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Invited commentary

Left ventricular size as a predictor of vascular events

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In the May issue of this journal Dykun et al. [1] reported that left ventricular size indexed to body surface area (LVI), measured on a non-enhanced chest CT scan, was a predictor of future cardiovascular events in the Heinz Nixdorf Recall (HNR) study. The HNR is a population observational outcome study conducted in the Ruhr area in North West Germany for nearly a decade. This study has generated a large number of relevant cardiovascular epidemiological data, and the current report adds interesting new facts to the well-known prognostic significance of LV hypertrophy as previously reported in several publications [2–4].

In total the authors recorded 265 events (122 coronary artery disease events, 59 cardiovascular deaths and 84 strokes), among 3926 subjects without prior history of cardiovascular disease followed for an average of 8 ± 1.5 years. The highest quartile of LVI was predictive of events independent of traditional cardiovascular risk factors and coronary artery calcium (CAC); no interaction between CAC and LVI was detected. Of interest, LVI appeared to be a better predictor of events in subjects with a low volume of CAC then in those with greater amounts.

In analyses of events per 1000 patient-years LVI was equally predictive of events in men and women. Although LVI was an independent predictor of events it was not incremental to traditional risk factors. The latter observation suggests that a larger LVI is not the end-result of an accumulation of risk factors and is independently associated with vascular disease. In fact, the same authors previously reported that traditional risk factors provided a limited explanation for the variance of LVI in the same population cohort [5]. What is then the link between LV size and vascular disease? It should be remembered that observational studies do not establish directionality of risk. Prior reports have linked inflammation as well as endothelial dysfunction [6,7] with left ventricular hypertrophy in chronic kidney disease. A modern pathogenetic model posits that long-term inflammation and immune-activation of T-effector lymphocytes [8] are necessary for the development of systemic hypertension. The latter is one of the main causes of LV enlargement and stroke. Vitamin D deficiency has been associated with development of hypertension and left ventricular dysfunction [9] and, very poignant to the article being editorialized here, myocardial infarction [10] and sudden death [11]. Subclinical coronary artery disease is associated with increased vascular stiffness [12] that may cause left ventricular hypertrophy and diastolic as well as systolic dysfunction. Therefore it is entirely possible that increasing LV size may be dependent upon the same systemic mechanisms leading to atherosclerosis. Finally, it is also conceivable that coronary artery disease may lead to left ventricular hypertrophy and/or enlargement [4], as associations may be bidirectional.

Hence, although potentially surprising the association of a simple measure of LV size with vascular events including stroke is tenable. One of the main limitations of the method used by the authors is the inability to diagnose LV hypertrophy, as the CT area-method used by the authors measures the surface of a single axial slice of the LV and does not provide mass measurements. Others have demonstrated a fair correlation of LVI with LV mass measured by cardiac magnetic resonance [13], but the correlation was modest. A few other limitations of the report by Dykun et al. [1] are worth mentioning. Among the many outcomes, the authors did not collect data on development of congestive heart failure which would have been very interesting in relation to increasing LV size. Another marker of risk of cardiovascular events that can easily be measured on non-contrast enhanced CT scans is epicardial adipose tissue (EAT) [14]. Although data on EAT and its prognostic impact as a marker of risk of coronary artery disease are available in the HNR study and others [15,16], the authors did not report any information on EAT in this paper. Probably the authors needed to expand their

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statistical power and included all events in their models. However the 265 events the authors recorded occurred in 219 patients and one wonders if it is correct to count more than one event, potentially dependent upon the same mechanism, in the same patient. Despite these limitations the report is stimulating and adds valuable epidemiological information on the significance of left ventricular size as a marker of vascular risk. LV size and mass is a relatively easy measurement to obtain with the numerous non-invasive imaging modalities in our armamentarium and it should be seen as more than a potential hazard for congestive heart failure alone.

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