

The Prognostic Significance of Left Ventricular Geometry: Fantasy or Reality?

Ramón Castelló Brescane

Research Florida Associates, Apex Cardiovascular Group, Jacksonville, Florida, USA

Hypertension is the most prevalent chronic disease in developed countries and affects more than 25% of the adult population. Its association with the later risk of cardiovascular events has been more than demonstrated. The World Health Organization (WHO) estimates that the risk attributable to inadequately controlled hypertension affects 7.1 million lives per year, and underlies 62% of cardiovascular events and 49% of cases of ischemic heart disease.¹

There are multiple pathophysiological mechanisms by which hypertension causes such high morbidity and mortality rates. Hypertrophy, both arterial and muscular, is closely associated with the greater prevalence of cardiovascular events. Hypertrophy and interstitial fibrosis are thought to cause the subsequent onset of heart failure, ventricular dysfunction—both diastolic and systolic—myocardial infarction, and fatal ventricular arrhythmias.

For these reasons, identifying patients with left ventricular hypertrophy is considered essential when stratifying risk for hypertensive patients. In the last 30 years, the prognostic relevance of left ventricular hypertrophy has not only been demonstrated, but integrated into clinical practice guidelines for managing the hypertensive patient.

Left ventricular hypertrophy can be diagnosed in several ways. Magnetic resonance imaging is the standard technique, although its use in large populations is naturally limited by its high cost and complex logistics. Electrocardiography lies at the other end of the spectrum, and has very acceptable sensitivity and specificity in large populations when applied in the form of a score.

Echocardiography plays a key role in managing the hypertensive patient. Unlike electrocardiographic criteria, echocardiography enables the direct measurement of wall thicknesses and ventricular diameters and, thus, calculation of left ventricular mass, which is the parameter that determines whether left ventricular hypertrophy is present.

The adaptation of the left ventricle to hypertension leads to the development of different geometric patterns. These left ventricular structural patterns are based on the following 2 parameters: *a*) the presence or absence of an increased left ventricular mass score (hypertrophy); and *b*) relative wall thickness in relation to the left ventricular cavity (index of concentricity or thickness relative to the wall). Thus, 4 different left ventricular geometry groups can be distinguished: normal geometry, concentric remodeling, concentric hypertrophy, and eccentric hypertrophy.²

The prognostic relevance of left ventricular geometry has been known for some time and has been demonstrated in numerous studies. The different geometric patterns are used as a risk stratification tool, especially in hypertensive patients, and have been incorporated into most guidelines for managing the hypertensive patient.

The prevalence of the different geometric patterns varies depending on the population studied. Thus, the prevalence of hypertrophy is closely associated with age and the severity of hypertension, and ranges between 6% in those less than 30 years of age and 43% in those older than 69 years.³ However, other factors, such as race, diabetes, coronary disease, or cardiomyopathy determine the relative prevalence of the 4 geometric groups.

The prognostic value of the different geometric patterns is immense, but, unfortunately, this is not well recognized in daily clinical practice. This prognostic value has been mainly demonstrated in hypertensive patients, but also in other groups at high cardiovascular risk. In hypertensive patients, left ventricular hypertrophy is an index of cardiovascular complications and greater mortality than blood pressure itself.⁴ Hypertrophy in hypertensive patients entails a risk of cardiovascular

SEE ARTICLE ON PAGES 246-54

Correspondence: Dr R. Castelló,
Research Florida Associates, Apex Cardiovascular Group,
6428 Beach Blvd, Jacksonville FL 32216, USA
E-mail: castello.ramon@gmail.com

events 20 times greater than when left ventricular geometry is normal.²

What is extremely attractive to the cardiologist is that left ventricular hypertrophy has significant prognostic value in clinical situations traditionally not associated with the presence of hypertrophy. The risk of mortality or non-fatal complications increases between 2 and 4 times in the presence of left ventricular hypertrophy in patients with coronary disease or noncomplicated myocardial infarction. For example, Liao et al⁵ studied 1089 patients with coronary disease who had undergone cardiac catheterization. Naturally, the factors that were significantly associated with prognosis after stepwise multiple regression analysis were ejection fraction (relative risk [RR] = 2) and the number of vessels with stenosis (RR=1.6), but the factor that had the greatest impact was left ventricular hypertrophy (RR=2.4). In one of the first studies on the dismal effect of left ventricular hypertrophy, Carluccio et al⁶ demonstrated that, in patients with preserved ejection fraction (>50%) after myocardial infarction, the number of events after the infarction was directly associated with the presence of left ventricular hypertrophy. Specific analyses conducted during the SOLVD (Studies of Left Ventricular Dysfunction) study in patients with ischemic cardiomyopathy also showed that increased left ventricular mass was significantly associated with prognosis, even after adjusting the population for ejection fraction.⁷

Recently, the VALIANT (VALsartan In Acute myocardial iNfarctiOn) study confirmed, once again, the prognostic relevance of left ventricular geometric patterns, this time in patients with an ejection fraction <35% after infarction.³ Ventricular remodeling in patients following infarction initially presents as infarct expansion and then as ventricular dilatation. The geometric changes occur via myocyte hypertrophy and also by increased fibrosis and apoptosis.⁸ Obviously, patients with greater remodeling also have a worse prognosis, which in turn is also associated with a more altered geometry in the form of concentric and eccentric hypertrophy.

It is of interest that the results obtained in this population of infarct patients overlap with those obtained in hypertensive patients. Patients with normal ventricular geometry had a lower risk of cardiovascular events, but this significantly increased in patients with concentric remodeling (hazard ratio [HR] = 3), eccentric hypertrophy (HR=3.1) and concentric hypertrophy (HR=5.4). Thus, it would appear important to incorporate these geometric patterns into risk stratification not only in hypertensive patients, but also in a wide variety of situations within clinical cardiology.

Perhaps what is of the greatest interest from the clinical standpoint, is that the entire dismal

prognostic value of the left ventricular geometry can be changed by partial or complete reversal with appropriate treatment. This fact has been well demonstrated in hypertensive patients. Verdecchia et al⁹ demonstrated that, in the long term, patients in whom initial hypertrophy disappeared during antihypertensive treatment had the same risk of adverse cardiovascular events as patients without hypertrophy at the beginning of follow-up.

In my view, this fact changes the clinical management of hypertensive patients. Many clinicians think that the only aim of hypertensive treatment is effective control. In view of these results, this aim, although important, is not entirely sufficient. Optimal treatment should be directed not only at controlling blood pressure (a sine qua non), but also at reversing the abnormal ventricular geometry, as far as this is possible. In this regard, it also seems clear that not all antihypertensive drugs have a similar effect. The LIFE (Losartan Intervention For Endpoint reduction) study demonstrated that, similar to the situation of blood pressure control, there are significant differences in the “reversibility” of abnormal geometry.

A key aspect for the echocardiography specialist is the intrinsic difficulty involved in measuring the ventricular mass accurately, especially in serial studies. In this regard, echocardiography has been criticized as a technique due to the significant variability in measurements. Unfortunately, for this reason, many new drug studies that attempt to analyze hypertrophy regression are designed using other techniques, such as resonance, due to the “perceived” variability of echocardiography.

Even though the American Society of Echocardiography¹⁰ has published precise guidelines for ventricular wall measurement, everyday experience indicates that the difficulties remain significant. The main problem is obliquity to the left ventricle long axis, especially when the M mode is used.

This “lack of perpendicularity” has little effect when parameters, such as the shortening or ejection fractions are measured, even when this is done serially, but leads to serious errors when absolute values are sought, such as mass or ventricular volume. A measurement error of 1 cm in ventricular diameter implies a 30% error in the calculation of left ventricular mass.

The work of Tovillas-Morán et al¹¹ published in this issue of *Revista Española de Cardiología*¹¹ presents a very interesting long-term follow-up study (12 years) of a cohort of primary health care hypertensive patients. Approximately 1 of every 2 patients had at least 1 major cardiovascular event, occasionally fatal, during follow-up. The investigators did not find a significant relationship

between geometric patterns and the incidence of cardiovascular events.

These results seem to cast doubt on the data reported up to now in relation to the prognostic value of ventricular geometry. The study is, in many respects, similar to that of Koren et al,² but the results differ substantially. The authors draw attention to the great differences in methodology, especially regarding the fact that the sample studied was randomized instead of being a consecutive series of patients.

However, the most substantial differences involved the following: *a*) the distribution of geometric patterns in the population studied; and *b*) the incidence of cardiovascular events during follow-up. Concentric remodeling is the most frequent geometric pattern in untreated hypertensive patients. Koren et al reported a figure of 50%, whereas this was 25% among patients with hypertrophy, with a cumulative incidence of events ranging between 12% and 24%. In the present study, the high incidence of cardiovascular events (43.7%) was striking, but of special note was the prevalence of left ventricular hypertrophy (63.8%), and above all that of eccentric hypertrophy, as this was the most common pattern, occurring in 40% of cases.

How can these differences be explained? Do the results need reconciling or are we perhaps viewing the same event at different times?

It is clear that differential factors in relation to race or population, or hospital versus ambulatory care could be suggested. It could even be considered that ventricular adaptation to hypertension varies from one side of the Atlantic to the other. However, a more plausible alternative is to consider that we are analyzing a more advanced stage of the disease. At the beginning of hypertension, essentially characterized by the presence of concentric remodeling, the incidence of cardiovascular events is relatively low and the differences between different patterns (normal vs remodeled vs hypertrophy) are clearer. When the disease progresses and hypertrophy reaches a population prevalence of 64%, the prognosis worsens considerably and the differences between patterns become far less clear. Alternatively, the possibility could be explored of there being errors in the echocardiographic measurements. The high incidence of ventricular hypertrophy could be explained by excessive obliquity which would lead to falsely elevated values of ventricular mass. This would be a reasonable hypothesis if the incidence of events had been similar to that of previous series. However, the high incidence of events in the present study probably indicates an association between "worse geometric distribution" and the consequent worst prognosis.

If this hypothesis is correct, then there could be a serious epidemiological problem. Is hypertension,

even at a primary level, being detected at the right time? Is it being done sufficiently early? It is possible that the current results are indicating a considerable delay in the diagnosis and treatment of hypertension, even in primary prevention. Shouldn't these results act as a spur to raising awareness still further of the relevance to public health of the early detection of hypertension? The consequences for both morbidity and mortality and for public spending could be significant.

In conclusion, echocardiography has a key role in the current management of the hypertensive patient. When assessing left ventricular geometric patterns, it is the best current tool for stratifying risk in these patients. The current treatment of hypertensive patients should be directed not only toward the strict control of blood pressure, but also toward attempting to reverse abnormal ventricular geometry when present.

It is also essential for clinical cardiologists to recognize the value of the presence of hypertrophy in clinical situations not involving hypertension. It is very intriguing, and innovative, to consider that the assessment of hypertrophy could enable risk stratification in patients with coronary disease, myocardial infarction, or heart failure, even after adjusting for the traditional risk variables in such clinical conditions. Echocardiography specialists are especially suited to the task of effectively disseminating this information such that it becomes firmly established in the clinical cardiology community.

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