With increased hemodynamic stress, the heart must adjust to meet the greater demands placed upon it. This adjustment frequently involves an alteration or remodeling in its structure or geometry, which augments its performance and helps to maintain adequate function under changing conditions. One of the most important forms of remodeling that the heart may undergo is an increase in muscle mass in response to a pressure or volume overload or myocardial injury.

This increase in muscle mass is known as left ventricular hypertrophy (LVH). LVH is of great importance from a risk selection perspective for two reasons: it is common, and it is associated with a significant increase in both morbidity and mortality risk. Thus, it is critical that both underwriters and medical directors be aware of this form of remodeling, its causes, diagnosis and consequences.

LVH results from the hypertrophy or enlargement of existing myocytes rather than the formation of new muscle cells. The key trigger for this change appears to be some form of a mechanical stress. Enlargement is the consequence of an alteration in the number and arrangement of the sarcomeres, the cellular structures that are responsible for the shortening or contraction of the muscle fibers.

When the heart is subjected to a pressure overload, as occurs with hypertension or aortic stenosis, new sarcomeres or contraction units are added in a parallel or side-to-side arrangement. This increase in the number of sarcomeres is known as concentric hypertrophy and results in both a thickening of the ventricular wall and an augmentation in the force of cardiac contraction.

In contrast, a volume overload, as might be encountered in aortic or mitral regurgitation, leads to the addition of sarcomeres in series (an end-to-end arrangement). In this case, the result is eccentric hypertrophy in which the heart cavity dilates but wall thickness remains relatively unchanged.

With either concentric or eccentric hypertrophy, there is also a modification of the connective tissue matrix that surrounds the myocytes. An alteration in the number and arrangement of collagen fibers, increases in interstitial edema and tissue fibrosis are commonly found. The overall result of this remodeling process is an increase in the mass of the ventricle.1

**DIAGNOSIS**

The principal method for diagnosing LVH is the echocardiogram, since this test pro-
Table 1. LV Mass Calculations

<table>
<thead>
<tr>
<th>Formula</th>
<th>Mean (g/m²)</th>
<th>Upper Limit (g/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penn Formula</td>
<td>92</td>
<td>131</td>
</tr>
<tr>
<td>American Society of Echocardiography (ASE) Formula</td>
<td>86</td>
<td>119</td>
</tr>
</tbody>
</table>

* Framingham data.

** LV mass index = LV mass/body surface area.

Table 2. Normal Values* – LV Mass Index**

<table>
<thead>
<tr>
<th>Formula</th>
<th>Mean (g/m²)</th>
<th>Upper Limit (g/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penn</td>
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<td>119</td>
</tr>
</tbody>
</table>

WHAT CAUSES AN INCREASE IN LV MASS?

An increase in LV mass is normal in growing children, pregnant women and trained athletes (athletic heart). Ventricular mass will decrease in the postpartum period and with the cessation of athletic training. The most common pathologic conditions resulting in an increase in LV mass are obesity and hypertension. In hypertensives, LVH correlates better with the long-term average of blood pressure readings than single values obtained at the time of examination. In that sense, the measurement of LV mass serves as an integrated measure of average blood pressure control over time, much like using glycosylated hemoglobin to assess glucose levels in diabetes.

LVH prevalence increases in the elderly (33% of men and 49% of women over age 70 have hypertrophy). However, this increase is most likely due to co-morbid conditions and not an effect of the aging process itself.

Other conditions associated with LVH include:

- Coronary artery disease (especially myocardial infarction)
- Valvular heart disease
Diabetes
Alcohol abuse (in men)
Insulin resistance and smoking

Nevertheless, much of the variance from normal in LV mass for a given individual cannot be explained by underlying co-morbidities—suggesting that a likely, as yet unidentified, genetic component is also at work.3

### PHYSIOLOGIC CONSEQUENCES

Several adverse physiologic findings are characteristic of LVH. One is diastolic dysfunction. Ventricular remodeling can have significant effects on diastolic filling. Myocardial relaxation is an active, energy-requiring process that is impaired as LV mass increases. In addition, the pliability of ventricular tissue diminishes as walls thicken and collagen deposits alter the normal architecture. The result is often delayed relaxation. This may be detected by echocardiography as a reversal of the usual pattern of ventricular filling. Most filling normally occurs early (E) in diastole, before atrial (A) contraction. LVH frequently results in a reversal of this E:A ratio (E<A), thus increasing the reliance on atrial contraction.1,9

Eventually, filling may be so impaired that diastolic heart failure results. This condition, which represents about one half of all congestive heart failure (CHF) cases, results from the inability to fill the ventricle sufficiently to maintain adequate forward blood flow. The ejection fraction or the percentage of the ventricular volume pumped per beat is normal, but the amount of blood present at the onset of systole is reduced. This condition is especially common in older women.1,10

LVH may also predispose the individual to the development of ischemia. The combination of excess muscle mass, fibrosis and pressure load increases myocardial oxygen demand. At the same time, coronary reserve (the ability to increase blood flow in response to demand) is reduced. The result may be the exacerbation of established coronary artery disease (CAD) or the development of subendocardial ischemia in the face of normal coronary arteries. This latter phenomenon may explain many of the so-called “false-positive” stress tests encountered in hypertensive individuals.3,11

### ASSESSING THE RISK

Physiologic derangements due to LVH increase morbidity and mortality risk. Numerous studies have demonstrated that an increase in LV mass is an independent risk factor for the development of cardiovascular disease, cardiovascular mortality and all-cause mortality. Data from the Framingham study indicated a relative risk (adjusted for age and risk factors) for cardiovascular mortality and all-cause mortality of 1.73 and 1.49 for men and 2.12 and 2.01 for women for each increase of LV mass of 50 g/m^2.12 Another study indicated a hazard ratio for all-cause mortality of 1.4 per 40 g/m^2 increase in LV mass.13 All-cause death is also related to the degree of diastolic dysfunction. For impaired relaxation (E:A ratio < 0.6), the multivariate relative risk is non-significantly increased (RR 1.23). In contrast, when restrictive filling of the ventricle occurs (E:A ratio > 1.5) the risk increases significantly (RR 1.73).14 This influence of LVH on mortality is operative regardless of the presence of concomitant CAD. However, the relative impact on outcome is greater in those without CAD (Table 3).7,15

### Table 3. LVH Mortality Risk* – Adjusted Relative Risk

<table>
<thead>
<tr>
<th></th>
<th>All-cause Mortality</th>
<th>Cardiovascular Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No CAD</td>
<td>CAD</td>
</tr>
<tr>
<td>Ghali, et al.</td>
<td>4.14</td>
<td>2.14</td>
</tr>
<tr>
<td>Liao, et al.</td>
<td>2.7–3.5</td>
<td>1.4–2.0</td>
</tr>
</tbody>
</table>

* LVH defined by ECG Criteria.
with the method used in diagnosis. For example, all-cause mortality associated with hypertrophy defined by ECG voltage criteria alone is about half of that found in individuals with the combination of increased voltage and major ST-T wave changes (strain pattern).\textsuperscript{17}

LVH has also been associated with an increased risk of sudden death (RR 2.16)\textsuperscript{18} and all-cause mortality in the presence of asymptomatic ventricular arrhythmias (RR 1.62).\textsuperscript{19} Some authors have detected mortality variations with different patterns of hypertrophy (ie, a greater risk with concentric than eccentric enlargement). However, this conclusion remains controversial.\textsuperscript{3,6,20,21}

**TREATMENT AND REVERSING LVH**

Treating the condition causing the pressure and/or volume load on the heart may lead to LVH regression. Valve replacement and normalization of systolic load in aortic stenosis and insufficiency may lead to a significant reduction (35% or more) in the degree of hypertrophy within a few weeks and near total reversal over time. Medical therapy for hypertension may also reduce the degree of hypertrophy, although generally to a lesser degree than with valve replacement. The reduced benefit from hypertension treatment is most likely due to incomplete control of blood pressure.

Four different classes of antihypertensive drugs have been shown to cause regression of LVH. These include the ACE inhibitors, diuretics, beta-blockers and calcium channel blockers. Despite similar degrees of reduction of systolic and diastolic blood pressure, the ACE inhibitors were significantly more efficacious than the others in reducing LV mass. Blockade of the renin-angiotensin system, which is a growth stimulus to myocardial cells, may be the reason for this increased benefit. Currently, it is not known if reducing the degree of LVH with therapy will lower morbidity and mortality risk.\textsuperscript{1,3,10,22,23}

**SUMMARY**

- LVH is a common condition, especially in the elderly.
- Hypertension and obesity are the most common impairments leading to pathologic LVH.
- Increased LV mass may be a normal variant in growing children, pregnancy and trained athletes.
- Echocardiographically determined LV mass, adjusted for body surface area or height, is the most accurate diagnostic tool.
- LVH may predispose an individual to diastolic heart failure.
- LVH may produce a positive stress test in the absence of angiographic CAD.
- LVH is an independent risk factor for cardiovascular morbidity and mortality, all-cause mortality and sudden death in those with and without CAD. The relative risk is greater in those without CAD.
- There is an increase in mortality risk of approximately 50% in men and 100% in women for each 50 g/m\textsuperscript{2} increase in LV mass index.
- The risk associated with ECG-defined LVH is twice as great in those individuals with major ST-T changes as it is in those with voltage criteria alone.
- Treatment of the underlying condition can lead to regression of LVH, but it is uncertain if this will reduce the associated risk.

**REFERENCES**


