60 Evaluation of Myocardial Disease in the Cardiac Catheterization Laboratory

James J. Ferguson III and Tomas Klima

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Key Points

- Dilated cardiomyopathy is characterized by cardiac enlargement, and left ventricle (LV) systolic dysfunction, usually resulting in congestive heart failure (CHF).
- Restrictive cardiomyopathy is characterized by diastolic dysfunction, resulting in impaired ventricular filling.
- Hypertrophic cardiomyopathy is myocardial hypertrophy in a nondilated ventricle, often including the interventricular septum.
- Endomyocardial biopsy may be helping in identifying diagnosis in patients with myocarditis, systemic disease processes involving the heart, including amyloidosis, sarcoidosis, and hemachromatosis; in distinguishing restrictive from constrictive pericarditis; in identifying rejection in the transplanted heart; in identifying cardiac toxicity from Adriamycin and similar agents; and in identifying cardiac tumors.

Cardiomyopathies are a group of diseases of unknown etiology that are characterized primarily by involvement of heart muscle in the disease process.[1–3] There are three general categories of cardiomyopathies (Table 60.1): dilated cardiomyopathies (otherwise known as congestive cardiomyopathies); restrictive or infiltrative cardiomyopathies (with scarring and fibrosis of the ventricle and diastolic dysfunction); and obstructive, or hypertrophic, cardiomyopathies (HCMs), characterized by left ventricular (LV) hypertrophy with normal and supernormal systolic function and usually abnormal diastolic function.[1–3] There may be areas of overlap among these three general categories, such as patients with extreme hypertrophy who manifest restrictive diastolic abnormalities.

Hypertensive heart disease, valvular heart disease, congenital heart disease, pericardial disease, and ischemic heart disease are not usually included among the cardiomyopathies. The term *ischemic cardiomyopathy* has been applied to the LV chamber dilatation and heart failure resulting from multiple myocardial infarctions with associated diffuse fibrosis and LV dysfunction.[4] However, ischemic cardiomyopathy is not usually included among the cardiomyopathies.

It is also possible to classify the cardiomyopathies on the basis of etiology. Primary cardiomyopathies have an underlying pathologic process involving the heart muscle that does not involve other organs or the cause of which is unknown. Secondary cardiomyopathies involve a known systemic disease or disease process, one manifestation of which is cardiac involvement (such as amyloidosis and hemochromatosis).[3]

This chapter describes the hemodynamics and cardiac catheterization laboratory findings in the cardiomyopathies. The hemodynamic pictures of dilated, restrictive, and obstructive cardiomyopathies are discussed, as is the role of endomyocardial biopsy with specific examples of important pathology.

General Hemodynamic Assessment

In the modern era, hemodynamic measurements are frequently accomplished noninvasively. However, given the frequent use of endomyocardial biopsy, coronary angiography, and shunt measurements, it can also be done efficiently, rapidly, and comprehensively in the catheterization laboratory.

In general, the hemodynamic assessment in the catheterization laboratory of a patient with cardiomyopathy should include right and left heart catheterization, with

TABLE 60.1. Usual features characterizing dilated, restrictive, and hypertrophic cardiomyopathy

	Dilated cardiomyopathy	*Restrictive cardiomyopathy*	*Hypertrophic cardiomyopathy*
Chamber size	↑↑	Normal	↓ normal, or ↑
Systolic function	Impaired	Normal or ↓	Hyperdynamic
Diastolic function	Elevated filling pressures Passive congestion	Impaired (throughout diastole, L > R may be brought out by exercise)	Impaired (may be similar to restrictive if hypertrophy is severe)
Wall thickness	↓	Increased	Increased (may be very increased), sometimes with further asymmetric septal thickening

measurements of cardiac output, intracardiac pressures, and pulmonary and systemic vascular resistances. When the left ventricle and right ventricle are entered with catheters for pressure measurement, care should be taken not to provoke ventricular arrhythmias, which may be very poorly tolerated in patients with compromised LV function. The pressure measurement system should be designed to provide the highest possible frequency response and optimal damping. The highest natural frequency for a pressure measurement system is obtained by using a stiff, short, wide-bore catheter directly connected to a pressure transducer without stopcocks or tubing; rigorous attention must be paid to avoid air bubbles in the measurement system.[5]

Superior vena cava (SVC), inferior vena cava (IVC), right atrial, right ventricular (RV), and pulmonary arterial oxygen saturations should be measured to detect right-to-left shunting. A saturation step-up of 7% or greater between SVC/IVC and the right atrium should be considered abnormal and indicates the presence of a significant left-to-right shunt at the atrial level. A saturation step-up of 5% or greater between the right atrium and the right ventricle indicates the presence of a significant left-to-right shunt at the ventricular level. A saturation step-up of 5% or greater between the right ventricle and the pulmonary artery indicates the presence of a left-to-right shunt at the level of the great vessels.[6] Coronary angiography, biplane left ventriculography, and endomyocardial biopsy (discussed later) are also considered as part of the usual evaluation of patients with cardiomyopathy, although the need for contrast studies or biopsy should be individually tailored to the patient's medical status and the diagnosis being considered. In some situations (such as restrictive cardiomyopathy), hemodynamic monitoring during supine bicycle exercise may be a valuable part of the diagnostic evaluation in order to elicit otherwise inapparent hemodynamic abnormalities.

Dilated Cardiomyopathy

Dilated cardiomyopathy, otherwise known as congestive cardiomyopathy, is characterized by cardiac enlargement and LV systolic dysfunction, usually resulting in congestive heart failure. Although the underlying cause is often not identifiable, this syndrome probably represents the end stage of a variety of causes of myocardial damage, some of which may be reversible and some of which are not reversible.

Underlying inciting factors for dilated cardiomyopathy include metabolic causes (e.g., uremia, hypophosphatemia, hypocalcemia), toxic causes (e.g., alcohol, cobalt), and infectious causes (e.g., myocarditis). The course of dilated cardiomyopathy is usually progressively downhill (unless a reversible cause can be identified), and 75% of patients will be dead within 5 years of the onset of symptoms.[7]

The hemodynamic findings in dilated cardiomyopathy are fairly nonspecific. Cardiac catheterization usually demonstrates elevated left-sided filling pressures, including elevations in the LV end-diastolic left atrial and pulmonary capillary wedge pressures.[8] Moderate pulmonary hypertension is often present. As the disease progresses and the degree of congestive heart failure worsens, right-sided hemodynamic abnormalities may also develop, including elevations in the right ventricular (RV) end-diastolic, right atrial, and central venous pressures.

Left ventriculography shows a dilated, diffusely hypokinetic left ventricle. Although focal wall-motion abnormalities (mimicking coronary artery disease) can be found,[8,9] the usual picture is one of global LV systolic dysfunction, with reduction of the ejection fraction and increases in the absolute LV end-diastolic and end-systolic volumes. Mitral regurgitation may be present on the basis of LV dilatation and chamber distortion; LV thrombi may also be present. Again, as the disease progresses to include right-sided involvement, there will be RV dilatation and perhaps associated tricuspid regurgitation.

Coronary arteriography is an important part of the diagnostic evaluation to exclude ischemic causes, particularly if focal wall-motion abnormalities are present. Coronary angiography is usually normal in patients with dilated cardiomyopathy,[8] although coronary artery vasodilator reserve may be impaired[10] and the potential exists for coronary emboli arising from an LV thrombus.

Restrictive Cardiomyopathy

The characteristic abnormality in restrictive cardiomyopathy is diastolic dysfunction, resulting in impaired ventricular filling.[11,12] In contrast to the dilated cardiomyopathies with abnormal systolic function, systolic function in restrictive cardiomyopathy is usually normal or near normal. There are a number of specific pathologic causes of restrictive cardiomyopathy (Table 60.2), and the abnormal diastolic dysfunction is usually the result of infiltration, fibrosis, or hypertrophy. However, the exact etiology of the underlying pathologic process frequently remains unknown.[13] The many potential primary causes of restrictive cardiomyopathy include amyloidosis, hemochromatosis, endomyocardial fibrosis, glycogen storage diseases, sarcoid (and other collagen vascular diseases), fibroelastosis, and pseudoanthoma elasticum.[13,14]

TABLE 60.2. Usual primary causes of restrictive cardiomyopathy

Amyloid	Glycogen storage disease
Hemochromatosis	Mucopolysaccharidoses
Endomyocardial fibroelastosis	

The hemodynamic features of restrictive cardiomyopathy can be very similar to those of constrictive pericarditis, and close attention should be paid in the cardiac catheterization laboratory to obtaining accurate hemodynamic tracings. Outside of the catheterization laboratory, other tests, including rapid-speed computed tomographic scanning, and particularly magnetic resonance imaging, may be useful in distinguishing between restrictive cardiomyopathy and constrictive pericarditis[15,16] by demonstrating the presence or absence of increased pericardial thickness. In the catheterization laboratory, both syndromes manifest as a diastolic filling abnormality.[13] The diastolic abnormality in constrictive pericarditis involves left and right ventricles equally and begins in early to mid-diastole, with normal or supranormal early filling, whereas in restrictive cardiomyopathy, the diastolic abnormality persists throughout diastole and the left ventricle may be more involved than the right ventricle (Fig. 60.1). Both syndromes are characterized by a rapid early decline in ventricular pressure at the onset of diastole, with a subsequent rapid plateau, the so-called square root sign (Fig. 60.2), although some high-fidelity LV diastolic pressure recordings do not show a clear-cut early diastolic dip.[17] On atrial and central (or pulmonary) venous tracings, rapid early diastolic filling of the ventricles will be expressed as a prominent *y* descent (Fig. 60.2). Both syndromes are also usually associated with elevations in pulmonary and systemic venous pressures. One major clinical feature distinguishing the two is that in restrictive cardiomyopathy with infiltrative involvement of both ventricles (left more than right because of its greater mass), there is usually a divergence between LV and RV pressures, with left exceeding right by at least 5 mm Hg, especially with exercise (see Fig. 60.1). In contrast, in constrictive pericarditis, the RV and LV diastolic pressures are usually within 5 mm Hg of each other, and often there is a relative equalization of pressures such that the mean right atrial, RV end-diastolic, pulmonary artery diastolic, and mean pulmonary wedge pressures are almost identical.

Other hemodynamic features can help to distinguish restrictive cardiomyopathy from constrictive pericarditis.[18] Pulmonary artery systolic pressure can often be greater than 45 mm Hg in restrictive cardiomyopathy but is less than 45 mm Hg in constrictive pericarditis. Finally, the height of the RV diastolic plateau is often less than one third of the RV peak systolic pressure in restrictive cardiomyopathy, whereas in constrictive pericarditis, it is usually greater than one third of the RV peak systolic pressure (Table 60.3).

Hypertrophic Cardiomyopathy

The characteristic feature of HCM is myocardial hypertrophy in a nondilated ventricle, which often involves the interven-

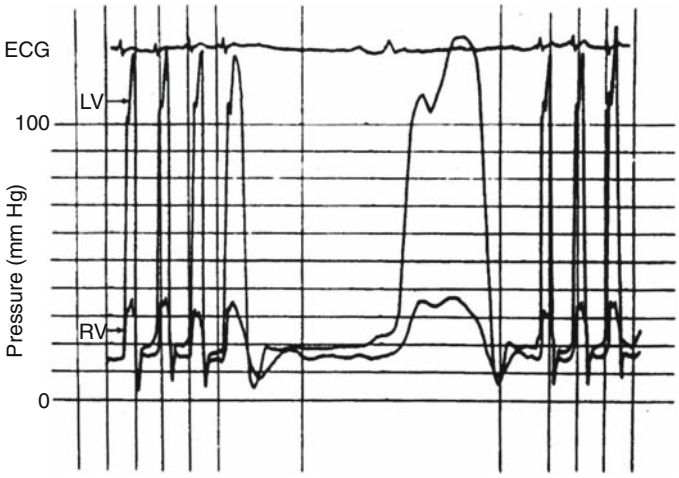


FIGURE 60.1. Simultaneously right ventricular (RV) and left ventricular (LV) pressure tracings in a 43-year-old patient with restrictive cardiomyopathy. Note prominent dip and plateau of both pressure recordings. There is more of a divergence of diastolic pressures in late diastole with the LV pressure significantly higher than the RV pressure.

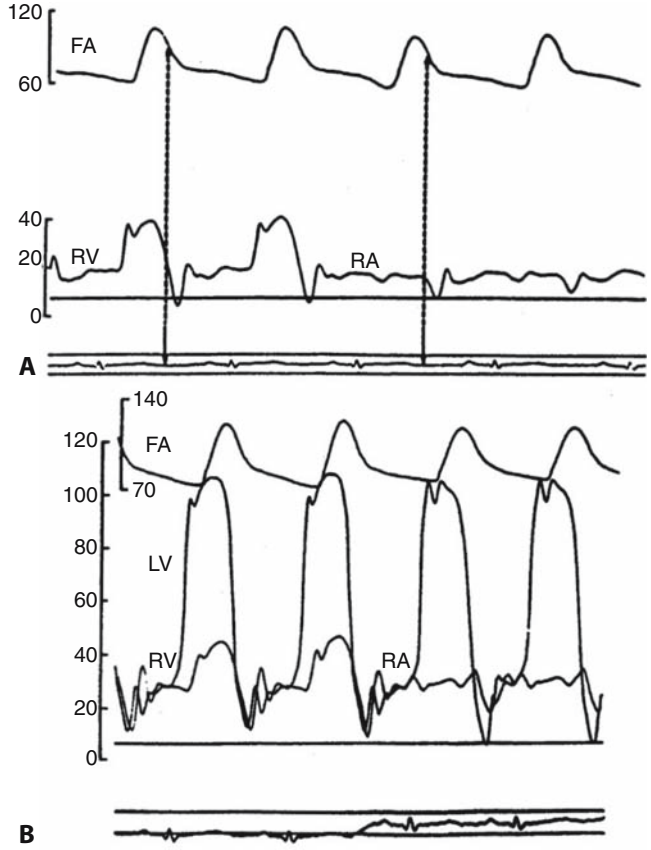


FIGURE 60.2. (A) Prominent *y* descent on a right atrial pressure tracing in a patient with restrictive cardiomyopathy. (B) Simultaneous pressures in the femoral artery (FA) and right ventricle (RV) pulled back to the right atrium (RA) show rapid *y* descent. Superimposed left ventricular (LV) pressure demonstrates a square root configuration.

TABLE 60.3. Usual hemodynamic features of restrictive cardiomyopathy and constrictive pericarditis

	Restrictive cardiomyopathy	*Constrictive pericarditis*
Diastolic filling	Dip and plateau	Dip and plateau
Venous	Prominent *y* descent	Prominent *y* descent
Diastolic pressures	LV exceeds RV by at least 5 mm Hg	LV within 5 mm Hg of RV
PA systolic pressure	>45 mm Hg	<45 mm Hg
RV pressure	Plateau less than one third of RV systolic pressure	Plateau greater than one third of RV systolic pressure

LV, left ventricle; PA, pulmonary artery; RV, right ventricle.

tricular septum.[19,20] A subaortic pressure gradient has been noted in a subset of these patients, giving rise to the terms *idiopathic hypertrophic subaortic stenosis*, *muscular subaortic stenosis*, and *hypertrophic obstructive cardiomyopathy*.[21] Although some patients may exhibit a distinct gradient, many patients show no evidence of LV outflow obstruction at rest (Fig. 60.3), and the gradient may be prominent after provocative maneuvers (Fig. 60.4). There is a strong genetic linkage of this disorder, with approximately 25% of the first-degree relatives of patients with HCM exhibiting some evidence of the

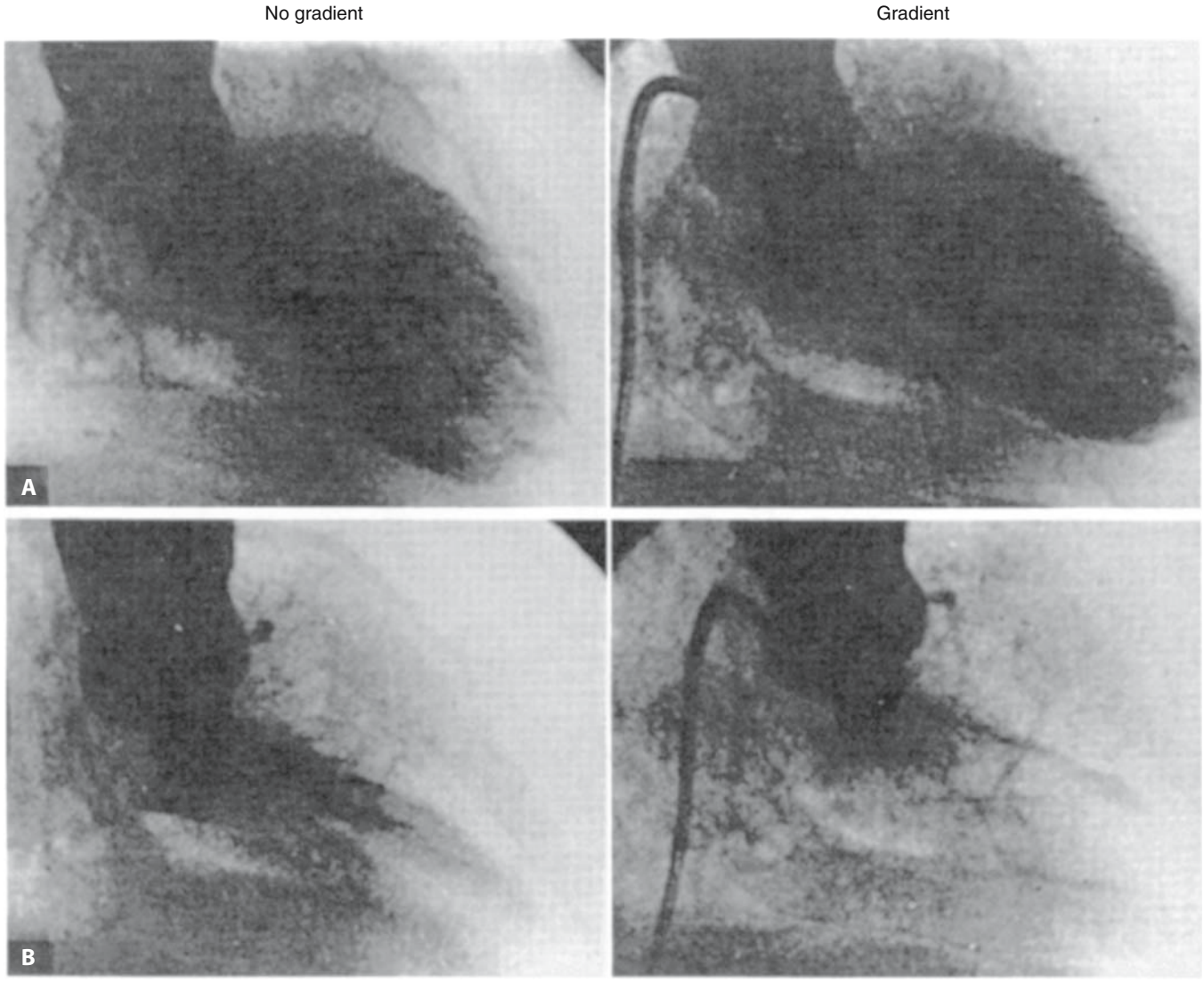


FIGURE 60.3. Right anterior oblique contrast ventriculograms in a patient with hypertrophic cardiomyopathy. End-diastolic (A) and end-systolic (B) frames with no gradient (left) and after induction of an 87 mm Hg gradient with nitroprusside (right). In both studies, there is obliteration of the left ventricular cavity, more so after nitroprusside administration.

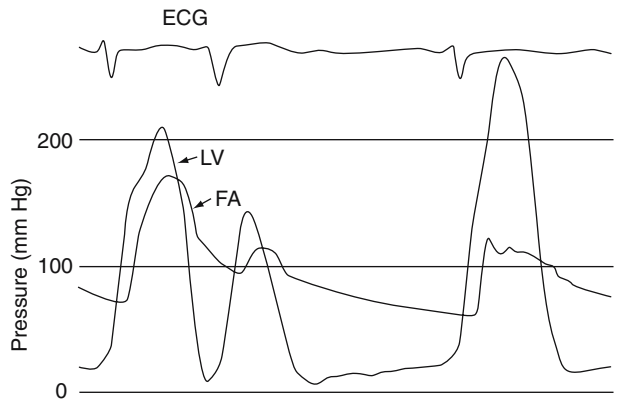


FIGURE 60.4. Simultaneous left ventricle (LV) and femoral artery (FA) pressure tracings in a patient with hypertrophic cardiomyopathy. Note that after the extrasystolic beat, there is an increase in the gradient, a more prominent spike-and-dome configuration to the peripheral pulse contour, and narrowing of the pulse pressure.

disease.[22] It is inherited as an autosomal dominant trait with incomplete penetrance, and the gene responsible has been shown to be present on chromosome 14.[23,24]

The issue of "obstruction" continues to engender significant controversy; there are experimental data indicating that most of the ventricular ejection has already taken place by the time any significant gradients are measured,[25–29] but other studies have suggested that systolic obstruction may be a significant component of the abnormality in some patients.[30–34]

From a functional standpoint, there are usually two primary abnormalities: hyperdynamic LV systolic function and impaired LV diastolic function. The extensive hypertrophy seen in this disorder also results in increased stiffness of the ventricle during diastole and in impairment of LV filling.

The arterial pressure tracing in HCM may demonstrate a "spike-and-dome" appearance, which is a manifestation of the hyperdynamic ejection ("spike") and Windkessel properties ("dome") of the proximal aorta (Fig. 60.4). A gradient may be present between the body of the ventricle and the aorta or aortic outflow tract (see Fig. 60.4). This gradient, if present, is characteristically labile. Because this gradient is, to a large extent, dependent on the ejection characteristics and size of the ventricle, there are four main factors that influence it: preload, afterload, atrioventricular synchrony, and contractility.[20,35] Provocations that decrease preload (Valsalva maneuver), decrease afterload (nitroglycerin), and increase contractility (isoproterenol), or any positive inotropic intervention (including cardiac glycosides) all increase the gradient, although most provocative maneuvers can have mixed effects on preload, afterload, and contractility. Similarly, maneuvers that increase preload (Mueller maneuver), increase afterload (handgrip or squatting), and decrease contractility (beta-blockade) decrease the gradient. The lability of the gradient is usually what distinguishes HCM from other fixed forms of outflow obstruction, although some patients with otherwise classic HCM can have a fixed gradient.

In the catheterization laboratory, postextrasystolic potentiation is one of the best techniques for provoking an otherwise inapparent gradient. The postextrasystolic augmentation of contractility far outweighs the increase in preload, and a gradient (and murmur) may be recorded. In addition to provocation of a gradient, the characteristic spike-and-dome arterial pressure waveform becomes more manifest, and there is no change in (or even a narrowing of) the pulse pressure (Brockenbrough-Braunwald-Morrow sign) (Fig. 60.4).[36] The lability of the gradient is what distinguishes HCM from fixed valvular aortic stenosis, as well as the fact that in valvular aortic stenosis, the postextrasystolic arterial pressure contour will be unchanged, and the pulse pressure will be increased.

In measuring LV pressure, care must be taken to avoid catheter entrapment (particularly with end-hole catheters), which may produce an artifactual gradient. Left ventriculography usually demonstrates a small LV cavity with vigorous contraction that may obliterate the LV cavity, and hypertrophied walls with prominent papillary muscles. However, the left ventricle may be very large in some patients. The mitral valve often moves anteriorly during systole (systolic anterior motion pattern), impinging on the LV outflow tract, with associated mitral regurgitation (Fig. 60.5), also generating a characteristic echocardiographic pattern (Fig. 60.6).

There is often evidence of LV diastolic dysfunction, with elevation of the LV end-diastolic pressure or even an abnormal LV diastolic pressure contour. With impaired LV filling, there are resulting elevations in left atrium and pulmonary capillary wedge pressures. Approximately 25% of patients have pulmonary arterial hypertension. Moreover, dynamic obstruction can be present in the LV outflow tract as well and has been reported in as many as 15% of patients with LV outflow gradients.[20,37] Visualization of the interventricular septum can be facilitated by simultaneous right and left ventriculograms obtained in a left anterior oblique projection with cranial angulation.

The coronary arteries may demonstrate atherosclerotic obstructions but also frequent exhibit "blanching" of the

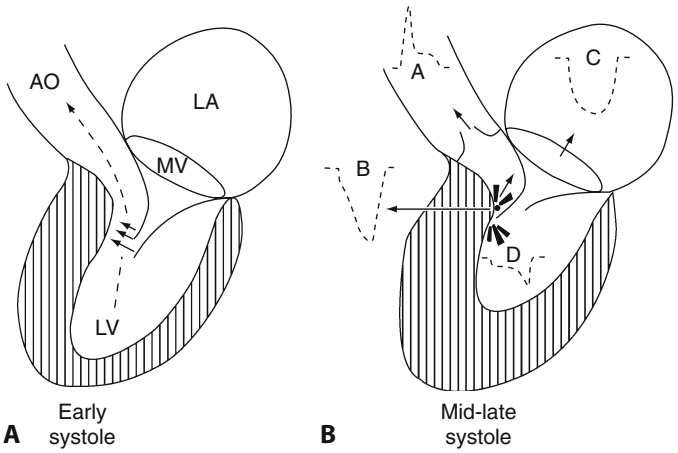


FIGURE 60.5. Schematic representation of the dynamics of mitral leaflet systolic anterior motion, outflow obstruction, and mitral regurgitation in hypertrophic cardiomyopathy. (A) Outflow tract is narrowed owing to septal hypertrophy, and ejection velocity is increased. The resulting Venturi forces draw the anterior and posterior mitral leaflet toward the septum, ultimately resulting in anterior leaflet septal contact. AO, aorta; LA, left atrium; LV, left ventricle; MV, mitral valve. (B) Septal contact results in outflow obstruction and mitral regurgitation. The *dashed lines* illustrate Doppler velocity recordings at the ascending aorta (A), at the level of mitral leaflet-septal contact (B), in the left atrium (C), and at the left ventricular apex (D).

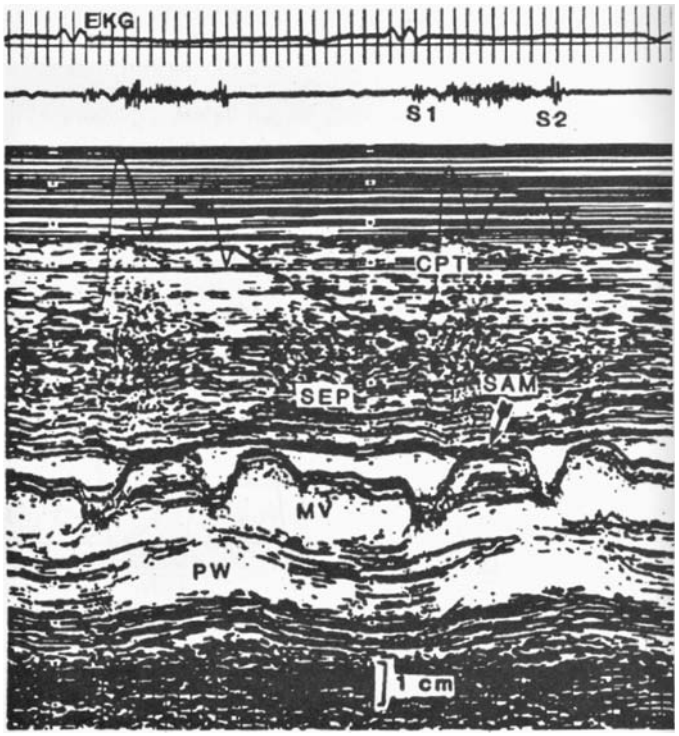


FIGURE 60.6. Simultaneous carotid pulse tracing (CPT), phonocardiogram, and M-mode echocardiographic recording at the level of the mitral valve (MV) in a patient with hypertrophic cardiomyopathy. The septum (SEP) is disproportionately thickened, there is systolic anterior motion (SAM) of the mitral valve, there is systolic retraction on the CPT, and a systolic murmur is noted. ECG, electrocardiogram; PW, posterior wall; S_1, S_2, first and second heart sounds.

septal vessels and intramyocardial left anterior descending artery during systole. The large epicardial coronary arteries in patients with HCM are usually free of atherosclerotic obstruction, but small intramural arteries exhibit intimal thickening and medial hypertrophy in some patients.[38] Furthermore, patients with HCM and angiographically normal epicardial coronary arteries still exhibit regional myocardial thallium-201 defects and metabolic evidence of myocardial ischemia during rapid atrial pacing.[39]

Endomyocardial Biopsy

Nonsurgical biopsies of the heart were initially obtained in the early 1960s using percutaneous needle techniques similar to those utilized for liver or kidney biopsy.[40,41] These procedures had an approximately 10% incidence of major complications. In 1962, Sakakibara and Konno[42] developed a flexible transvenous endomyocardial biopsy device that allowed much safer access to myocardial tissue. Since that time, there have been considerable technical improvements in the devices and technique, to the point where transvenous endomyocardial biopsy is a standard procedure that can be performed as part of the diagnostic evaluation in most catheterization laboratories.[43] Biopsy specimens can be obtained from both the right and the left ventricle. Multiple biopsy specimens should be obtained because of the nonhomogeneous nature of some disease processes.

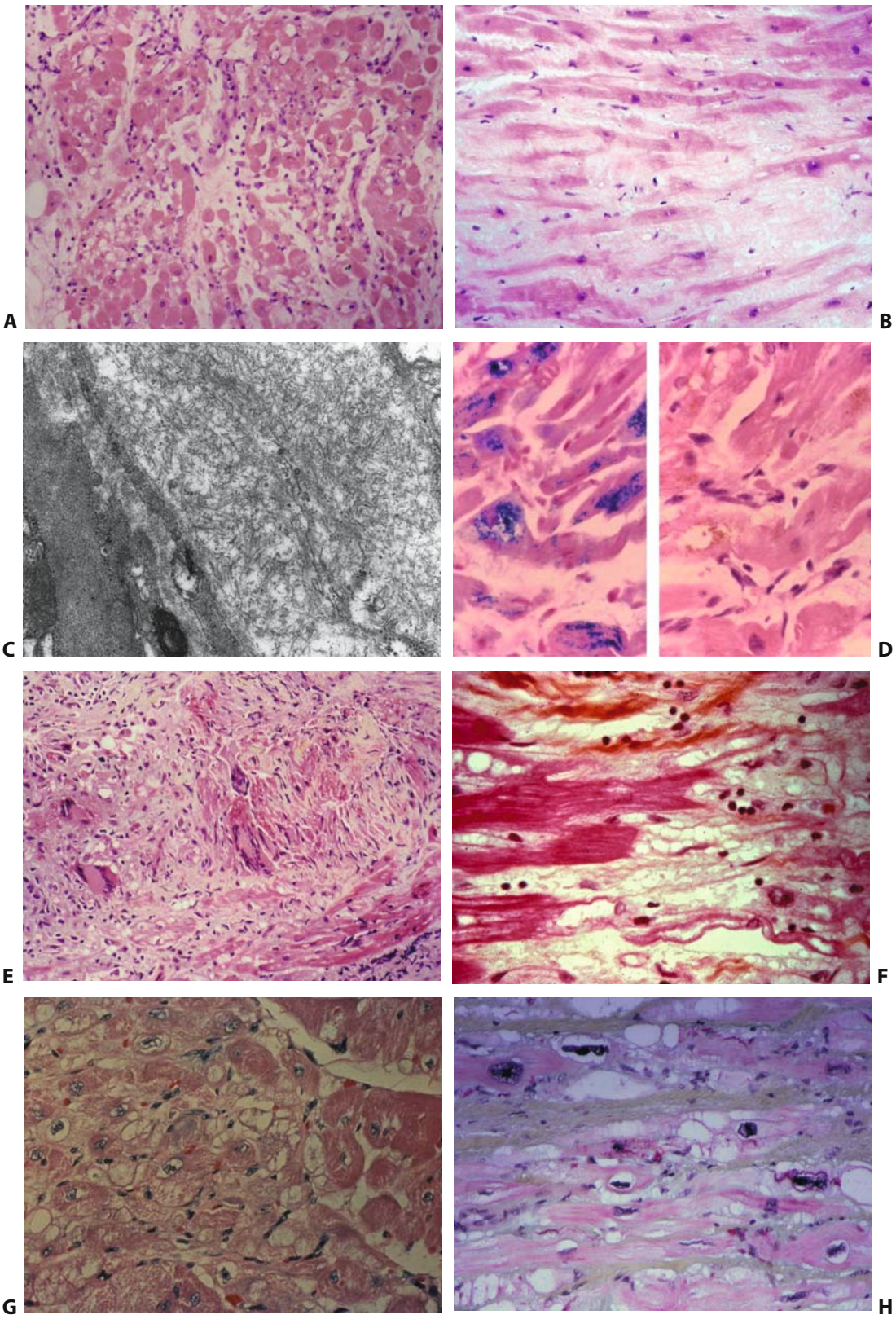
The routine use of endomyocardial biopsy in patients with cardiomyopathies remains controversial, but it can clearly be of benefit in identifying specific causes of cardiac pathology.[43,44] While not every patient with cardiomyopathy needs a tissue diagnosis, most specific heart muscle abnormalities can only be definitively diagnosed with myocardial biopsy (Fig. 60.7).

A biopsy may be most helpful in the following situations:

1. Myocarditis, cardiomyopathy, and ischemic heart disease
2. Diagnosing cardiac involvement in systemic disease processes, such as amyloidosis, hemochromatosis, and sarcoid
3. Distinguishing restrictive cardiomyopathy from constrictive pericarditis
4. Postcardiac transplant evaluation for identification of rejection
5. Cardiac tumors
6. Identifying cardiotoxic effects of agents such as Adriamycin and alcohol
7. Other less common entities such as endocardial fibroelastosis and glycogen storage disease

Endomyocardial biopsy may also be particularly helpful in patients with new LV dysfunction and patients with rapidly worsening congestive heart failure despite therapy.

FIGURE 60.7. Histology of disorders noted on endomyocardial biopsy. (A) Acute lymphocytic myocarditis. The cardiac myocytes exhibit varying degrees of degeneration. The interstices are edematous and diffusely infiltrated with lymphocytes. [Hematoxylin and eosin (H&E), ×40.] (B) Amyloid. There are diffuse interstitial deposits of amyloid. The cardiac myocytes are diffusely attenuated. (H&E, ×100.) (C) Electron microscopy of amyloid. Rail-like structures within the sarcoplasm are diagnostic of amyloid. (D) Hemochromatosis. Sarcoplasmic deposits of brown iron pigment are noted. Left, H&E, ×200. Right, ferrocyanide stain, ×200. (E) Sarcoidosis. Granuloma-containing multinucleated giant cells. (H&E, ×160.) (F) Alcohol toxicity. Severe vacuolar degeneration of the sarcoplasm is noted. (H&E, ×200.) (G) Adriamycin toxicity. There are degenerated myocytes with vacuolated cytoplasm. (H&E, ×100.) (H) Congestive cardiomyopathy. The myocytes are mostly enlarged, but their sarcoplasm is depleted and focally vacuolated. The nuclei are enlarged and bizarre. (H&E, ×100.) (I) Ischemic cardiomyopathy. Extensive vacuolar changes of cardiac myocytes. (H&E, ×200.) (J) Type IV glycogen storage disease. The sarcoplasm contains glycogen deposits. [Periodic acid-Schiff (PAS), ×100.] (K) Endocardial fibroelastosis. Thick fibroelastic endocardial layer that compresses the underlying myocardium. (H&E, ×40.) (L) Mild rejection (left) and severe rejection (right). Mild rejection is characterized by perivascular infiltrates of mononuclear cells, with occasional degeneration of cardiac myocytes. Severe rejection is characterized by lymphocytic and leukocytic infiltrates associated with severe cardiac myocyte degeneration. (H&E, ×80, left; ×80, right.) (M) Higher magnification of severe rejection. The interstitial infiltrate contains many polymorphonuclear leucocytes. The cardiac myocytes are severely degenerated, and some are necrotic. (H&E, ×140.)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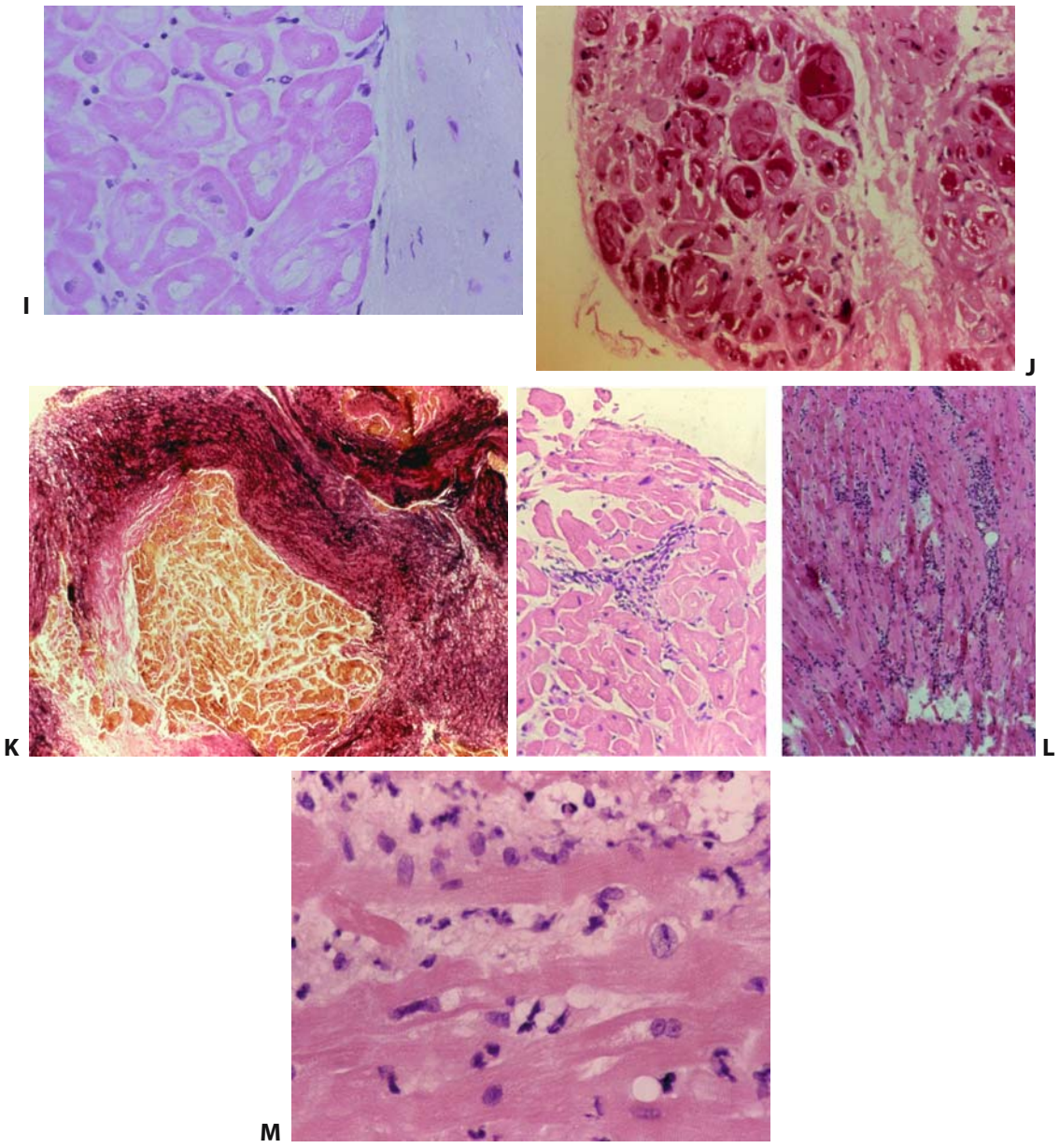

FIGURE 60.7. (continued)

Thus the use of endomyocardial biopsy can help to facilitate the diagnosis of specific underlying causes of cardiomyopathy, particularly myocarditis and infiltrative disorders, and it is an important part of the diagnostic workup in those patients.

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