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Why is Regression of Left Ventricular Hypertrophy Convenient?



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According to our experience, approximately 40% of hypertensive outpatients assisted by our group, have left ventricular hypertrophy and, approximately 10% (of them), have a concentric remodeling. However, it is very important to consider that this concept is not based on solid medical evidence, since the relationship between left ventricular hypertrophy and cardiovascular risk is linear and continuous, as with any biologic variable. Thus, this is an arbitrary criterion and with it we found this prevalence. Nevertheless, when comparing the average left ventricular mass index in patients with concentric remodeling (13%) against those subjects with normal geometry, it is significantly higher in the former. Consequently, concentric remodeling may not be what its name suggests but rather, a subclinical form of left ventricular hypertrophy, that we are wrongly diagnosing with the current concept. In that case, less than 50% of hypertensive patients have a normal left ventricular geometry [1-2].

For almost twenty years, it has been shown that the rate of cardiovascular death, death for any cause and cardiovascular events is significantly higher in patients with left ventricular hypertrophy compared to subjects who do not have hypertrophy. In addition, patients with concentric remodeling have a higher rate of events than those who have normal geometry. According to more recent studies, such as the PIUMA study, those subjects with regression of left ventricular hypertrophy with treatment had a lower incidence of events for every 100 patients and they had a better free of events survival, during follow-up, compared to those in whom ventricular hypertrophy did not show regression. On the one hand, left ventricular hypertrophy increases cardiovascular risk in people and, on the other hand, regression of the left ventricular hypertrophy reduces cardiovascular risk. This was proved by a very large study, the HOPE study. The sample was divided into two groups: one group consisted of people that had regression—or no progression—of left ventricular hypertrophy and the other one consisted of people with persistence or de novo development of left ventricular hypertrophy. The primary endpoint and heart failure were significantly lower in those who had no progression or even regression of left ventricular hypertrophy. As a final conclusion to this introduction, it can be said that for every 25 g per meter to the 2.7 power (per height to the 2.7 power) that left ventricular mass index is reduced, primary endpoints of total mortality, myocardial infarction or cerebrovascular events are reduced in 20%

[3-5]. Considering this conclusion, we ask ourselves why regression of left ventricular hypertrophy is convenient in hypertensive people; and this is so because it undoubtedly reduces cardiovascular morbimortality. But the most interesting issue and, the one I will address and I consider must be deeply discussed, is why regression of left ventricular hypertrophy reduces cardiovascular morbimortality.

The impact of regression of left ventricular hypertrophy will be evaluated on

- the incidence of atrial fibrillation,
- the incidence of cerebral infarction,
- the incidence of heart failure, and
- the incidence of sudden death.

Regression of ventricular hypertrophy and atrial fibrillation

Some studies carried out in our group indicated that left ventricular mass index is the variable which has a higher correlation with the left atrial size, measured in its anteroposterior axis. This left ventricular mass index can be either corrected for height to the 2.7 power, which is the way in which it should be corrected in obese subjects, or by body surface. In both cases, this statistically significant

relationship ranges from 0.60 to 0.50 and the correlation was higher than when considering levels of blood pressure, patients' height, body mass index, presence of diabetes, etc. That is to say, left ventricular mass index is the clinical variable which has a higher correlation with left atrial size and, as a conclusion, it can be said that left ventricular hypertrophy leads to left atrial dilation [6].

The LIFE study divided the population into two groups: those who had left ventricular mass reduction and those who, after one year of treatment, had no reduction. The group that had a reduction, showed a reduction of left ventricular diameter, as well as the interventricular septal and posterior wall thickness. Left atrial diameter was reduced in those subjects who had a regression of left ventricular mass index and did not change in subjects who had no regression of left ventricular mass index. That is to say, left ventricular hypertrophy dilates the left atrium and the treatment of the left ventricular hypertrophy and its regression reduces the left atrial size. According to the LIFE study, atrial fibrillation was present in 0.4% of the subjects with normal-sized left atrium and in 3% of the patients with dilated left atrium [7-8]. Hence, figure 1 shows a model expressing a proposal of the physiopathological development of hypertensive cardiopathy: left ventricular hypertrophy leads to atrial dilation and the regression of left ventricular hypertrophy prevents the whole process.

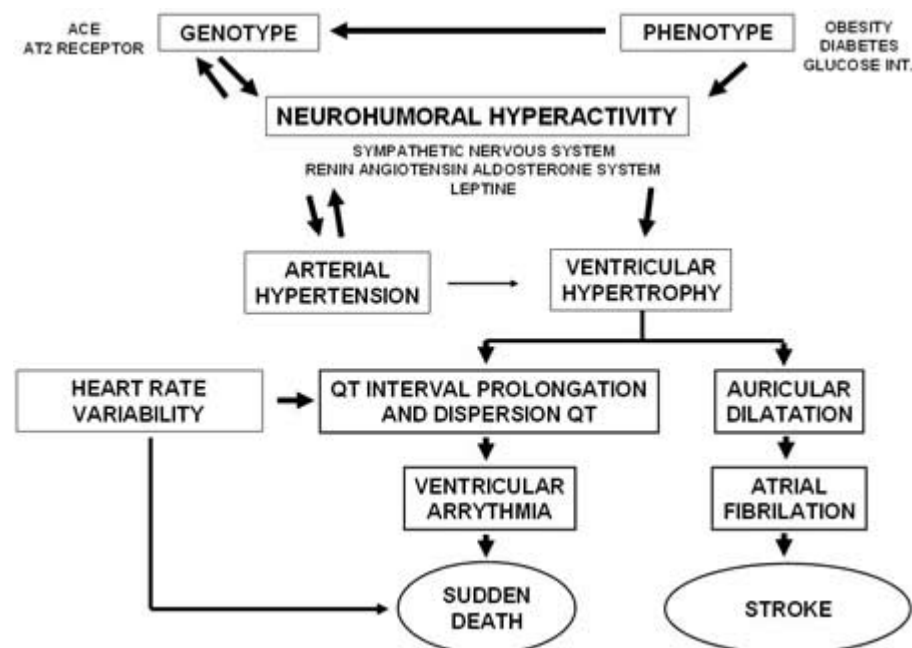


Figure 1: Physiopathology of hypertensive cardiopathy and related clinical events.

Regression of ventricular hypertrophy and cerebral infarction

In the LIFE study, 8% of the enrolled patients had atrial fibrillation: 4% developed it at randomization and the other 4% developed a de novo atrial fibrillation. The incidence of cerebral infarction in those subjects who were in sinus rhythm during the whole study was 5%. On the other hand, subjects who developed a de novo atrial fibrillation or had a baseline atrial fibrillation had a 16% rate of having cerebral infarction; this means that they had a three times higher incidence of cerebral infarction. However, when we evaluate the total population and we see that 7% of patients in the LIFE study had cerebral infarction (5% in sinus rhythm, 1% with atrial fibrillation from the beginning of the study and 1% with atrium fibrillation for the first time), we realize that cerebral infarction is related to this left ventricular hypertrophy and atrial fibrillation mechanisms that lead to cerebral infarction in 28% of patients.

What happened in the LIFE study? Treatment reduced the risk of having cerebral infarction in the global population by 25%. The risk of cerebral infarction was reduced with treatment in 25% in the global population but those who had atrial fibrillation had almost 50% reduction of the risk of infarction. It can be stated that in 1 out of 3 hypertensive patients, cerebral infarctions are related to ventricular hypertrophy and that regression of left ventricular hypertrophy by or due to this reverse remodeling of the heart lowers the incidence of cerebral infarctions.

Regression of ventricular hypertrophy and heart failure

In the epidemiologic HyperGen study, the ventricular function of 1300 hypertensive patients was evaluated and the results were: nearly 86% of patients had normal ejection fraction, 10% of them had a moderate depression of their ejection fraction and only 4% had a severely depressed ejection

fraction [9].

What is happening in the left ventricle? For this to happen in the left ventricular geometry remodeling, as left ventricular mass index gradually increases, the ventricular function deteriorates— both in males and females subjects. Nonetheless, this is not due to the increase of the septal or posterior wall thickness but mainly to left ventricular cavity dilation; in fact, in hypertensive patients, the fall of the ejection fraction in hypertensive patients is mainly caused by left ventricular dilatation not specifically related to hypertension. The typical or characteristic hypertensive patient model of heart failure is the model of diastolic dysfunction, which, from the beginning, is always accompanied by at least cellular systolic dysfunction, or myocytic dysfunction.

What happened in the LIFE analysis in which patients were divided according to the reduction or increase of their left ventricular mass? There was an improvement of the isovolumetric relaxation time, peak E wave/A wave velocity ratio and deceleration time in subjects with left ventricular mass reduction. Neither of these facts occurred in subjects who did not have regression of left ventricular hypertrophy [7–8]. Hence, left ventricular hypertrophy causes deterioration of the left ventricular systolic and diastolic functions and its regression causes a significant and clear improvement in the left ventricular systolic and diastolic functions.

Regression of ventricular hypertrophy and sudden death

In some studies carried out by our group, we have been able to identify, in an objective way a linear, positive, continuous and statistically significant correlation between the left ventricular mass index corrected by body surface or by height to the 2.7 power and the maximum corrected QT so that there is a corrected QT interval prolongation as an increase of the left ventricular mass index occurs [10]. In several epidemiologic studies, it could be observed that in subjects with sudden death, there was a higher prevalence of left ventricular hypertrophy than in subjects who survived and in those who died of a non-sudden death. In addition, in the latter ones, the QT interval dispersion was much higher (59 msec and 65 msec, respectively) than in the former ones. The complexity of ventricular arrhythmias in patients who suffered from left ventricular hypertrophy and high QT dispersion was significantly greater and this may be the reason why these patients have sudden deaths [11].

Also, in other studies done by our group, we could notice an inverse—and negative—relationship between cardiac frequency variability and left ventricular mass index and we know that reduced cardiac frequency variability is a way of expressing the existence of sympathetic hyperactivity in subjects. Then, we divided our patients into those who had reduced frequency variability (SDNN value lower than 100 milliseconds) and the ones who had normal cardiac frequency variability (SDNN value higher than 100 milliseconds); patients with reduced frequency variability had a significantly higher prevalence of prolonged maximum corrected QT: nearly 70% against 25% [12-13].

Therefore, the left ventricular hypertrophy model might lead to QT interval prolongation and dispersion; this can cause left ventricular arrhythmia and this, in turn, might cause sudden death. In this context, cardiac frequency variability may be warning us about QT prolongation and dispersion and about the fact that the patient may have a sudden death as well.

Final comments

To get to a final conclusion, we may try to answer the question why regression of left ventricular hypertrophy is convenient by saying that regression of left ventricular hypertrophy reduces the incidence of atrial fibrillation, cerebral infraction, heart failure and, finally, of sudden death. Therefore, in the future, in the treatment of hypertensive patients, we need to target not only atrial pressure values but also left ventricular mass index and besides, by achieving the reduction of blood pressure we should achieve the regression of left ventricular hypertrophy.

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