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COMMENTARY

Inappropriately high left ventricular mass: marker of very high cardiovascular risk in patients with chronic kidney disease?

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There is increasing knowledge of the burden of cardiovascular (CV) diseases affecting patients with chronic kidney disease (CKD). CV diseases are the main cause of death in the CKD population, and the majority of patients with CKD die before ever reaching the end-stage renal disease; in fact, for patients with CKD, the risk of a fatal CV event is much higher than the risk to develop end-stage renal disease.[1,2] Although patients with CKD manifest a high prevalence of traditional CV risk factors, this does not fully account for the burden of CV diseases in CKD. Other factors, which are typical of the CKD condition, such as secondary hyperparathyroidism, anaemia or oxidative stress, are associated with enhanced CV damage and mortality.[3] Traditional CV risk factors, however, have a central role. Hypertension, often together with diabetes, is today the first cause of CKD. Hypertension has a major role in cardiac damage in CKD via induction of the left ventricular hypertrophy (LVH),[4] whose prevalence is very high in patients with advanced CKD, with very high values of LV mass[5](Figure 1). As in other populations, in CKD patients, the presence of LVH is predictive of a worse CV prognosis.[6]

In recent years, the traditionally defined LVH has been joined by the concept of 'inappropriate' LV mass, resulting from the ratio of observed to predicted LV mass. From a haemodynamic view, LVH is primarily considered an adaptive remodelling process, compensating for an increase in cardiac work. In this view, LV mass can be considered as inappropriate (i.e., inappropriately high) when exceeding the amount needed to adapt to stroke work for a given gender and body size; in detail, LV mass is defined as inappropriate when the ratio observed/predicted LV mass is $>128\%$.[7]

In this regard, it should be highlighted that LV growth, and eventually the development of LVH, depend not only on haemodynamic factors, but also on several non-haemodynamic factors (that remain in part unidentified), including genes and neuro-humoral systems. In this complex picture, some pathological conditions, such as CKD, may have a very important role contributing to the structural changes of the left ventricle that lead to the development of LVH and/or of inappropriately high LV mass, and most importantly, in determining the functional LV alterations that may pave the way to overt heart failure.

In this issue of *Hypertension Research*, the article by Chen *et al.*[8] investigates the CV prognostic importance of the ratio observed/predicted LV mass in 485 patients with CKD stage 3–5. Previous papers by other research groups have shown that inappropriate LV mass has a negative impact on CV prognosis of hypertensive patients[9] and is linked with the presence and severity of CKD.[5,10] In the interesting study by Chen *et al.*,[8] inappropriate LVM is highly prevalent (68.5%) and is independently related to CKD severity, in agreement with previous findings.[5,10] Further, the presence of inappropriately high LV mass is independently associated with CV events.[8] Other independent predictors of CV events in this study are old age, history of coronary artery disease, heart failure or atrial fibrillation, wide pulse pressure, low albumin, low haemoglobin and left atrium diameter.[8] Without any doubt, this study gives interesting findings and expands existing data on the topics of the

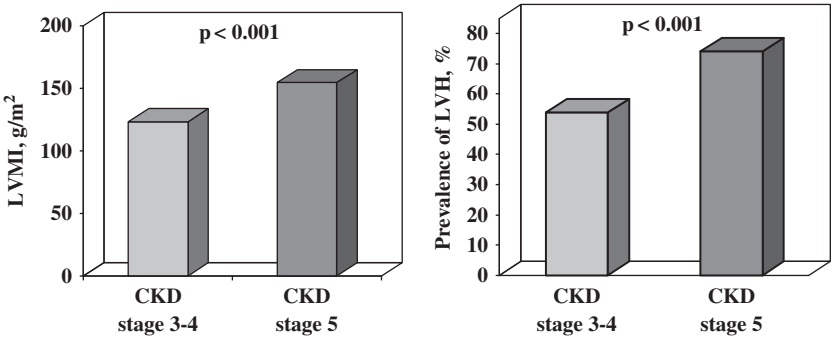

Figure 1 Left ventricular mass indexed by body surface area (LVMI) and prevalence of left ventricular hypertrophy (LVH) in patients with different stages of chronic kidney disease (unpublished personal data).

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relationships between LV mass and CKD, and of CV risk of patients with CKD.

However, the reading of papers focussing on inappropriate LV mass may sometimes be accompanied by silent questions in the reader's mind:

Is the evaluation of inappropriateness of LV mass indeed reliable?

In regard to this question, the predicted LV mass is estimated by means of an equation including height (m),[2,7] gender and stroke work. Stroke work is estimated starting from stroke volume and systolic blood pressure (BP).[7] The reliability of this evaluation has been tested in a study by Muiesan *et al.*[11]; in this study, a difference of –22 or +20% in the ratio of observed/predicted LV mass, measured on two different days, had a 90% probability to identify a true biological change. However, in our opinion, it is incontestable that a single BP measurement may have a great impact on the calculation of the predicted (i.e., 'appropriate') LV mass. In other words, should the single BP measurement obtained on the day of the echocardiographic examination be considered as representative of the BP load that, during months or years, contributed to cause the increase of LV mass in that patient? This can be considered the main limitation of the concept and use of inappropriate LV mass. In this regard, Chen *et al.*[8] suggest that the use of average ambulatory BP instead of a single clinical BP measurement could be more reliable. Further, they correctly acknowledge that also low LV ejection fraction may influence the calculation of inappropriate LV mass.

Despite these limitations, inappropriate LV mass has shown to be associated with CV prognosis in different populations,[8–9] thus it seems to correspond to something biologically plausible. In this regard, and adding a provocative comment, it should be noted that the concept of inappropriate LV mass could be in part comparable to the concept of very high LV mass, and the observation that CV risk increases linearly with the increase of LV mass is yet known in the literature.[12] Beyond these concerns on the 'inappropriate' LV mass, it is still topical to draw attention on CV risk in patients with CKD, and on the need for early and effective treatment in this population.

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