coronary Artery Disease (CAD) is the leading cause of death in Switzerland¹. Early detection and appropriate management of risk is of prime importance. Detection of vulnerable subjects with atherosclerosis is however challenging, since flow limiting disease is not necessarily present in high risk subjects: coronary plaques with positive (not flow limiting) plaque remodelling infers higher risk, because plaques with positive remodelling contain larger lipid pools and more macrophages, and are more unstable². Although detection of subjects with ischemia has prognostic impact, the dilation of the coronary segment that causes ischemia will not improve the cardiovascular prognosis³, since most myocardial infarctions occur in coronary segments of seem-

¹ EHJ 1997;18:1231 / CVDiseaseMortalityEurope.pdf

² Circulation 2002;105:993 / 26020203.pdf

³ BMJ 2000;321:73 / 1607001.pdf

ingly healthy subjects without angiographic stenosis over 70%⁴. Therefore, ischemia is a marker of CAD risk only in subjects with flow limiting disease and it can be inferred, that the more ischemia is present, the higher is the global plaque burden and the higher is a subjects risk.

Tests with a sensitivity below 80% to detect ischemia, namely exercise electrocardiography, dobutamin and dipyridamol echocardiography, will thus miss ischemia in 1:4 subjects. Missed ischemia will have a strong prognostic impact in the long term, because effective atherosclerosis therapy (aspirin, statins, ACE-I) might be withheld because the test failed to diagnose CAD.

Rationale

In subjects with chest pain, a test performed to detect ischemia is used to establish or rule out the diagnosis of CAD and helps to decide, if coronary angiography is warranted. In subjects with known CAD, ischemia testing is added to the clinical work up in symptomatic patients.

Pretest Probabilities

Pretest probability for the presence of CAD is defined by patients gender, age, and symptoms^{5,6}. In subjects with chest pain and known CAD, the type of chest pain can be used in a similar way. A surrogate marker of ischemia is exercise induced dyspnea and might be weighted as typical angina.

Age, y	Nonanginal Chest Pain		Atypical Angina		Typical Angina	
	Men	Women	Men	Women	Men	Women
30–39	4	2	34	12	76	26
40–49	13	3	51	22	87	55
50–59	20	7	65	31	93	73
60–69	27	14	72	51	94	86

*Each value represents percent with significant CAD on catheterization.

Data from (1) Diamond GA, Forester JS. Analysis of probability as an aid in the clinical diagnosis of coronary-artery disease. *N Engl J Med.* 1979;300:1350–1358. (2) Chaitman BR, Bourassa MG, Davis K, Rogers WJ, Tyras DH, Berger R, Kennedy JW, Fisher L, Judkins MP, Mock MB, Killip T. Angiographic prevalence of high-risk coronary artery disease in patient subsets (CASS). *Circulation.* 1981;64:360–367.

⁴ Circulation 1996;93:2205

⁵ George Diamond. *N Engl J Med* 1979;300:1350

⁶ Chaitman B. *Circulation* 1981;64:360., ref 0106995.pdf, page 2835

Test Performance

The commonly used tests to detect ischemia are exercise electrocardiography on bicycles or a treadmill, exercise or pharmacological stress testing in conjunction with imaging (nuclear, echocardiography).

The following table gives the sensitivities, and specificities of various tests, if performed on a state-of-the-art level.

	Sensitivity	Specificity
Exercise MPS ⁷ MIBI SPECT ⁸	91	80
Pharmacological MPS MIBI SPECT ⁹	90	75
Radionuclide-Angiography (RNA) ¹⁰	90	73
Exercise echocardiography ¹¹	85	77
Dobutamin echocardiography ⁹	80	84
Exercise electrocardiogram ⁹	68	77

The choice of a test has to be made on the base of test performance, subject characteristics, availability, local expertise, and cost.

E.g., in a subject with LBBB, the electrocardiogram during exercise is not interpretable. Likewise, specificity is decreased using exercise echocardiography in subjects with a hypertensive response to exercise¹². Poor specificity has been described for dobutamin echocardiography for the myocardial segments supplied by the right coronary artery¹³. Pseudoischemia is also well known from RNA studies occurring in older subjects¹⁴, and in subjects with significant valvular heart disease¹⁵ as well as in a number of other clinical conditions (various forms of cardiomyopathy, female gender, cystic fibrosis and sudden exercise or elevated resting ejection fraction). Further, low sensitivity of exercise and dobutamin echocardiography is expected in subjects with a poor acoustic window¹⁶ and supine exercise echocardiography is more sensitive than post exercise treadmill echocardiography¹⁷.

Expertise and familiarity with the method used by a medical doctor is of high importance. Especially wall motion abnormalities called “unspecific” occurring during physical exercise or pharmacological stress testing are very difficult to discern from ischemia especially in the inferior, posterior and lateral wall, but may have a strong prognostic impact in the long term.

Thus, to perform exercise or pharmacological stress testing, an individual has to show 100 controlled studies at an accepted institution (university hospital) and has to perform > 30 studies/year, possibly having also reported sensitivities and specificities for his own skills in the literature¹⁸.

⁷ MPS denotes myocardial perfusion study

⁸ Compilation of the literature 1989-93: Wackers, JNM 1989;30:301. Hoffmann AJC 1993;72:555. Pozzoli AJC 1991;67:350. Höffken JNM 1990;29:135. Kahn Circulation 1989;79:1282. Iskandrian AJC 1989;64:270. Kiat AHJ 1989;117:1. Later studies showed lower specificities because of the post test referral bias.

⁹ Am Heart J 2001;142:934 / 28020201.pdf

¹⁰ Compilation of the literature: direct comparison of RNA with Thallium. Johnston AJC 1980;45:113. Jengo AJC 1980;45:535. Bodenheimer Circulation 1979;60:1270. Caldwell Circulation 1980;61:610. Candell E Heart J 1990;11:980.

¹¹ Fleischmann, JAMA 1998;280:913

¹² JACC 2002;39:323 / 20020209.pdf. Exercise induced hypertension was defined for men > 220 mm Hg, for women > 190 mm Hg or diastolic hypertension > 90 mm Hg in both genders.

¹³ Mayo Clin Proc 1995;70:16

¹⁴ NEJM 1980;303:1133

¹⁵ Am J Cardiol 1981;47:861

¹⁶ Circulation 1999;99:763

¹⁷ JACC 1999;33:1485

¹⁸ Circulation 2000;102:1726

Image quality defines the feasibility of a test. With nuclear imaging, feasibility is almost 100%. In subjects with poor acoustic windows, image quality precludes the use of echocardiography to detect ischemia. Thus, subjects, in whom over 1 segment is not visible on the resting echocardiogram, should possibly be imaged with nuclear techniques. Segments have been recently defined by the American Heart Association in a scientific statement¹⁹.

Posttest Probabilities

The test performance should be used to calculate the posttest probability for the presence of CAD and by inference, of ischemia²⁰. In subjects with a normal exercise electrocardiogram, but a pretest probability of over 30%, posttest probability remains high (over 15%), and imaging of ischemia has to be considered. Similarly, in subjects with a normal imaging study, posttest probability remains over 15% in subjects with a pretest probability of over 63% (MPS study). However, short- to intermediate-term prognosis is excellent in these subjects and in general, further diagnostic work-up (coronary angiography) can be safely deferred. Imaging of the carotid plaque area²¹ may however be very helpful in these subjects with high pretest probability and a normal imaging study, in order to detect subjects who need to be treated with aspirin and a statin.

Guidelines

These guidelines can be applied to subjects, where exercise electrocardiography does not give conclusive results or cannot be performed because of patient characteristics. The guidelines are based on the literature reports and published papers in Europe and the U.S. to detect subjects with CAD or ischemia in subjects with known CAD. Depending on patients ability to exercise or not, the imaging test will be performed pharmacologically. No guideline ever was published, that allows for pharmacological testing in subjects able to exercise physically to the prespecified levels.

	MPS	ECHO ²²	CA ²³
Stable angina	1	1	3
Unstable angina	1(Aden?)	2	1
Exercise induced Hypertension ²⁴	1	2 (Dob)	3
LBBB ²⁵	1(Aden)	2 (Dob)	3
Unable to exercise	1(Aden)	2 (Dob)	3
Poor acoustic window	1	---	2
Post MI or LVEF < 40%	1(Aden?)	---	1
Exact ischemia location before PTCA	1(Aden ?)	2	---
Preoperative risk stratification	1(Adeno ?)	1 (Dob)	2

Conclusions

Coronary heart disease is the most frequent cause of death in Switzerland. Therefore, medical doctors aiming at diagnosing CAD in there clinical practice non-invasively, have a high responsibility for not missing the disease.

¹⁹ Circulation 2002;105:539 / 29010202.pdf

²⁰ Calculation: www.kardiolog.ch/bayes.xls or <http://www.health.usyd.edu.au/ebm/bayes.htm>

²¹ David Spence. Stroke 2002 (in press).

²² The gradation is made for the condition, that image quality is excellent. For exercise echocardiography, the test should be performed on a supine bicycle ergometer with the possibility to turn the patient to the left

²³ CA denotes coronary angiography

²⁴ > 220 mm Hg in men, > 190 mm Hg in women: consider MPS instead of stress-echocardiography

²⁵ LBBB denotes left bundle branch block