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Left Ventricular Hypertrophy, Ischemic Heart Disease and the Incidence of Cardiovascular Events in Japanese High-Risk Hypertensive Patients

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Although blood pressure (BP) is the main variable determining cardiovascular (CV) risk in hypertensive patients, recent guidelines emphasize that management of hypertension should be related to quantification of the total CV risk[1] This concept is based on the fact that, when concomitantly present, BP and other risk factors augment the risk and lead to a greater CV risk than the sum of the individual components[2]

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The most common clinical variables that should be used in stratification are risk factors, target organ damage, diabetes and established CV or renal disease. High total CV risk is a subgroup of patients with a previous diagnosis of CV disease, besides the subgroups of patients with diabetes mellitus and with severely elevated single risk factors[1] In addition, it is widely accepted that subclinical organ damage plays a crucial role in determining the CV risk of hypertensive patients. Of these, there has been further confirmation of the adverse prognostic role of left ventricular hypertrophy (LVH), together with evidence that it is fairly common in hypertensive patients[3] Accordingly, evaluation of cardiac complications, such as previous CV disease and the presence of LVH, is useful for detecting hypertensive subjects at increased risk of CV disease. However, whether each component cardiac complication has separate implications on the outcome of long-term CV events in hypertensive patients is not known with certainty.

Ueshima et al, reporting in this issue of the Journal[4], provide the interesting piece of information that each of 2 cardiac complications, LVH and ischemic heart disease (IHD), has a different effect on the incidence of future CV events in Japanese high-risk hypertensive patients. By using enrolled participants of the Candesartan Antihypertensive Survival Evaluation in Japan (CASE-J) trial, the authors evaluated 2,030 and 2,673 high-risk hypertensive patients with and without cardiac complications. The incidence of CV events, represented as a composite of sudden death, cerebrovascular, cardiac, renal and vascular events, was compared between patients with and without the complication of LVH and/or IHD in this post-hoc study. During 3.2 years of follow-up, the authors proved that cardiac complications as a whole are associated with the CV events rate, and further, both LVH and IHD are independent predictors for CV events. Moreover, the authors found that there are different effects on each event category of CV events between LVH and IHD. After adjustment for baseline characteristics, LVH is linked to cerebrovascular events, but not to CV death or other cardiac events, whereas IHD is associated with cardiac death, especially sudden death, and other cardiac events, but not with cerebrovascular events. Neither LVH nor IHD related to the onset of renal and vascular events.

An extensive body of population studies has provided consistent evidence that LVH confers increased risk for CV events, including heart failure, myocardial infarction, sudden death, arrhythmia and cerebrovascular events[1,3,5] LVH, a measure of hypertensive target organ damage in the heart, is considered to be a valuable surrogate index for CV events, reflecting longstanding exposure to hypertension. Also, retrospective analyses of prospective trials have shown that treatment-induced reduction in LVH is accompanied by a reduced incidence of those same CV events[1,6] In spite of this, Ueshima et al demonstrated that LVH was associated exclusively with the onset of cerebrovascular events, but surprisingly, failed to predict the onset of other CV events[4] Although this finding seems to open new perspectives in assessing the CV risk in hypertension, caution is needed in the interpretation of the result because of some study limitations. First, the number of CV events was small in their study, partly because of strictly controlled BP and the short follow-up period of 3.2 years. Total CV risk models do not consider the duration of exposure to a risk factor or to diseases; however, several computerized methods for estimating total CV risk notify the absolute chance of having a CV event usually over 10 years[1] Furthermore, CV risk factors are traditionally derived from studies in Western societies. The profile of CV disease tends to be different in Japan, where there are more cerebrovascular events than IHD events[7] The age-adjusted death rate resulting from IHD in Japan has been estimated as one-sixth that observed in the United States[7] In fact, the total number of cardiac events was smaller than that of cerebrovascular events by 20% in this study. Second, the definition of ECG-LVH was relatively lenient and there were small numbers of subjects who underwent echocardiography. The significance of target organ damage in determining the calculation of overall risk depends on how carefully the damage is assessed. Also, it has been suggested that echocardiography is more sensitive than ECG in diagnosing LVH and predicting CV risk[5]

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Nevertheless, this finding raises an important aspect of the management of hypertension in the Japanese population. To lower the comparatively high incidence of cerebrovascular events in Japan, reduction of LVH ought to be a key treatment strategy in the treatment of hypertensive patients. Recently, Ishikawa et al[8] reported that the Cornell Product ECG-LVH predicted future cerebrovascular events, but not myocardial infarction, in the Japanese general population by using more than 10 years of follow-up, providing a further clue to the close relationship between LVH and the incidence of cerebrovascular events in Japanese.

Another important information from the study by Ueshima et al[4] is that a history of prior IHD is an independent predictor for cardiac death and other cardiac events, but not for cerebrovascular events. Patients with IHD have a greater risk of subsequent coronary events if BP is raised[9] The important role of BP lowering in patients with IHD is also supported by the results of several recent placebo-controlled trials showing that, irrespective of the type of treatment, in hypertensive patients with known IHD the incidence of CV events decreases steeply in relation to the achieved BP value! Because BP was fairly well controlled in these CAST-J trial patients, other risk factors for CV death and cardiac events may contribute to the present finding. Although there are no follow-up data, nearly 45% and 31% of participants in the CAST-J study had hyperlipidemia and smoking habit, respectively, at baseline![10] Consequently, this emphasizes the importance of risk factor control, as well as BP control, in Japanese hypertensive patients with IHD.

Despite these still open problems and limitations, Ueshima et al present important data highlighting the different implications of complicated LVH and IHD on the incidence of each event category of CV events: the strong association of LVH with cerebrovascular events, and that of IHD with cardiac death and events. This may provide new perspectives on prognostic stratification and will lead to individual therapeutic strategies for Japanese high-risk hypertensive patients, while we wait for future studies to address these issues in more depth.

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