Chapter 4
Diagnosis of Coronary Artery Disease (CAD)

Keywords Diagnosis · Type of angina · Probability of coronary artery disease · Noninvasive testing · Blood-borne biomarkers

Evaluation of the patient with known or suspected cardiovascular disease begins with their medical history and a targeted physical examination as well as basic ancillary studies that are sufficient for the physician to understand the aetiology of any chest pain. A history and symptoms of angina are important in order to determine which tools should be used for diagnosis and treatment. The major signs and symptoms associated with cardiac disease include chest discomfort, dyspnoea, fatigue, oedema, palpitations and syncope. Then the type of angina needs to be characterized based on the clinical classification listed in Table 4.1. Anginal pain is characterized depending on the pain location, the quality, the duration of pain and any exacerbating or alleviating factors [63–65].

If the angina lasts longer and has the symptoms mentioned in Table 4.1, it can be classified as typical angina. If only two symptoms are presented, it can be called atypical angina, and with even fewer symptoms it is described as noncardiac chest pain. Once the physician determines that the appropriate symptoms are present, then the probability of CAD is assessed. For example, a history of CAD in the family, the patient's age, gender and symptoms are all important to determine the probability of having coronary artery disease as shown in Table 4.2. In addition, physicians may use other risk algorithms that are available based on the location and race of the patient.

A description of the symptoms and determining the probability are important elements for the understanding of the occurrence of CAD, its severity, comorbidities and complications. But alone they are not sufficient to diagnose CAD. The Canadian Cardiovascular Society (CCS) has proposed that the appropriate diagnosis and management of stable ischemic heart disease (SIHD) also includes the need for basic ancillary studies, such as fasting lipids, a resting 12-lead electrocardiogram and possibly a chest X-ray. For example, for patients $\gtrsim$ 40 years of age, the

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Table 4.1 Clinical classification of chest pain [63]

Type of angina	Symptoms
Typical angina	1. Retrosternal chest discomfort 2. Increased pain with exertion or emotional stress 3. Relief with rest or nitroglycerin
Atypical angina	Exhibits 2 of the above symptoms
Noncardiac chest pain	Exhibit 0 or 1 of the above symptoms

Table 4.2 Probability of coronary artery disease (CAD) by age, gender and symptoms [63]

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

CCS has suggested the use of noninvasive testing in patients with classical anginal chest pain symptoms to diagnose SIHD as explained in Fig. 4.1 and acute coronary syndrome (ACS) as presented in Fig. 2.6 [64]. Depending on the situation, some invasive diagnostic testing can be used by physicians, such as fractional flow reserve (FFR) and intravascular ultrasound, as suggested by the American College of Cardiology Foundation (ACCF) and the American Heart Association (AHA) in their 2012 document describing the guidelines for the appropriate criteria for using diagnostic catheterization [66].

There are many advanced diagnostic tools available now such as stress electrocardiography, echocardiography, myocardial perfusion imaging, magnetic resonance imaging, coronary computed tomography and cardiac catheterization. The selection of the initial test depends on the patient's characteristics, potential contraindications to testing, limitations of each modality, local availability and local expertise. Figure 4.2 describes the comprehensive flow chart for the diagnosis as well as treatment of the patient with chest pain. One should take a note that only around 1–11% of patients admitted to hospital with chest pain are due to coronary artery disease (CAD) or acute coronary syndrome (ACS). Physicians might also use the sensitivity and specificity data of any diagnostic test, as listed in Table 4.3, to decide which test is to be used for which patient [64, 67].

For a suspected CAD patient, a treadmill exercise test with a 12-lead ECG and a blood pressure monitor is a useful option as it is simple, low cost and easily available. But pharmacological testing with vasodilator perfusion imaging or dobutamine echocardiography is preferred for those who cannot exercise to an adequate workload due to various reasons such as obesity, orthopaedic limitations, balance

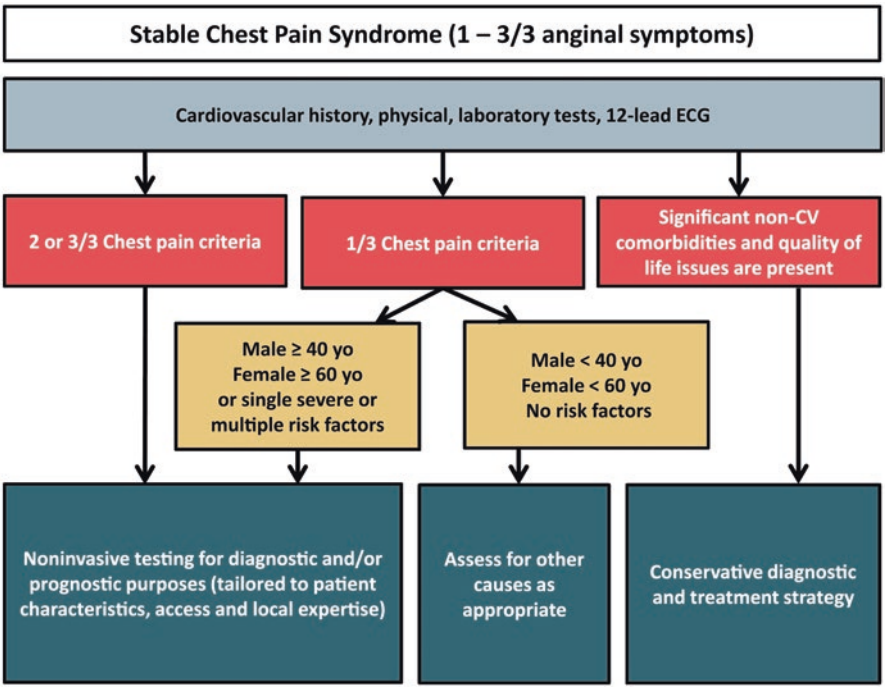

Fig. 4.1 Noninvasive testing for diagnosis and prognostic purposes in patients with classical chest pain symptoms (*CV* cardiovascular, *ECG* electrocardiogram) [64]

issues, pulmonary limitations, frailty or limb dysfunction. Vasodilator perfusion imaging or anatomical imaging for diagnostic purposes is an appropriate method when complete left bundle branch block (LBBB) or paced ventricular rhythm is present. Computed tomography (CT) can be used to detect coronary calcium or to generate a coronary angiogram, but coronary computed tomography angiography (CCTA) is preferable for individuals who have a probability of being in an intermediate risk category for CAD. One thing to consider is that CCTA should also be avoided for patients with arrhythmia, significant renal dysfunction or contrast media allergies. Invasive coronary angiography is the benchmark investigative technique to detect the presence of CAD causing luminal blockage, but not for the detection of early atheroma. It should not be offered to patients who are not candidates for revascularization [64, 68–70].

Other than the above-mentioned diagnostic tools, blood-borne biomarkers are also helpful to access the diagnosis and prognosis as well as to monitor the successful treatment of CAD. For example, inflammatory biomarkers such as high sensitivity C-reactive protein (CRP) and interleukin-6 are tools for the prognosis of future cardiac events. Biomarkers of myocardial injury, such as troponin T and I levels,

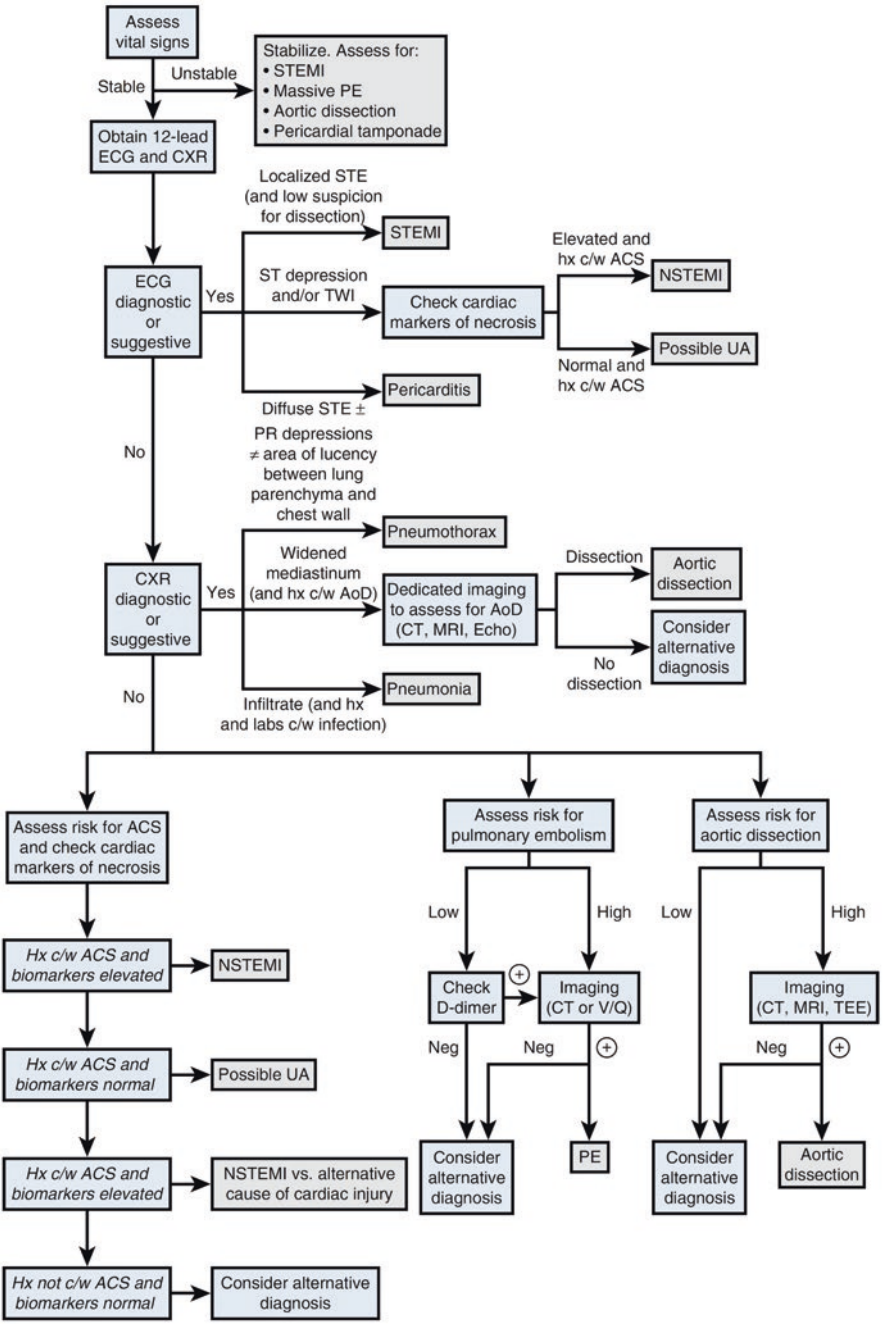

Fig. 4.2 A comprehensive approach to the diagnosis and treatment of patients with chest pain

Table 4.3 Summary estimates of pooled sensitivity and specificity data for cardiac tests (with 95% confidence interval) used in the diagnosis of CAD [64]

Technology[a]	Sensitivity	Specificity
Exercise treadmill	0.68 (0.23–1.0)	0.77 (0.17–1.0)
Attenuation-corrected SPECT	0.86 (0.81–0.91)	0.82 (0.75–0.89)
Gated SPECT	0.84 (0.79–0.88)	0.78 (0.71–0.85)
Traditional SPECT	0.86 (0.84–0.88)	0.71 (0.67–0.76)
Contrast stress echocardiography (wall motion)	0.84 (0.79–0.90)	0.80 (0.73–0.87)
Exercise or pharmacologic stress echocardiography	0.79 (0.77–0.82)	0.84 (0.82–0.86)
Cardiac computed tomographic angiography	0.96 (0.94–0.98)	0.82 (0.73–0.90)
Positron emission tomography (PET)	0.90 (0.88–0.92)	0.88 (0.85–0.91)
Cardiac MRI (perfusion)	0.91 (0.88–0.94)	0.81 (0.75–0.87)

[a]*MRI* magnetic resonance imaging, *SPECT* single photon emission computed tomography

also have potential prognosis features associated with stable CAD, and are specific markers for myocardial injury. Biomarkers of vascular function and neurohumoral activity, such as B-type natriuretic peptide (BNP) and the N-terminal fragment of its prohormone named NT-proBNP, can be used for risk assessment related to vasoactive function, which can be an important surrogate for determining the severity of heart failure. Biomarkers such as Atrial Natriuretic Peptide (ANP), Adrenomedullin (ADM) and Growth Differentiation Factor-15 (GDF-15), novel omics-based biomarkers of renal function such as Estimated Glomerular Filtration Rate (eGFR) and Cystatin C, and lipid biomarkers such as total cholesterol (TC), high density lipoprotein cholesterol (HDL-C), LDL-C and triglycerides (TGs), can all play a part in determining the risk level of suspected CAD patients as illustrated in Fig. 4.3 [71].

All the above-mentioned biomarkers have their own specific roles and characteristics for the diagnosis and prognosis of CAD but they are not yet recommended for routine clinical practice due to their limitations compared to other established diagnostic tools. Advances in research continue to make them more effective, which will enable them to be translated into clinical practice in the future.

Fig. 4.2 (continued) *ACS* acute coronary syndrome, *CT* computed tomography, *CXR* chest X-ray, *ECG* electrocardiogram, *MRI* magnetic resonance imaging, *NSTEMI* non-ST-elevated myocardial infarction, *PE* pulmonary embolism, *ST* is a segment of the ECG pulse and is not defined, *STE* ST elevation, *STEMI* ST-elevated myocardial infarction, *TEE* transoesophageal echocardiogram, *TWI* T wave inversion, *UA* unstable angina, *V/Q* ventilation/perfusion, *Hx* history, *c/w* consistent with [67]

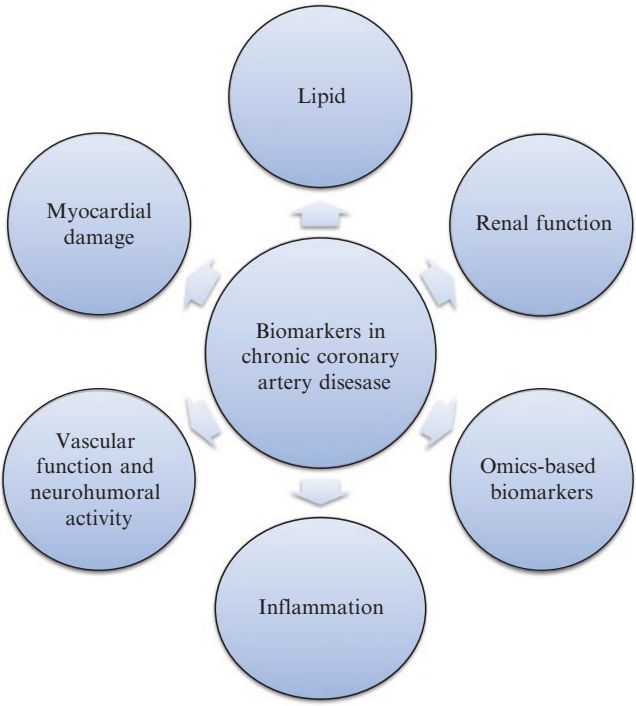

Fig. 4.3 Established and novel biomarkers for chronic coronary artery disease [71]