Coronary Flow Reserve

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9.1 Historical Background and Physiological Basis

The seminal concept of coronary flow reserve (CFR) was proposed experimentally by Lance K. Gould in 1974 [1]. Under normal conditions, in the absence of stenosis, coronary blood flow can increase approximately four- to sixfold to meet increasing myocardial oxygen demands. This effect is mediated by vasodilation at the arteriolar bed, which reduces vascular resistance, thereby augmenting flow. Coronary reserve is the capacity of the coronary circulation to dilate following an increase in myocardial metabolic demand and can be expressed by the difference between the hyperemic flow and the resting flow curve. In most clinical applications, hyperemia is induced pharmacologically, not via an increase in oxygen demand. A combined anatomical and physiological classification can ideally identify four separate segments in the hyperemic curve (Fig. 9.1): (1) the hemodynamically silent range of 0–40 % stenosis, which does not affect CFR (>2.5) to any detectable extent; (2) the clinically silent zone, where stenosis ranging from 40 to 70 % may marginally reduce the CFR without reaching the critical threshold required to provoke ischemia with the usual stresses; (3) the severe stenosis range (70–90 %), where critical stenosis reduces CFR less than 2.0 and myocardial ischemia is usually elicited when a stress is applied; and (4) the very severe stenosis range (>90 %), producing a marked transstenotic pressure drop at rest, with a reduction of baseline myocardial blood flow and a CFR close to 1, or even less; in these patients, the administration of a coronary vasodilator actually decreases the poststenotic flow for steal phenomena. This experimental paradigm can be accurately reproduced clinically in highly selected series of patients with single-vessel disease, no myocardial infarction, no coronary collateral circulation, normal baseline function, no left ventricular hypertrophy, and no evidence of coronary vasospasm and who are off therapy at the time of testing. In these patients, the more severe the stenosis, the more profound the impairment in CFR. The correction of the stenosis improves CFR, and perfect dilation normalizes the CFR. The perfect, predictable relationship found in the experimental animal and in a very selected patient population [2] falls apart in the clinical

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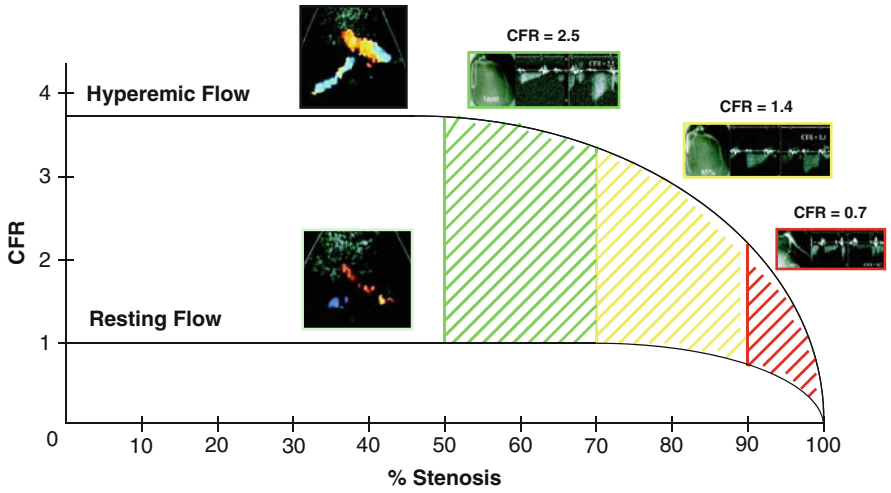

Fig. 9.1 The curve of CFR with the four segments: hemodynamically silent (0–40 % stenosis), clinically silent (40–70 % stenosis), hemodynamically significant (70–90 % with CFR <2.0), and very severe stenosis (>90 %, with CFR <1.0) (Redrawn and adapted from Gould and Lipscomb [1] and Pizzuto et al. [17])

arena [3], where many variables can modulate the imperfect match between epicardial coronary artery stenosis and CFR. Among others, these variables include:

1. The geometric characteristics of the stenosis
2. The presence of coronary collateral circulation
3. The microvascular component of coronary resistance
4. Left ventricular hypertrophy modulating the myocardial extravascular component of coronary resistance
5. The viable or necrotic state of the myocardium distal to the stenosis
6. The presence of coronary macrovascular or microvascular spasm
7. The presence of concomitant anti-ischemic therapy

In fact, this impressive scatter of data leads to the need to reconsider our original view of ischemic heart disease focused on coronary stenosis [4]. According to that view, each level of stenosis precisely predicts the level of impairment in coronary blood flow. This concept has some corollaries: stenosis is the disease, and dilating the stenosis means curing the disease; the probability of subsequent occlusion depends on the severity of the stenosis; the stress test accurately maps the area at risk for subsequent infarction. Although reasonable, all these corollaries are at least partially wrong; the stenosis is only the fruit of the atherosclerotic plant, which has deep genetic, metabolic, and hemodynamic roots that must be identified and treated in order to better cure this disease. Critical stenosis may occlude, but the majority of clinically catastrophic occlusions occur in previously noncritical stenosis; the stress test accurately identifies the area at risk of subsequent infarction in only a minority

Table 9.1 Methods of assessing CFR

	Measurements of flow	Radiation exposure	Cost	Availability	Accuracy	Interest
PET	Absolute	2–5 mSv	Very high	–	+++	Research
SPECT	Relative	10–20 mSv	High	++	++	Clinical cardiology
CMR	Relative	0	High	±	++	Clinical cardiology
Intracoronary Doppler	Relative	5 mSv	High	±	+++	Cath lab
Transesophageal Doppler	Relative	0	Low	+	++(+)	Echo lab
Transthoracic echocardiography	Relative	0	Very low	+++	++(+)	Clinical cardiology

CXR chest radiograph, *mSv* millisievert, *PET* positron emission tomography, *SPECT* single-photon emission computed tomography, *CMR* cardiovascular magnetic resonance

(four out of ten) of patients. In two out of ten patients, the stress test is right for the wrong reason (the test results are positive, and the patient develops infarction, but in an area different from the induced ischemia), and in four out of ten, the test is wrong (normal findings in a patient who subsequently develops infarction) [5]. The appeal of coronary flow reserve is to gain insight into a key physiological variable that integrates functional assessment during a stress [6]. This assessment can be obtained clinically, with six different basic approaches (Table 9.1): positron emission tomography (PET), myocardial scintigraphy, magnetic resonance perfusion imaging, intracoronary Doppler flow wire, transesophageal echocardiography, and transthoracic echocardiography. PET is highly accurate and allows a quantitative assessment of absolute myocardial blood flow but is exorbitantly expensive, technically demanding, and available in very few centers and exposes the patient to radiation biohazards. Single-photon emission computed tomography (SPECT) is less expensive and is also less accurate than PET, with a high radiation burden of 500–1500 chest X-rays for a sestamibi or thallium scan, respectively. Intracoronary Doppler flow wire is invasive, risky, and expensive, requiring intracoronary catheterization; radiation exposure is required for intracoronary catheter placement, although not directly for CFR measurement. Instead, transesophageal echocardiography has the limitation of being semi-invasive, while transthoracic echocardiography has the merit of being noninvasive, nonionizing, and compatible with other forms of functional testing for induction of wall motion abnormalities in the echocardiography laboratory. All these approaches are based on the theoretical prerequisite that the imaging technique combined with hyperemic stress will generate a signal whose intensity is correlated (possibly in a linear, direct fashion) with coronary flow, especially in the high-flow range that is the most important one for diagnostic purposes. Unfortunately, none of the available techniques for noninvasive assessment of CFR allows a truly accurate quantitative assessment [7] (Fig. 9.2). For instance, a 40 %

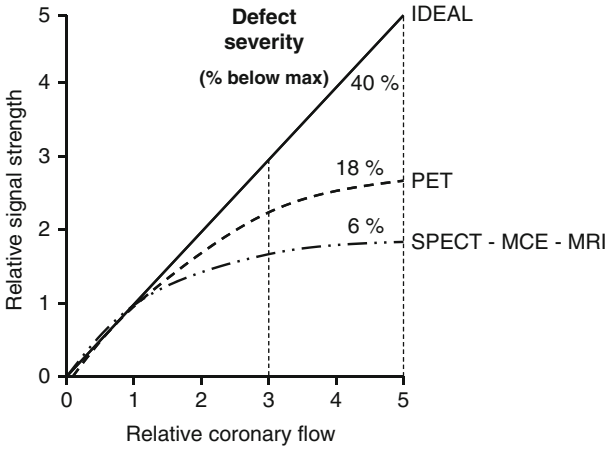

Fig. 9.2 Relationship between the true increments of coronary flow and the flow signal strength obtained with the currently available imaging techniques. All techniques, including the most sophisticated and expensive ones, are considerably far from the ideal, in which the signal increases in a linear and direct fashion with flow. In the high-flow range – the most important one following a vasodilatory stimulus – the relationship between flow and signal tends toward a plateau, implying only minimal (if any) signal differences. For instance, if the flow is fivefold higher in the normal coronary vessel and only threefold in the stenotic vessel, the recorded flow difference will be 18 % by positron emission tomography (*PET*) and around 10 % by SPECT, myocardial contrast echocardiography (*MCE*), transthoracic echo Doppler flowmetry, and magnetic resonance imaging (*MRI*) (Adapted and modified from Gould [7])

reduction in CFR compared with normal values (i.e., a flow reserve of 3 in diseased myocardium compared to a flow reserve of 5 in the normal myocardium) will yield a difference in signal intensity of only 6 % with SPECT (comparable to myocardial contrast echocardiography) and of 18 % with PET, whose results correlate well with intracoronary, transesophageal, and transthoracic echocardiography Doppler techniques [8]. We are still far from the ideal test of CFR. Nevertheless, the possibility of a reasonably accurate estimation of CFR during a stress targeted on functional testing for wall motion analysis opens new, exciting clinical and research opportunities.

9.2 Coronary Flow Reserve in the Echocardiography Lab

With either transesophageal (sampling the proximal tract) or transthoracic echocardiography (exploring the mid-distal tract), the left anterior descending coronary blood flow velocity profile recorded with pulsed-wave Doppler is consistent with the pathophysiological premises. Coronary flow velocity by Doppler assessment appears to be biphasic, with a lower peak during systole and a higher peak during diastole. Myocardial extravascular resistance in fact is higher in systole and lower in diastole due to the effect of myocardial contraction (Fig. 9.3) [9]. The flow

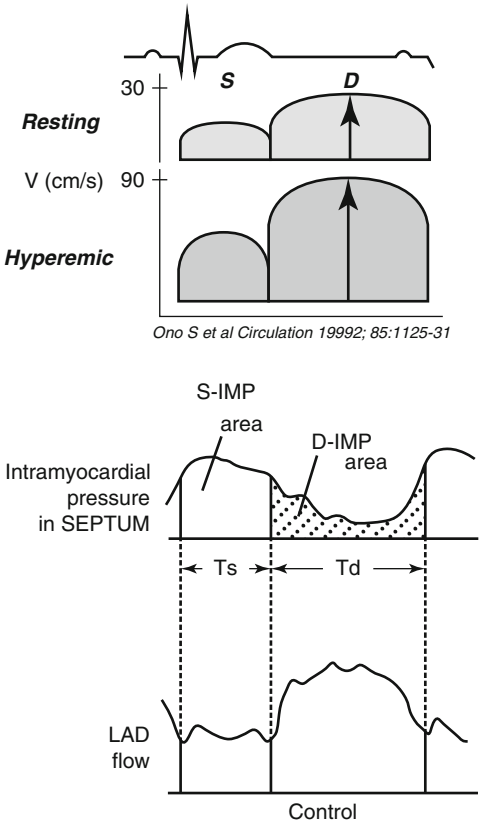

Fig. 9.3 Schematic representation of coronary flow velocity profile obtained with transthoracic Doppler of the mid-distal left anterior descending coronary artery and measurement of the CFR through peak diastolic flow velocity. The coronary blood flow velocity is higher in diastole. The *lower panel* shows the experimental data obtained with intramyocardial pressure monitoring and left anterior descending flowmetry in the dog (From Ono et al. [9], with permission)

velocity variations are proportional to the total blood flow if the diameter of the vessel lumen is kept constant. In reality, the diameter of epicardial coronary arteries increases by an average of 30 % in healthy subjects following adenosine infusion [10]. Therefore, failure to take into account epicardial coronary artery vasodilation during hyperemia may cause a nonsystematic underestimation of CFR, which can be more accurately calculated as velocity time integral cross-sectional area [10]. In practice, and with an unavoidable approximation, the coronary flow velocity reserve (CFVR) between baseline and peak effect of a coronary vasodilator makes it possible to derive an index of CFR in the left anterior descending artery territory. Several parameters might be measured from Doppler tracings of left anterior descending artery flow, including systolic flows, time–velocity integrals, and mean flows [8]. However, the best parameter is peak diastolic flow; it is not only the simplest parameter to be measured and the easiest to obtain but also the most reproducible and the one with the closest correlation with coronary perfusion reserve measured with Doppler flow wire [11] and PET [12]. The signal of coronary flow on the left anterior descending coronary artery was first made possible by transesophageal echocardiography, with excellent diagnostic results [11,

12], but only recently has there been increased clinical interest in the development of the transthoracic method [13–17]. There were technological factors that allowed the totally noninvasive transthoracic imaging of the mid-distal left anterior descending coronary artery: second-harmonic imaging, which provides better definition of smaller structures such as the left anterior descending coronary artery, and high-frequency transducers (up to 8 MHz), which provide improved resolution imaging of near-field structures (Fig. 9.4). The availability of contrast agents also improved the signal-to-noise ratio, increasing the feasibility of transthoracic imaging of the left anterior descending coronary artery above the threshold of potential clinical impact.

The Doppler assessment of CFVR has some limitations. The assessment of absolute blood velocity can be limited in some patients by the large incident angle between the Doppler beam and blood flow. However, calculation of the flow reserve allows assessment of flow patterns without the need for absolute values. More importantly, the velocity ratio is used as a surrogate of flow reserve; flow within the coronary artery is not calculated because cross-sectional visualization of the vessel does not accurately measure the diameter of the vessel. The estimated flow reserve can be accurate if the coronary artery functions only as a conduit, with no change in its diameter during drug infusion. The variability and heterogeneity in coronary artery diameter response following administration of adenosine [10] or dobutamine [18] introduce a remarkable source of error, which is amenable to correction only through direct measurement of epicardial vessel diameter changes with

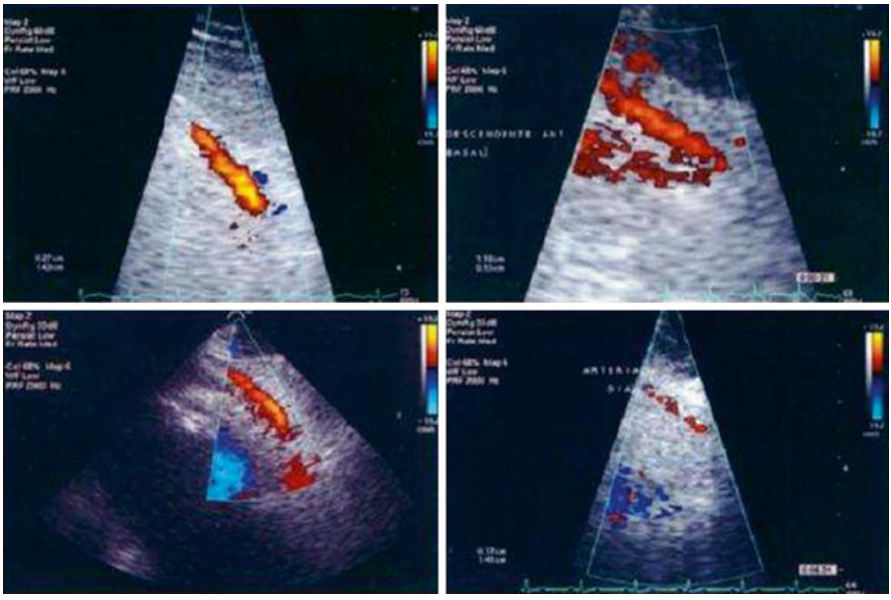

Fig. 9.4 Color Doppler flow imaging of the left anterior descending artery, visualized in its middle-to-distal portion to a variable extent in four different patients (Courtesy of Dr. Jorge Lowenstein)

high-resolution imaging [10]. However, the positive correlation between true CFR and CFVR, together with the lower method variability of the latter, makes it suitable for a robust assessment of CFR in most experimental and clinical settings [19].

9.3 Methodology

Stress testing of CFVR introduces a change in the choice of the stress, the use of transducers, and the methodology of testing.

After stress, the balance between exercise, dobutamine, and vasodilators clearly goes in the direction of vasodilators (Fig. 9.5), which fully recruit CFR [20] (Fig. 9.6) and minimize the factors polluting image quality [21]. Among vasodilators, dipyridamole is better tolerated subjectively than adenosine [22]; it induces less hyperventilation (which may pollute the echocardiography images), costs much less in most countries, and has a longer-lasting vasodilatory effect [23] (Fig. 9.7), which is more convenient for dual flow and function imaging (Table 9.2).

A broadband transducer (2–7 MHz) or two transducers (with low-frequency imaging of wall motion and high-frequency imaging of left anterior descending coronary artery flow) must be used, allowing alternative opening of imaging windows on coronary flow and left ventricular function [24, 25]. Besides the classic projections for stress echocardiography testing, specific projection for left anterior descending coronary artery imaging should be integrated into the cardiac imaging sequence (Fig. 9.8). The posterior descending artery (Fig. 9.9) and the left circumflex artery (Fig. 9.10) can be imaged with dedicated imaging projections but with greater difficulty and a lower success rate. The imaging protocol methodology also changes, with a shift from left anterior descending coronary artery flow to left ventricular function. This is more technically demanding but also more thrilling for the skilled stress echocardiographer, as it combines the two different aspects of flow and functional imaging into a single test [24–26]; the split brain of imaging formally finds its conceptual corpus callosum in the echocardiography laboratory (Figs. 9.11 and 9.12). The normal values are quite similar for all three coronary arteries and are clearly normal when above 2.5, borderline between 2.0 and 2.5, and clearly

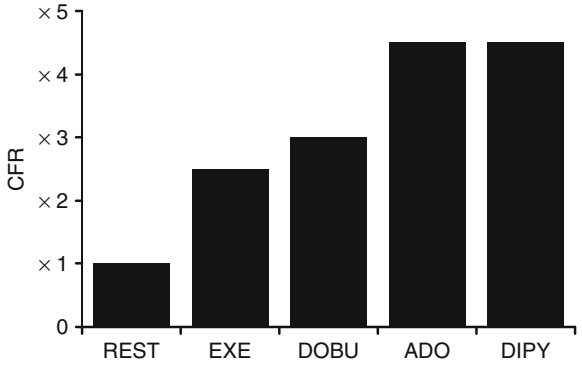

Fig. 9.5 CFVR and stresses: vasodilators [adenosine (*ADO*) or dipyridamole (*DIPY*)] evoke a greater recruitment of CFR, substantially higher than dobutamine (*DOB*) and exercise (*EXE*). They are more appropriate stressors for testing CFR (Modified from Iskandrian et al. [20], with permission)

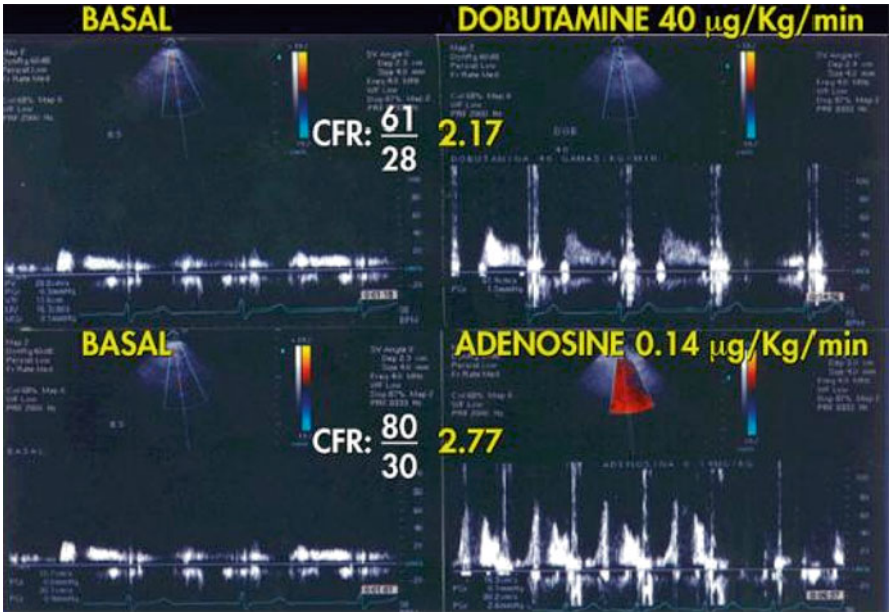

Fig. 9.6 CFVR assessed in the same patient with transthoracic echocardiography by dobutamine (*upper panels*) and adenosine (*lower panels*). *Left panels*, baseline signal. *Right panels*, peak stress signals. The increase in CFVR is substantially higher with adenosine than with dobutamine (Courtesy of Dr. Jorge Lowenstein)

abnormal below 2.0. Athletes show supernormal values (above 4.0). A reduction in CFVR can be linked to a significant epicardial coronary artery stenosis but also to microvascular disease or to factors increasing extravascular resistance and endoluminal compressive forces with normal coronary arteries, as happens in syndrome X, dilated or hypertrophic cardiomyopathy, and aortic stenosis [27].

9.4 Coronary Flow Velocity Reserve: The Diagnostic Results

Good results have been reported with CFVR evaluation during transesophageal [11, 12] or transthoracic echocardiography [13–17] for noninvasive diagnosis of coronary artery disease (Fig. 9.13). Nevertheless, the use of CFVR as a stand-alone diagnostic criterion suffers from major pitfalls, since only the left anterior descending coronary artery is easily sampled in different tracts, and CFVR cannot distinguish between microvascular and macrovascular coronary disease [27]. Therefore, it is much more interesting (and clinically realistic) to evaluate the additive value over conventional wall motion for left anterior descending coronary artery detection. The assessment of CFVR adds sensitivity for left anterior descending coronary artery disease, with a modest loss of specificity [28–32]. In some ways, CFVR and wall

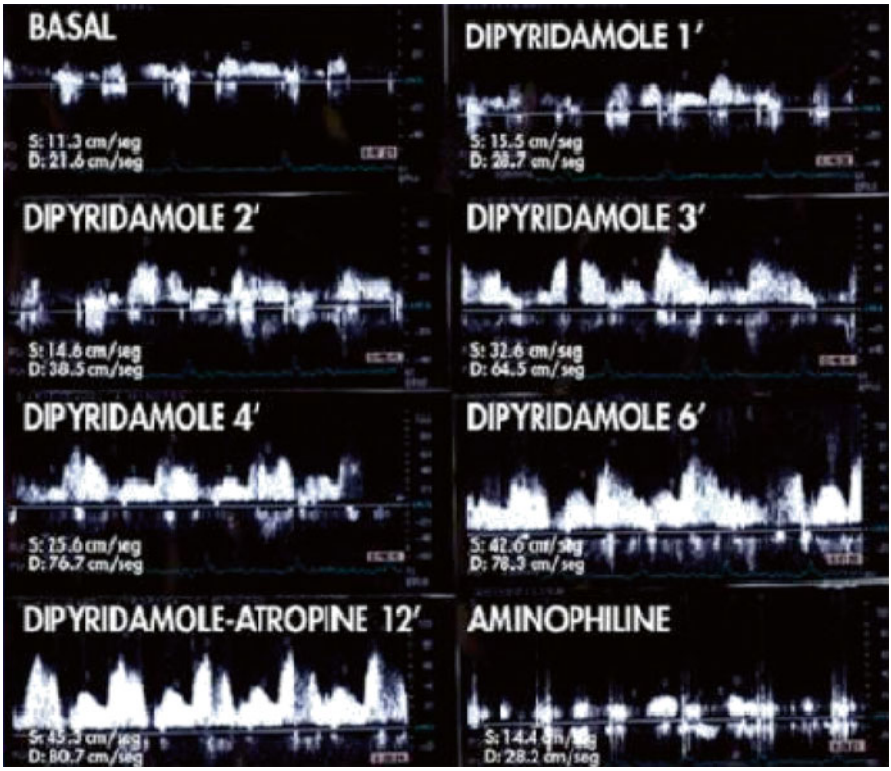

Fig. 9.7 The temporal sampling of CFVR by transthoracic echocardiography. There is a progressive, stepwise increase in CFVR peaking after the high dose and immediately reversed upon administration of aminophylline

Table 9.2 Vasodilator stress imaging

Drug	Adenosine	Dipyridamole
Patient tolerance	Lower	Higher
Vasodilator effect onset	Seconds	Minutes
Multiple coronary imaging	Difficult	Possible
Combined wall motion and CFVR	Difficult	Possible

CFVR coronary flow velocity reserve

motion analysis offer complementary information during stress echocardiography (Table 9.3). From the pathophysiological viewpoint, wall motion positivity requires ischemia as a necessary prerequisite, whereas CFR can be impaired in the absence of induced ischemia. Wall motion is easy to acquire but can be difficult to analyze. CFVR can be difficult to acquire, but it is usually straightforward in its quantitative interpretation of a Doppler signal. In the interpretation phase, a regional wall motion abnormality has higher positive predictive value for predicting the presence

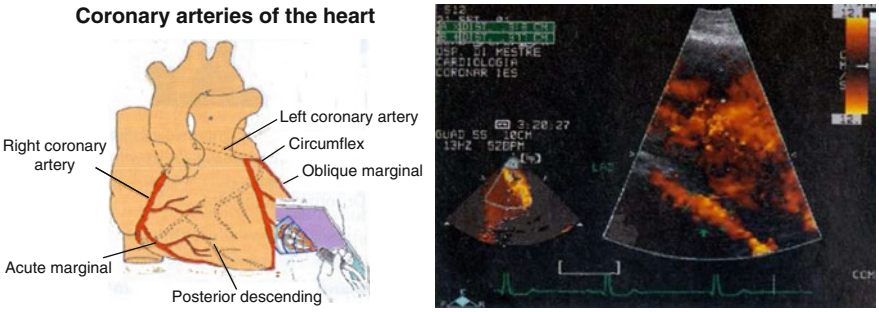

Fig. 9.8 *Left panel*: Artist's drawing illustrating transducer beam orientation to the left anterior descending coronary artery. The mid-distal tract is imaged from a modified apical 2-chamber view. *Right panel*: The corresponding echocardiographic image of left anterior descending color flow

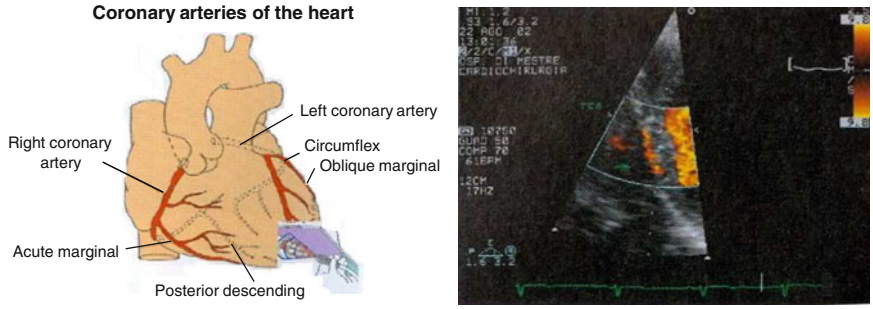

Fig. 9.9 *Left panel*: Artist's drawing illustrating transducer beam orientation to the posterior descending coronary artery. The mid-distal tract is imaged from a modified apical 2-chamber view with counterclockwise rotation and anterior angulation of the probe. *Right panel*: The corresponding echocardiographic image of posterior descending color flow

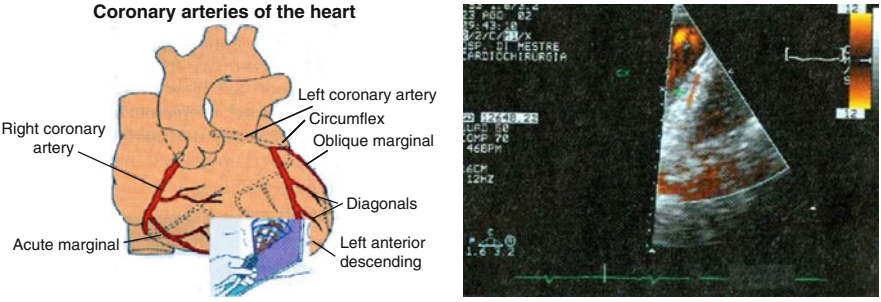

Fig. 9.10 *Left panel*: Artist's drawing illustrating transducer beam orientation to the left circumflex coronary artery. The mid-proximal tract of the left circumflex artery is imaged from a modified apical 4-chamber view with 50–80° clockwise rotation and posterior angulation of the probe. *Right panel*: The corresponding echocardiographic image of left circumflex color flow

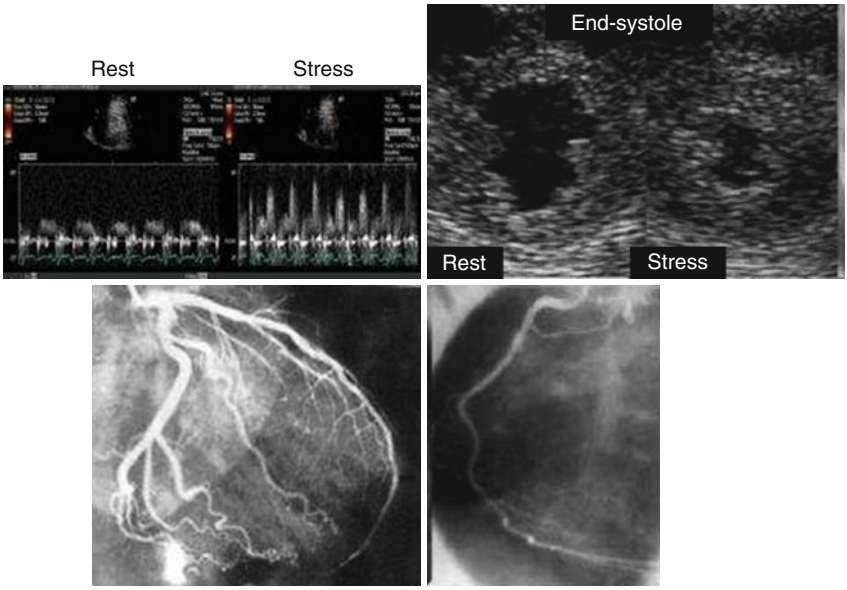

Fig. 9.11 A typical example of a normal regional wall motion and CFVR pattern from a patient with normal coronary arteries. The end-systolic frames from parasternal short-axis view show a normal thickening at rest (*left upper panel*) and during stress (*right upper panel*). On the *left*, pulsed Doppler shows a threefold increase in Doppler peak diastolic flow velocity from baseline (*left lower panel*) to peak dipyridamole (*right lower panel*)

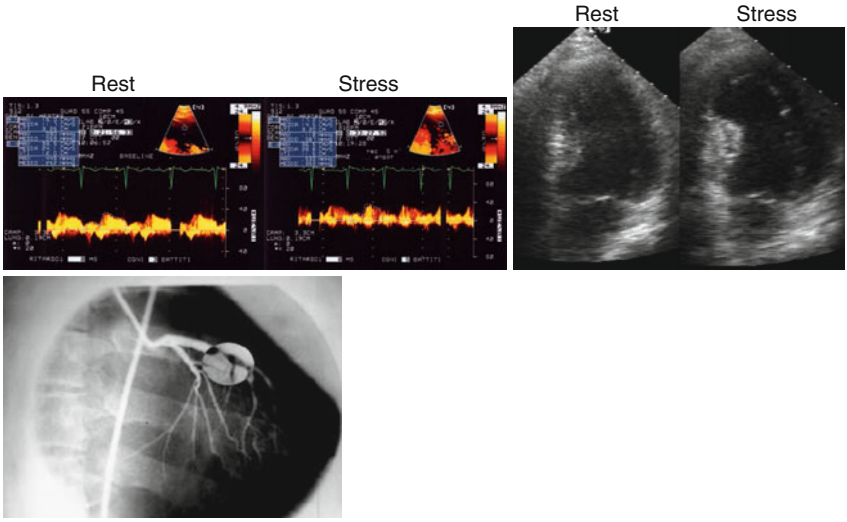

Fig. 9.12 A typical example of a regional wall motion (*right upper panel*) and CFVR (*left upper panel*) pattern from a patient with a tight proximal stenosis of the left anterior descending artery (*lower panel*). On the *right*, the end-systolic frames from the apical 4-chamber view show a normal thickening at rest and akinesia of the apex during stress. On the *left*, pulsed Doppler shows no significant increase in Doppler peak diastolic flow velocity from baseline (*left*) to peak dipyridamole (*right*)

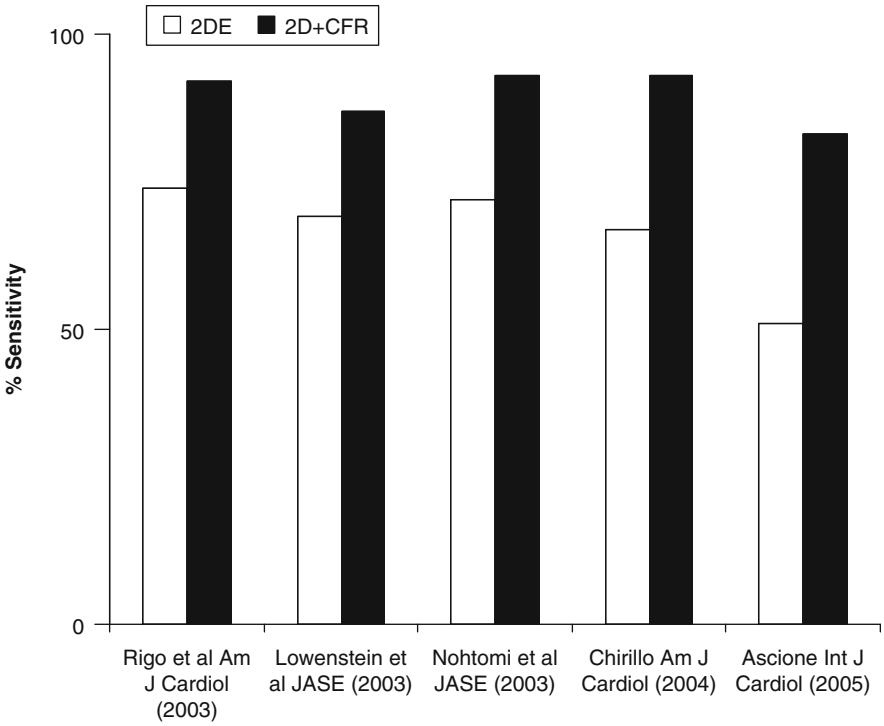

Fig. 9.13 The sensitivity for noninvasive detection of anatomic disease of the left anterior descending coronary artery on the basis of wall motion (2D echocardiography) and CFVR criteria in five different studies, all consistently showing the higher sensitivity achieved with the contribution of 2D echocardiography and CFR criterion versus 2D echocardiography alone (Redrawn and adapted from original data of [28–32])

Table 9.3 The two faces of stress echocardiography testing

	Wall motion	Coronary flow reserve
Specificity	Higher	Lower
Sensitivity	Lower	Higher
Technical difficulty	Lower	Higher
Interpretation	Difficult	Easier
Prognostic value	High	Unknown
Segmental positivity response	All or one	Continuous
Coronary arteries explored	All territories	Mostly LAD

LAD left anterior descending artery

of epicardial coronary artery stenosis. A normal CFVR has a higher negative predictive value. Therefore, the two pieces of information on flow and function can complement each other since a wall motion abnormality is highly specific and a normal CFVR is highly sensitive for coronary artery disease [28–32]. In addition, the flow information is relatively unaffected by concomitant antianginal therapy, which

markedly reduces sensitivity of ischemia-dependent regional wall motion abnormality [33] and does not influence CFVR except to a limited extent, if at all [34]. In this way, the CFR can already help in the difficult task of identifying patients with coronary artery disease. Obviously, such help will be greater with the potential of imaging all three major coronary arteries, with segments of the posterior descending and left circumflex coronary artery [35, 36] being more difficult for ultrasonic imaging at present.

9.5 The Prognostic Value of Coronary Flow Velocity Reserve

In patients with idiopathic dilated cardiomyopathy [37] or hypertrophic cardiomyopathy [38] and in patients with normal to nonsignificant coronary artery disease [39, 40], a severely depressed CFR is a predictor of poor prognosis. These studies were performed on small patient series, with a limited number of events, and employed complex and demanding techniques such as PET [37, 38] or the intracoronary Doppler flow wire technique [39, 40]. With the advent of CFVR in the stress echocardiography laboratory, in a few years a striking amount of information became available through large-scale multicenter studies, showing the impressive prognostic value of CFVR. This value has been proven in patients with stable angina [41, 42], in patients with intermediate stenosis of single-vessel disease [43, 44], and in several other challenging subsets characterized by negative wall motion response during stress echocardiography, such as patients with diabetes [45, 46] or hypertension [47], under antianginal therapy at the time of testing [48], with left bundle branch block [49], dilated cardiomyopathy [50], hypertrophic cardiomyopathy [51], or heart transplant [52]. The prognostic value has also been shown

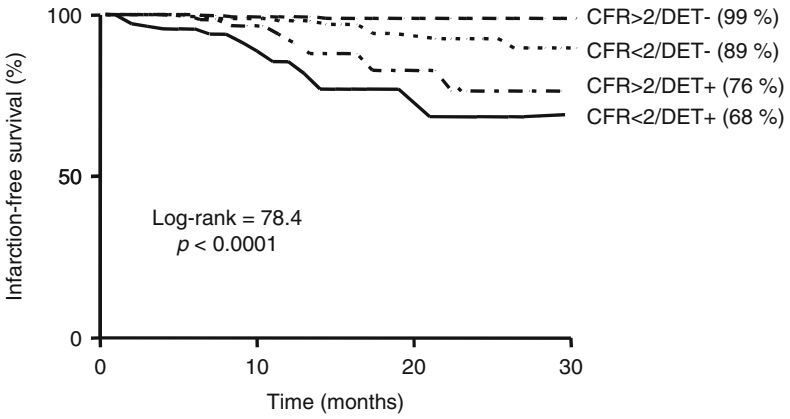

Fig. 9.14 Kaplan–Meier survival curves (considering only death and myocardial infarction as end points) in patients stratified according to normal (>2.0) or abnormal (<2.0) CFVR at Doppler echocardiography and the presence or absence of wall motion abnormalities by 2D echocardiography

for hard end points only [53] and adds incremental information over the value of inducible wall motion abnormalities (Fig. 9.14). The prognostic information provided by CFVR can be further expanded if the response is titrated according to a continuous spectrum rather than artificially dichotomized, with lowest quartiles (<1.8) identifying higher risk than higher quartiles with progressively more benign prognosis [54]. At this point, an evidence-based use of CFVR in clinically driven decision-making is possible and fully justified. Similar diagnostic and prognostic results can be obtained in the assessment of left ventricular wall motion and CFVR in left internal mammary artery and right internal mammary artery grafts [55–58].

9.6 Targets, Tips, and Traps in Coronary Flow Reserve Assessment

At present, different segments of native or grafted coronary arteries can be imaged transthoracically in the echocardiography laboratory. Each of the segments has different transducer frequency windows, different initial velocity range, different projections, and different technical difficulties (Table 9.4). There are biological and technical problems with CFR assessment. The CFR depends on a coronary as well as a myocardial component. Patent native arteries or graft with a low flow reserve supply myocardium that is partially scarred from previous infarction. Under these conditions, the vasodilating capacity of the recipient myocardium is probably reduced independently of any stenosis. In diagnostic terms, this may account for a reduced specificity of CFR (abnormal with patent arteries). Poststenotic CFR accurately reflects the residual vasodilatory capacity of that vascular bed which is specifically affected by the stenosis [24–27]. Prestenotic CFR can be diagnostically

Table 9.4 CFVR in the echocardiography laboratory: technicalities and targets

Vein graft	LAD	LCx	PD	LIMA	RIMA	Saphenous
Success rate	90 %	50 %	60 %	90–100 %	90–100 %	80–90 %
Transducer	Modified	Modified	Modified	Left supra	Right	Modified
Position	Apical	Apical 4-chamber	Apical 2-chamber	Clavicular area	Supraclavicular area	Parasternal
Transducer frequency (MHz)	5–7	3.5	3.5	5–7	5–7	3–5
Best CFR cutoff for stenosis detection	<2.0	<2.0	<2.0	<1.9	<1.9	<1.6

CFR coronary flow reserve, *LAD* left anterior descending artery, *LCx* left circumflex artery, *PD* posterior descending artery, *LIMA* left internal mammary artery, *RIMA* right internal mammary artery

unreliable, since the abnormal response in the poststenotic territory can be pseudonormalized by the normal vasodilatory response in the territories supplied by the branching vessels stemming off the main trunk between the sampling zone and the stenosis. CFR will yield the greatest information when combined with wall motion imaging. Contrast agent injection is sometimes – although not often – needed, and this will impact favorably on the cost-effectiveness profile of the method.

9.7 Stress Echo Response Patterns

Assessment of CFVR integrates and complements classic stress echocardiography founded on regional wall motion analysis. With the addition of CFVR to wall motion, the stress echocardiography response can be stratified into a severity code mirroring the ischemic cascade. On one end of the spectrum, there is the totally normal pattern, with hyperdynamic left ventricular function and preserved CFR, which is highly predictive of normal coronary anatomy and normal physiological response of coronary micro- and macrocirculation. At the opposite end of the spectrum, there is the totally abnormal pattern with regional wall motion abnormalities and abnormal coronary flow response, which is highly predictive of diseased epicardial coronary anatomy and impaired flow reserve. In between these extreme "black and white" responses, a gray zone can be found, more often with prognostically meaningful mild to moderate abnormal CFR and normal function (Fig. 9.15). At present, CFVR in coronary artery disease is a feasible, useful, and prognostically validated tool to be considered with standard wall motion analysis for the "two birds with one stone" approach of dual imaging in stress echocardiography. Its noninvasive, radiation-free nature also make it ideally suited for ethically immaculate, radiation-free research-oriented studies, especially when each subject or patient acts as his/her own control, allowing establishment of acute or chronic changes in CFR, induced, for instance, by acute food or beverage intake (such as alcohol or chocolate) or ingestion of medication in chronic therapeutic interventions, for instance, statins or antihypertensive drugs [59–61]. Although substantial technological and conceptual refinements are expected in the near future, for instance, with 3D imaging and the possibility of accurately assessing CFR with simultaneous evaluation of coronary flow velocity profiles and stress-induced changes in coronary diameter, there is little doubt that the technique is here to stay.

9.8 Pitfalls

The feasibility and clinical impact are highest for the mid-distal native left anterior descending coronary artery and the left internal mammary artery graft, while it is lowest (albeit still feasible) for posterior descending and left circumflex arteries. CFVR can be altered by changes in resting and hyperemic flows, which are

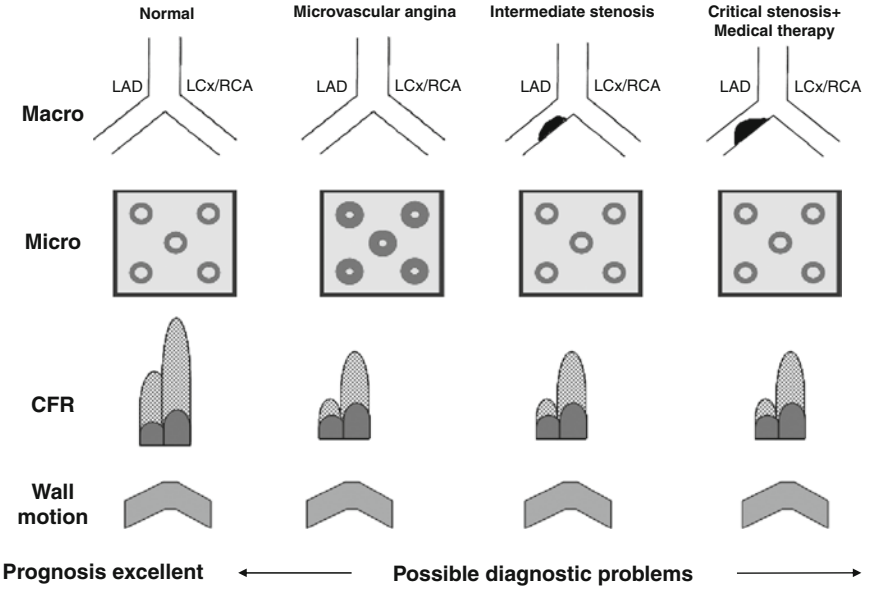

Fig. 9.15 Pathophysiological and prognostic heterogeneity behind normal wall motion response during stress. In the *upper panel*, we show epicardial coronary arteries: normal in the *first two columns*, with moderate disease in the *third column*, and moderate-to-severe disease but concomitant, effective anti-ischemic therapy in the *last column*. The myocardium is shown as a *square box*, with small vessels as *circles*. Coronary small vessel disease is shown (*second columns*) as *bold circles* (structural or functional impairment). All four very different pathophysiological conditions show the negativity of wall motion response. The abnormal CFVR response is present in the *last three columns*, with abnormality of micro- or macrocirculation. *Panel B*: Pathophysiological and prognostic heterogeneity behind abnormal wall motion response during stress. Symbols as in *panel A*. The CFVR can be normal in spite of wall motion abnormality when the left anterior descending artery is not significantly involved and the microcirculatory level is not impaired (*left panel*)

influenced by hemodynamics, loading conditions, and contractility. For example, tachycardia increases basal flow and decreases hyperemic flow, thus reducing CFVR by 10 % for each 15-beat increase in heart rate. The main problem with CFR in clinical practice resides in its lack of specificity for the epicardial vessel: an abnormal CFR value does not determine whether this abnormal flow velocity relates to the epicardial stenosis, to microvascular disease, or both [62].

9.9 Clinical Guidelines

ESC guidelines 2013 recognize that invasive measurements of CFR using a Doppler wire are complex and time-consuming and carry a small risk. Therefore, in angina with normal coronary arteries, objective evidence of ischemia of microvascular disease may be alternatively be obtained by measuring diastolic coronary blood flow in the LAD at peak vasodilation and at rest using transthoracic echocardiography

Doppler recordings [63]. A CFVR <2.0 strongly suggests coronary microvascular disease. Specialist guidelines endorse a more extensive application of CFR in the stress echo lab, suggesting that "whenever possible, it is recommended to perform dual imaging (flow and function) vasodilator stress echo" [64].

9.10 Future Directions

The possibility of mapping coronary flow velocity going from proximal to distal tract (Fig. 9.16) of LAD can highlight an abnormal coronary flow velocity due to an atherosclerotic plaque. More precisely, a recording on LAD of a higher velocity,

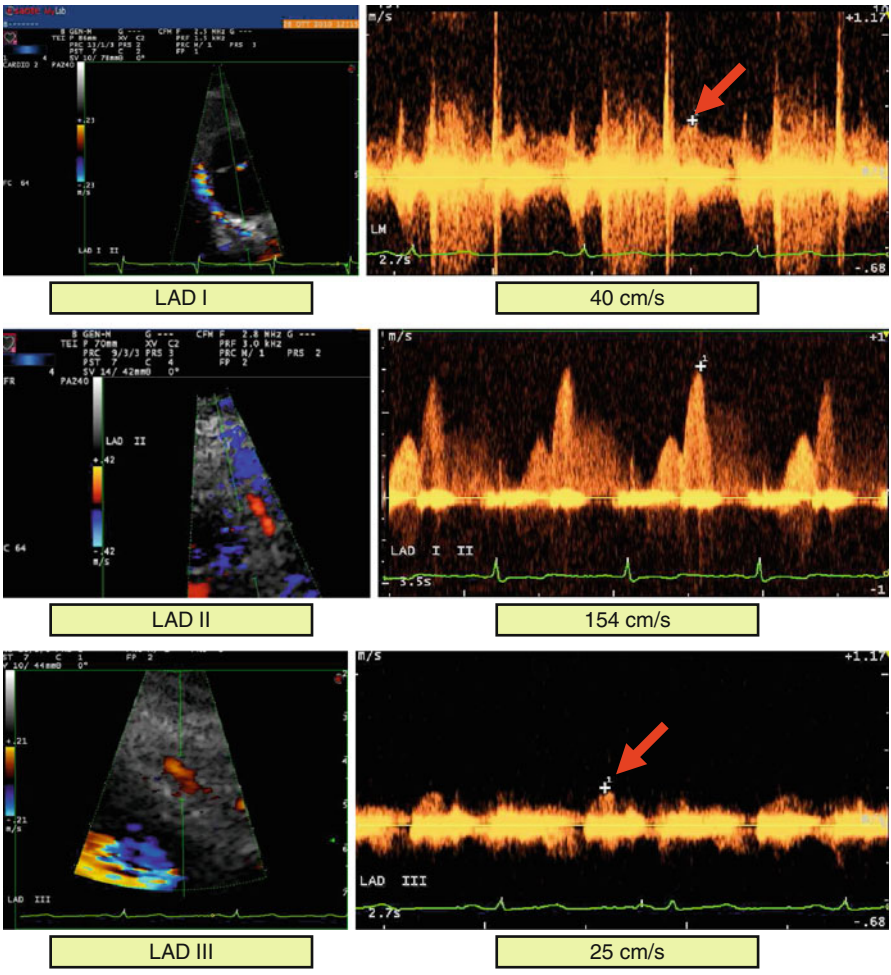

Fig. 9.16 Coronary flow velocity mapping, with color and pulsed Doppler, of proximal tract mid-distal tract of left anterior descending coronary artery in an abnormal case

more than 80 cm/s, especially in mid-distal tract of LAD, means a critical narrowing of coronary artery [65, 66].

Recently, some authors have proposed a new technique by applying Doppler flow wire, an innovative parameter labeled wave intensity analysis [67] that enables to highlight the different forces that drive coronary filling: proximal aortic pushing effect and distal suction effect. At present, matching coronary flow velocity information obtained by transthoracic echo Doppler recorded simultaneously with non-invasive arterial brachial pressure, both integrated electronically with a dedicated software, it is possible to define accurately the coronary filling. In so doing, we could better identify different coronary wave filling patterns that characterized different coronary artery diseases and therefore improve and tailor better our therapeutic strategy.

Table of Contents Video Companion

See in the section illustrative cases: cases number 13–18
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