In the prediction of the risk of cardiovascular events, the role of the left ventricle (LV) has been established for a long time, in the general population and especially in patients with heart failure. LV dimensions and systolic function, the latter mainly expressed as ejection fraction, were the first variables investigated; over the years, the role of predictors of cardiovascular outcomes has been extended to an increased LV mass (ie, hypertrophy) and altered chamber geometry, to an increase in stiffness and parallel reduction in filling properties (diastolic dysfunction), and more recently, to subclinical alterations of systolic function (myocardial strain and strain rate), in an attempt to identify predictors of risk at an early stage of dysfunction, when ejection fraction may still be normal.

See Article by Gonçalves et al

In the last 2 decades, the left atrium (LA) has also attracted considerable attention as a possible predictor of cardiovascular outcomes. The LA is known to dilate in response to mitral valve disease, arterial hypertension, increased LV mass, and in general any condition that increases the LV filling pressures.1–3 As such, LA size may be thought of as an indicator of the combined action of these factors over time and, therefore, also a possible marker of their integrated action on the risk of cardiovascular diseases. Indeed, LA enlargement has been associated with increased risk of death,4,5 stroke,5–7 heart failure,8,9 and development of atrial fibrillation.10–12

The assessment of LA size was initially performed using the antero-posterior diameter, as measured by transthoracic echocardiography at end-systole, when the dimension of the atrium is largest. Although easy to measure, reproducible, and therefore, suitable for both clinical purposes and large population studies, LA diameter is a poor indicator of the actual volume of the LA, which is known to enlarge in asymmetrical fashion in response to various stimuli. The assessment of LA volume by 2-dimensional echocardiogram represented, therefore, a substantial improvement in the evaluation of the LA size and associated risk of events, allowing measurements that were more accurate and less fraught with geometric assumptions. More recently, the introduction of 3-dimensional echocardiography has allowed the assessment of LA volume in real time throughout the cardiac cycle and, therefore, an accurate measurement of maximum and minimum atrial volumes and the analysis of functional parameters, such as the LA emptying fraction (LAEF).

In this issue of Circulation: Cardiovascular Imaging, Gonçalves et al report on echocardiographic parameters obtained by 2- and 3-dimensional echocardiography in a subgroup of elderly participants in the Atherosclerosis Risk in Communities (ARIC) study, examining differences among participants with no known cardiac disease or risk factors, hypertensive individuals, and individuals with heart failure.13 Although reporting on a host of LV, LA, and other echocardiographic parameters, the authors focused their investigation on LA volumes and LAEF. Atrial volumes were found to be smallest and LAEF highest in participants without cardiac disease or risk factors (healthy participants), whereas patients with heart failure were at the opposite end of the spectrum, showing the largest volumes and lowest LAEF. Hypertensive subjects were somewhere in the middle, showing larger volumes, but similar LAEF compared with healthy participants, which suggests that hypertension may have affected LA size before it did LA reservoir function. Worse LAEF was associated with lower LV systolic and diastolic function, and with higher plasma levels of N-terminal pro-B type natriuretic peptide.

The study has important strengths; first among them the thorough, state-of-the-art echocardiographic examination performed on a large cohort of elderly individuals, whose results provide information that is largely missing, or at a preliminary stage, in the literature. The presence of a sizeable group of individuals without known cardiac disease or cardiovascular risk factors is also remarkable in this age group, when risk factors and especially hypertension are highly prevalent. This group of healthy individuals is of crucial importance as a reference, allowing one to place the results observed in the other subgroups in the correct perspective. Also important is the attempt to identify structural and functional atrial parameters that could help in the risk stratification of elderly individuals for heart failure development and the attention paid to the inter-relation between LA and LV parameters on the observed results.

Still, some aspects of the study should be regarded with caution. The heart failure group is somewhat problematic. The diagnosis of heart failure was based on unadjudicated hospitalization International Classification of Diseases-Ninth Revision codes and Gothenburg criteria. In apparent contrast with their diagnosis, heart failure patients had normal mean LV ejection fraction on echocardiogram (over 63%); although this observation might be driven by a preponderant proportion of patients with heart failure and preserved ejection fraction (also
known as diastolic heart failure or heart failure with preserved ejection fraction), moderate diastolic dysfunction was present in only one third of cases, a proportion that was slightly but not significantly higher than that observed in hypertensive or even healthy individuals. Even so, heart failure patients did show significant LA dilatation and LAEF impairment compared with the other subgroups; however, there was no possibility to separate patients with heart failure and preserved LV ejection fraction from others. LA volumes and function may be affected differently in systolic and diastolic heart failure, especially when phasic volumes are considered. LA minimum (diastolic) volume has been shown to be more strongly associated with LV diastolic dysfunction,12 which seems reasonable given the fact that the atrium is directly exposed to the LV pressure during diastole, when the mitral valve is open. In Gonçalves et al’s article, LA minimum volume was strongly associated with LAEF in the entire study group, whereas LA maximum (systolic) volume was not associated with LAEF when pertinent covariates were taken into account (Table 2). LA minimum volume was the strongest correlate of LAEF in every diagnostic subgroup, whereas LA maximum volume was associated with LAEF only in hypertensive individuals and to a lesser degree than the minimum volume (Table 3).

Evidence has been accumulating that LA minimum volume may be a better predictor of outcome than the traditionally used maximum volume. LA minimum volume has been shown to be a better predictor of the development of atrial arrhythmias than the maximum volume.13,14, also, LA minimum volume has been shown to be more strongly associated than maximum volume with subclinical cerebrovascular disease detected by brain magnetic resonance imaging,17 providing an initial indication of its possible role as a stronger predictor of outcomes. The use of LA phasic volumes, and especially of the minimum volume in addition to the traditionally used maximum volume, is one of the important methodological aspects that the article by Gonçalves et al indirectly supports.

The study has some limitations that are inherent to the composition of the study cohort and to the study design and are, therefore, unavoidable. The older age of the studied cohort is at the same time an advantage and a limitation. If, on one hand, it allows the study of the variables of interest in the elderly, the age group that has the highest frequency of risk factors and cardiac abnormalities and the highest risk of heart failure development, on the other hand, it prevents the full appreciation of the effects of age on the variables under examination. Because of the race-ethnic composition of the study population (85% white), the generalization of the results to populations with a larger representation of minorities, and potentially different risk factors profiles, may not be possible. More importantly, as the authors remind us, this is a cross-sectional study and is, therefore, in the condition to suggest associations between variables, but not to establish causality, and to suggest, but not prove, the predictive value of the examined echocardiographic parameters for cardiovascular disease. In the end, the success of newer diagnostic modalities, such as 3-dimensional echocardiography, will lie in how much they can improve on what is already available. In the specific, 3-dimensional echocardiography has been shown to be more accurate than 2-dimensional echocardiography for LA volume determination18–20, the challenge will be to demonstrate that it can also perform better in the prediction of cardiovascular outcomes. The best echo- cardiographic variables, or combination thereof, will have to be defined from a host of available candidates of both atrial structure and function (phasic volumes; LAEF; LA global longitudinal strain), and their actual predictive power for clinical outcomes will have to be established in appositely designed outcome studies. If 3-dimensional echocardiographic imaging of the LA is to become a risk-stratification tool in individual patients, age- and sex-specific cutoffs of increased risk will have to be defined for the best predictive parameters. When those conditions are met, 3-dimensional assessment of LA structure and function may well become an invaluable tool for refining the prediction of cardiovascular risk.

Disclosures

None.

References


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