Hypertension

31

Eugenio Picano

31.1 Background

Uncontrolled and prolonged elevation of blood pressure can lead to a variety of changes in the myocardial structure, coronary vasculature, and conduction system of the heart. These changes can lead to the development of left ventricular hypertrophy, coronary artery disease, various conduction system diseases, and systolic or diastolic dysfunction of the myocardium, which manifest clinically as angina or myocardial infarction, cardiac arrhythmias (especially atrial fibrillation), and congestive heart failure. Patients with angina have a high tolerance for hypertension. Hypertension is an established risk factor for the development of coronary artery disease, almost doubling the risk [1]. Transthoracic echocardiography is especially helpful for an initial risk stratification, and identifies four key variables of recognized prognostic value [2]: (1) left ventricular hypertrophy, especially of the concentric type; (2) left atrial dilatation, often occurring in the absence of valvular heart disease or systolic dysfunction and may correlate with the severity of diastolic dysfunction; (3) diastolic dysfunction, common in hypertension, and usually, but not invariably, accompanied by left ventricular hypertrophy [3]; and (4) systolic dysfunction (Table 31.1).

To the information provided by resting transthoracic echocardiography and stress echocardiography adds critically important pathophysiologic, diagnostic, and prognostic information.

31.2 Pathophysiology

Arterial hypertension can provoke a reduction in coronary flow reserve through several mechanisms, which may overlap in the individual patient: coronary artery disease, left ventricular hypertrophy, and microvascular disease [4] (Fig. 31.1). Abnormal coronary flow reserve has been demonstrated in patients with essential hypertension, despite the presence of angiographically normal arteries and the absence of left ventricular hypertrophy [5].

E. Picano, *Stress Echocardiography*,

Table 31.1 Rest and stress echocardiography for risk stratification in hypertensive subjects with normal resting left ventricular function

	Higher risk	Lower risk
Resting echocardiography		
LVH (g m^{-2})	>125	<125
LA (mm^2)	>4.5	<4.5
DD (grade)	2–3	0–1
RWT	>0.45	<0.45
Stress echocardiography		
WMA	Yes	No
CFR	<2.0	>2.0

CFR coronary flow reserve, *DD* diastolic dysfunction (from 0 = absent to 3 = severe), *LA* left atrial volume (in apical biplane view), *LVH* left ventricular hypertrophy (by ASE-cube method), *RWT* relative wall thickness, *WMA* wall motion abnormalities

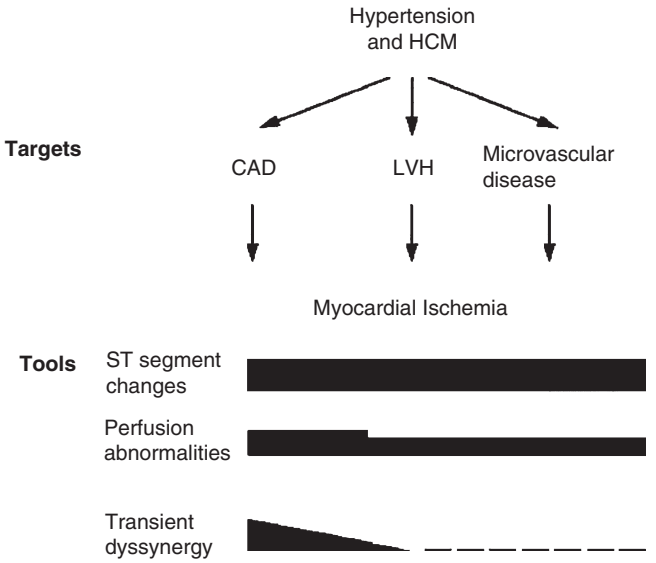

Fig. 31.1 Three main targets of hypertension: coronary artery disease (*CAD*), left ventricular hypertrophy (*LVH*), and microvascular disease. All three of these conditions can provoke stress-induced ST-segment depression and perfusion abnormalities, but only CAD evokes transient dyssynergy. (Modified from [9])

This observation has been attributed to both the remodeling of vascular and extravascular structures and to coronary hemodynamic alterations. The former includes remodeling of intramural arterioles and interstitial fibrosis, and leads to a decreased density of vessels in

the coronary microvasculature, whereas the latter is characterized by increased extravascular compressive forces and elevated systolic and diastolic wall stress and impaired relaxation. Coronary microvascular dysfunction in patients with hypertension is not necessarily related to the presence or degree of left ventricular hypertrophy [6, 7].

31.3 Diagnosis of Coronary Artery Disease

The noninvasive diagnosis of coronary artery disease in hypertensive individuals is particularly challenging for the cardiologist, because the coexistence of hypertension dramatically lowers the specificity of exercise electrocardiography and perfusion scintigraphy [8, 9]. Experience with diagnostic tests in these patients led to the frustrating conclusion in the prestress echocardiographic era that "no non-invasive screening test has been found to adequately discriminate between hypertensive patients with and without associated atherosclerosis" [10]. Furthermore, all exercise-dependent tests also show a markedly lowered feasibility in hypertensive patients; severe hypertension during the resting condition is a contraindication to exercise testing, and even in mild to moderate hypertension, the first step of exercise can induce an exaggerated hypertensive response that limits effort tolerance [10]. Stress echocardiography tests have proven to have a higher specificity than ECG [11, 12] or perfusion stress testing [13, 14], with a similar sensitivity (Fig. 31.2). In addi-

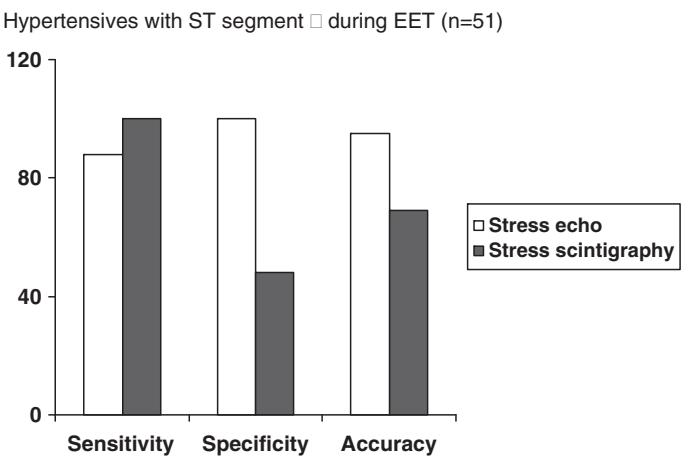

Fig. 31.2 Histogram showing sensitivity, specificity, accuracy, negative predictive value (NPV) and positive predictive value (PPV) of dipyridamole stress test with atropine (*black bars*) and exercise thallium perfusion scintigraphy (*white bars*) for coronary artery disease detection in hypertensive patients with chest pain and positive exercise test. *EET* exercise thallium perfusion scintigraphy. (Modified from [14])

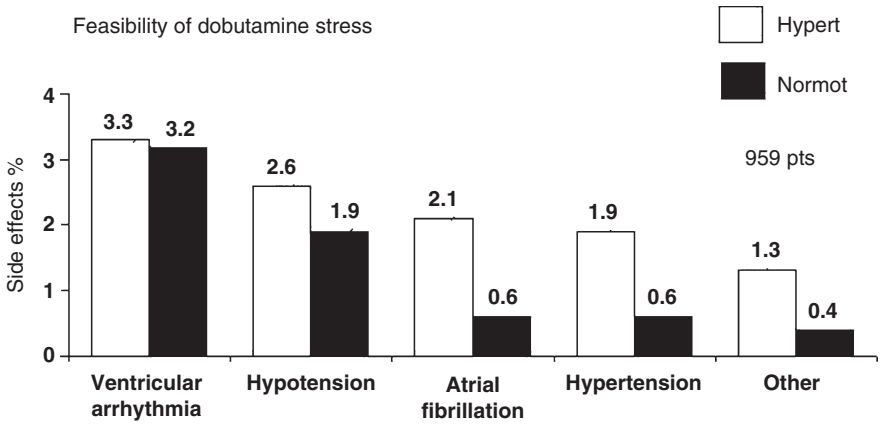

Fig. 31.3 Safety and tolerability profile of dobutamine stress testing in a large cohort of normotensive (*black bars*) and hypertensive patients (*white bars*): all side effects are more frequent in hypertensive subjects. (Modified from [15])

tion, pharmacological stresses have a significantly higher feasibility than exercise stress testing [11], especially with vasodilator testing, which does not evoke the often limiting hypertensive response that can be associated with dobutamine stress [15] (Fig. 31.3). The exaggerated systolic blood pressure rise is also a frequent determinant of wall motion abnormalities during exercise, lowering the specificity of the test [16]. Dipyridamole is less vulnerable to false-positive wall motion abnormalities since there is little or no systolic blood pressure rise during stress [17].

31.4 Prognostic Stratification

During stress, we have three signals of potential value in hypertensive patients: ST-segment depression, wall motion abnormalities, and coronary flow reserve. The pathophysiological significance of stress-induced, ischemic-like electrocardiographic changes remains uncertain [18]. This stress pattern is often found in these patients with normal coronary arteries and hyperkinetic wall motion. The electrocardiographic changes may merely represent nonspecific, innocent alterations or may reflect true subendocardial hypoperfusion. Such ischemic-like electrocardiographic changes occurring with angiographically normal coronary arteries have been associated with a reduced coronary flow reserve [19], a higher incidence of spontaneously occurring or stress-induced ventricular arrhythmias [20], higher values of left ventricular mass index, and, when left ventricular mass is normal, more pronounced structural and functional changes in systemic arterioles [21]. Regression

of structural changes of systemic arterioles achieved with any form of antihypertensive therapy is paralleled by the electrocardiographic negativity of a previously positive ECG stress test result [22, 23].

As with microvascular angina, resting and stress echocardiography can be very helpful for risk stratification in patients with chest pain and angiographically normal coronary arteries. The prognostic value of stress-induced wall motion abnormalities is strong and extensively documented. Hypertensive patients with inducible wall motion abnormalities (with or without underlying coronary artery disease) are at higher risk than those without [24–26] (Fig. 31.4). Within the subset with no wall motion abnormalities, patients with reduced coronary flow reserve assessed with transthoracic echocardiography are at intermediate risk (Fig. 31.5) and patients with neither wall motion abnormalities nor coronary flow reserve are at lowest risk [27] (Fig. 31.6).

When compared to other stress imaging techniques with comparable prognostic value, such as myocardial perfusion scintigraphy, stress echocardiography has three clear advantages: lower cost (approximately 1:3 compared with perfusion scintigraphy) [28, 29]; higher specificity (which is important to avoid a number of useless coronary angiographies) [13, 14], also maintained in challenging subsets such as patients with right bundle branch block [30]; and, most importantly, lack of radiation exposure, ranging from a dose equivalence of 500–1,500 chest X-rays for a stress scintigraphy with sestamibi or thallium, respectively, or 700–1,500 chest X-rays for cardiac computed tomography [31–33]. These

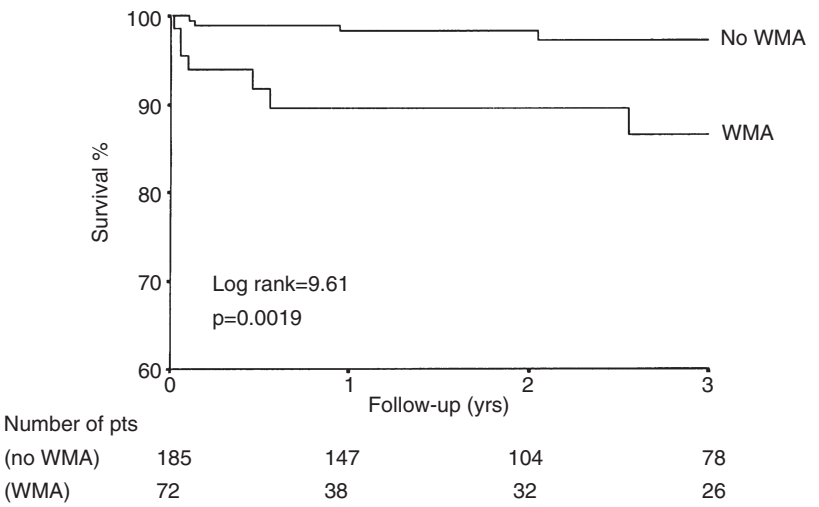

Fig. 31.4 The prognostic value of inducible wall motion abnormalities (*WMA*) in hypertensive patients. (Modified from [24])

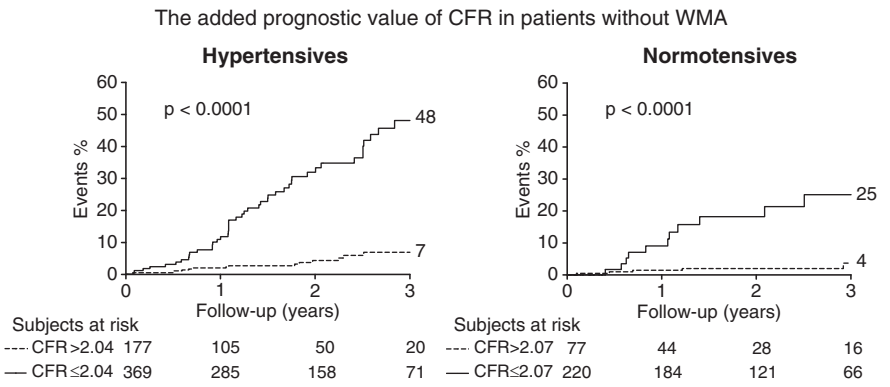

Fig. 31.5 The prognostic value of reduced coronary flow reserve (*CFR*) in hypertensives (*left panel*), and normotensives (*right panel*) with reduced coronary flow reserve. (Modified from [28])

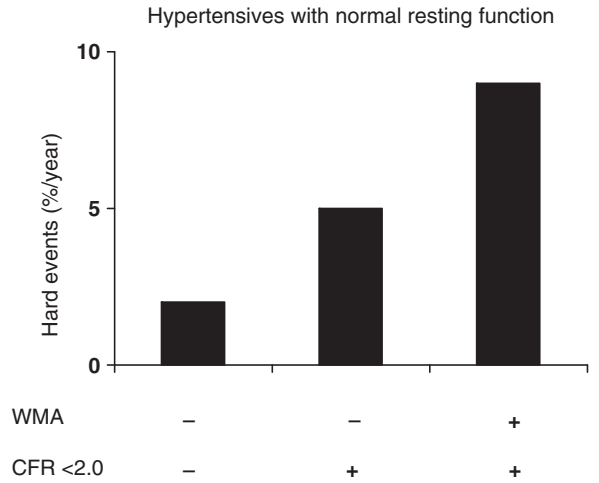

Fig. 31.6 Risk stratification in hypertensive patients based on the simple parameters: wall motion abnormalities (*WMA*) and reduction in coronary flow reserve (*CFR* <2.0). Both parameters can be identified during a single stress echocardiography test ("two birds with one stone"), more easily with a vasodilator stress

aspects are especially important in our cost-conscious and risk-conscious era, in particular if we consider that serial examinations are required in these patients since the results of a negative test are no longer valid after 12–24 months, and every test adds cost to cost, dose to dose, and risk to risk [34]. Stress echocardiography today appears to offer an advantageous trade-off between the top priority of granting the optimal care for our patients with the emerging need to optimize the economic and biological sustainability of our diagnostic strategies [35] (Figs. 31.6 and 31.7).

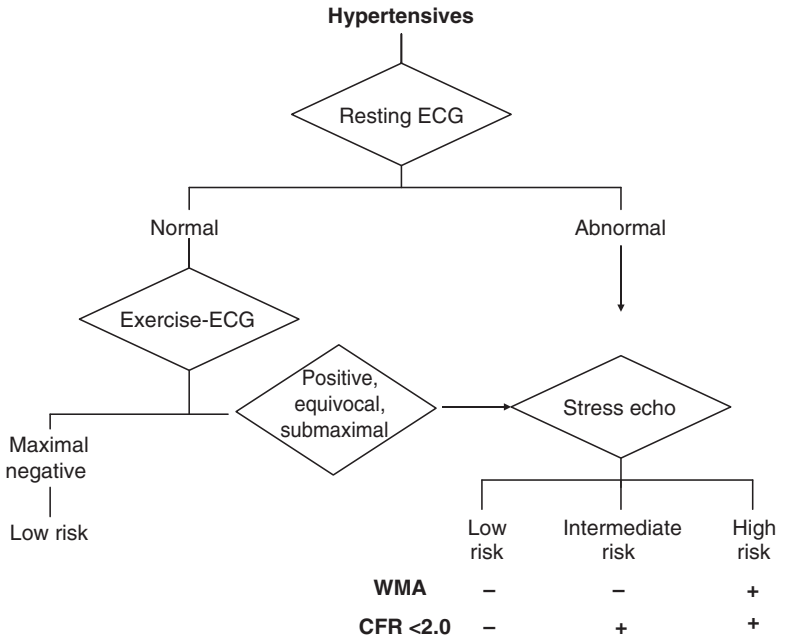

Fig. 31.7 The proposed diagnostic algorithm in hypertensive patients. Exercise electrocardiography remains the most informative first-line test, because of the wealth of information (blood pressure response, arrhythmias, exercise tolerance) provided beyond ST-segment changes. The negative predictive value is high in patients with interpretable and normal ECG at rest. In patients with abnormal or equivocal stress ECG findings, and in patients with resting ECG abnormalities, a stress imaging test is indicated as a gatekeeper to coronary angiography

References

1. Mancia G, De Backer G, Dominiczak A, et al; The task force for the management of arterial hypertension of the European Society of Hypertension, The task force for the management of arterial hypertension of the European Society of Cardiology (2007). 2007 Guidelines for the management of arterial hypertension: The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 28:1462–1536
2. de Simone G, Schillaci G, Palmieri V, et al (2000) Should all patients with hypertension have echocardiography? J Hum Hypertens 14:417–421
3. Galderisi M (2005) Diastolic dysfunction and diastolic heart failure: diagnostic, prognostic and therapeutic aspects. Cardiovasc Ultrasound 3:9
4. Marcus ML (1989) Importance of abnormalities in coronary flow reserve to the pathophysiology of left ventricular hypertrophy secondary to hypertension. Clin Cardiol 12:IV34–IV35
5. Strauer BE (1979). Ventricular function and coronary hemodynamics in hypertensive heart disease. Am J Cardiol 44:999–1006

6. Opherk D, Mall G, Zebe H, et al (1984) Reduction of coronary reserve: a mechanism for angina pectoris in patients with arterial hypertension and normal coronary arteries. Circulation 69:1–7
7. Brush JE Jr, Cannon RO III, Schenke WH, et al (1988). Angina due to coronary microvascular disease in hypertensive patients without left ventricular hypertrophy. N Engl J Med 319: 1302–1307
8. Vogt M, Motz W, Strauer BE (1992). Coronary haemodynamics in hypertensive heart disease. Eur Heart J 13(Suppl D):44–49
9. Lucarini AR, Picano E, Lattanzi F, et al (1991) Dipyridamole-echocardiography stress testing in hypertensive patients. Target and tools. Circulation 83(Suppl III):68
10. Prisant LM, Frank MJ, Carr AA, et al (1987) How can we diagnose coronary heart disease in hypertensive patients? Hypertension 10:467–472
11. Picano E, Lucarini AR, Lattanzi F, et al (1988) Dipyridamole echocardiography in essential hypertensive patients with chest pain. Hypertension 12:238–243
12. Lucarini AR, Lattanzi F, Picano E, et al (1989) Dipyridamole-echocardiography test in essential hypertensives with chest pain and angiographically normal coronary arteries. Am J Hypertens 2:120–123
13. Fragasso G, Lu C, Dabrowski P, et al (1999). Comparison of stress/rest myocardial perfusion tomography, dipyridamole and dobutamine stress echocardiography for the detection of coronary disease in hypertensive patients with chest pain and positive exercise test. J Am Coll Cardiol 34:441–447
14. Astarita C, Palinkas A, Nicolai E, et al (2001) Dipyridamole-atropine stress echocardiography versus exercise SPECT scintigraphy for detection of coronary artery disease in hypertensives with positive exercise test. J Hypertens 19:495–502
15. Cortigiani L, Zanetti L, Bigi R, et al (2002) Safety and feasibility of dobutamine and dipyridamole stress echocardiography in hypertensive patients. J Hypertens 20:1423–1429
16. Ha JW, Juracan EM, Mahoney DW, et al (2002). Hypertensive response to exercise: a potential cause for new wall motion abnormality in the absence of coronary artery disease. J Am Coll Cardiol 39:323–327
17. Picano E, Palinkas A, Amyot R (2001) Diagnosis of myocardial ischemia in hypertensive patients. J Hypertens 19:1177–1183
18. Picano E, Lucarini AR, Lattanzi F, et al (1990) ST segment depression elicited by dipyridamole infusion in asymptomatic hypertensive patients. Hypertension 16:19–25
19. Strauer BE, Schwartzkopff B, Kelm M (1998) Assessing the coronary circulation in hypertension. J Hypertens 16:1221–1233
20. Lucarini AR, Picano E, Bongiorni MG, et al (1991) Increased prevalence of ventricular arrhythmias in essential hypertensives with dipyridamole-induced ischemic-like S-T segment changes. J Hypertens 9:839–844
21. Virdis A, Ghiadoni L, Lucarini A, et al (1996) Presence of cardiovascular structural changes in essential hypertensive patients with coronary microvascular disease and effects of long-term treatment. Am J Hypertens 9:361–369
22. Lucarini AR, Picano E, Salvetti A (1992) Coronary microvascular disease in hypertensives. Clin Exp Hypertens A 14:55–66
23. Cannon RO 3rd (1996) The heart in hypertension. Thinking small. Am J Hypertens 9:406–408
24. Cortigiani L, Paolini EA, Nannini E (1998) Dipyridamole stress echocardiography for risk stratification in hypertensive patients with chest pain. Circulation 98:2855–2859
25. Marwick TH, Case C, Sawada S, et al (2002) Prediction of outcomes in hypertensive patients with suspected coronary disease. Hypertension 39:1113–1118
26. Bigi R, Bax JJ, van Domburg RT, et al (2005) Simultaneous echocardiography and myocardial perfusion single photon emission computed tomography associated with dobutamine stress to

predict long-term cardiac mortality in normotensive and hypertensive patients. J Hypertens 23:1409–1415
27. Rigo F, Cortigiani L, Gherardi S, et al (2008) Coronary flow reserve in hypertensives: the best diagnostic and prognostic cut-off values. Eur Heart J (abstract Suppl)
28. Gibbons RJ, Balady GJ, Bricker JT, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines) (2002) ACC/AHA 2002 guideline update for exercise testing: summary article: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1997 Exercise Testing Guidelines). Circulation. 106:1883–1892
29. Picano E (2005). Economic and biological costs of cardiac imaging. Cardiovasc Ultrasound 3:13
30. Cortigiani L, Bigi R, Rigo F, et al; Echo Persantine International Cooperative Study Group (2003) Diagnostic value of exercise electrocardiography and dipyridamole stress echocardiography in hypertensive and normotensive chest pain patients with right bundle branch block. J Hypertens 21:2189–2194
31. Picano E (2003) Stress echocardiography: a historical perspective. Special Article. Am J Med 114:126–130
32. Picano E (2004) Sustainability of medical imaging. Education and Debate. BMJ 328:578–580
33. Picano E (2004) Informed consent and communication of risk from radiological and nuclear medicine examinations: how to escape from a communication inferno. Education and debate. BMJ 329:849–851
34. Picano E, Vano E, Semelka R, et al (2007). The American College of Radiology white paper on radiation dose in medicine: deep impact on the practice of cardiovascular imaging. Cardiovasc Ultrasound 5:37
35. Brenner DJ, Hall EJ (2007). Computed tomography – an increasing source of radiation exposure. N Engl J Med 357:2277–2284