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EDITORIAL COMMENT

Global Longitudinal Strain

Ready for Clinical Use and Guideline Implementation*

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Cardiac function is a powerful prognostic marker. A great number of clinical decisions are based on the performance of the left ventricle, such as medication for heart failure (HF), primary prevention implantable cardiac defibrillator treatment, and timing of valve interventions, among others. The method for assessing left ventricular function has long been synonymous with the left ventricular ejection fraction (EF), a term with >70,000 hits on PubMed. Other methods to evaluate left ventricular function were introduced during the past years, but were most often discarded. Myocardial strain imaging was introduced in the 1990s and this method has persisted, although its path to acceptance by the medical community has been thorny (1,2). Global longitudinal strain (GLS) has emerged as a fine-tuned, highly reproducible, and operator-friendly method for quantification of left ventricular function and prognostication in a wide spectrum of cardiac diseases (3). Long ago accepted in the cardiac imaging research community and headlining numerous conferences over the last decade, the way toward guideline implementation of GLS moves slowly ahead. Skepticism against the specifics of the underlying technology (vendor secrecy) and potential vendor differences is legitimate (4), but seems to overshadow the growing pile of evidence for the clinical use and added value of GLS beyond EF.

In this issue of the *Journal*, Park et al. (5) assessed the value of GLS compared with EF for prediction of all-cause mortality in patients admitted to the hospital with a clinical diagnosis of acute HF. The

SEE PAGE 1947

investigators included a staggering 4,312 patients during an 8-year study period and quantified EF and GLS at admission. Patients were classified as having HF with reduced EF, HF with preserved EF (HFpEF), and the recently formed category of HF with mid-range EF (6,7). EF categories were compared with GLS tertiles and both parameters were also analyzed as continuous variables. A total of 1,740 (40%) patients met the primary endpoint of all-cause death during follow-up. Maybe not unexpectedly, GLS showed strong predictive value among well-known predictors of all-cause death in HF, whereas EF failed to predict mortality when adjusted for confounders. The superiority of GLS to EF in prediction of cardiovascular death has previously been demonstrated in this patient group, albeit not in the same scale (8). The main strength of the study by Park et al. (5) is the hitherto unmatched population size, representing one of the world's biggest echocardiographic studies.

HF is currently classified according to EF (6,7). However, HF classified according to EF becomes problematic when there is no reduction in EF. The term HFpEF indicates that there is "invisible" HF that is not detected by EF measurements. Furthermore, we teach our students that this "invisible" HF has a concerningly high mortality, maybe as high as in those with reduced EF (9). Deadly, invisible, and without a specific treatment, HFpEF has caused some confusion. Using both GLS and EF for assessing systolic function, several studies have now revealed that GLS may be reduced although EF is still preserved (10-12). Therefore, it is essential to differentiate

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between the terms systolic function and EF, which are not synonymous and not interchangeable. In hearts with mildly reduced function, EF is not sensitive enough to detect dysfunction. The fact that 84% of patients with preserved EF in the study by Park et al. (5) had reduced GLS highlights that GLS quantifies "invisible" HF with good precision and is strongly linked to prognosis, as shown in this and in other papers (13). When systolic function is severely reduced (i.e., when the patient has reduced EF), EF is an excellent marker of prognosis, as has been shown for many years in numerous reports (14). Importantly, in the situation of reduced EF, the prognosis is unfavorable and further quantification by GLS is unlikely to yield additional useful information. Therefore, we still need EF and do not anticipate the fall of a giant. However, a tool is needed to assess the mild reduction in cardiac function found in a large subset of patients with HF and here GLS is an excellent candidate.

What does the study by Park et al. (5) add to what is already known about GLS? Park et al. (5) award useful confirmative results on the prediction of mortality in acute HF, with the statistical power to adjust for a long list of possible confounders. If the medical community has ignored previous reports about the prognostic value of GLS, this paper should help convince those who are still in doubt. The design of the study and the number of included patients allow us to conclude that GLS is now ready to be implemented in daily clinical work and in the guidelines for diagnosis, monitoring, and assessment of prognosis in patients when cardiac function matters.

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