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EDITORIAL COMMENT

Global longitudinal strain: the best biomarker for predicting prognosis in heart failure?

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This article refers to 'Echocardiographic screening for non-ischaemic stage B heart failure in the community' by H. Yang *et al.*, published in this issue on pages 1331–1339.

The desire to predict who will develop heart failure (HF) has inspired researchers for a long time. Numerous so-called predictive biomarkers have been developed, studied, published, and forgotten. Various suggestions of biomarkers have been deemed to add little to clinical practice.[1–3] However, a few have reached current clinical practice, including NT-proBNP, troponins, and creatinine, which can be used as biomarkers for an unfavourable cardiac prognosis.

In this issue of the journal, echocardiographic biomarkers for HF development are presented.[4] Marwick and co-workers present a community-based study on 419 asymptomatic subjects with risk factors for HF who were screened with echocardiography. At baseline there was a considerable prevalence of stage B HF measured by LV hypertrophy, diastolic measures, global longitudinal strain (GLS), and left atrial enlargement. During 14 months of follow-up, new HF symptoms or death occurred in ~13% of the study population. The echocardiographic markers were tested for predictive value of outcome by a variety of statistical methods. The authors reported convincing evidence that echocardiographic markers, in particular GLS and LV mass, were useful for screening of incident HF. The study adds to an increasing number of studies demonstrating the superiority of GLS compared with EF,[5–8] and the usefulness of GLS in asymptomatic subjects.[9] While the EF is one of the most well established markers for cardiac prognosis, GLS obviously has advantages by a discriminative value for both death and occurrence of ventricular arrhythmias when systolic function is still relatively preserved.[5–7]

In fact, the Australian research team was one of the first to demonstrate the usefulness and the predictive value of GLS as a biomarker of cardiac prognosis.[7] Since the introduction of strain echocardiography almost two decades ago, the technique has struggled to become a clinical tool, which can partly be explained by scepticism in the cardiology community, time-consuming analyses, and questions regarding reproducibility. The transition from a pure research tool to clinical praxis has been cumbersome, but has been facilitated by evolving techniques and strain analyses that are now partly automated. The senior author has strongly contributed to the transition of strain echocardiography into clinical practice and was visionary in his belief in the clinical value of GLS, when the majority of the community remained sceptical.[7,10] The superior clinical value of GLS was again shown in the current article, and GLS has thereby strengthened its role as a reliable biomarker for HF.

The greatest advantage of GLS and why it may be the rising star of biomarkers in HF is the fact that GLS can be used as a direct measure of HF. While some biomarkers, such as NT-proBNP, measure hormonal consequences of atrial stretch and elevated filling pressures, GLS gives us an accurate measure of reduced myocardial function.

NT-proBNP is an excellent and easy to perform biomarker in patients with established HF, but has limited ability to assess HF in patients with normal EF.[11] This indicates that NT-proBNP is most useful in HF at a later stage, when EF already is reduced. The non-ischaemic failure of the left ventricle is a continuum, starting slowly in most patients, and when EF is finally reduced the process has been ongoing for some time. The poor sensitivity of EF to detect subtle myocardial dysfunction has led to the understanding that HF can exist without reduction in EF, i.e. HF with preserved EF (HFpEF). GLS has the ability also to assess mild systolic impairment and has revealed that patients with HFpEF already have reduced systolic function.[12] Therefore, with the help of GLS, our understanding of HF has changed to the more intuitive idea that HF is a disease affecting both systolic and diastolic function simultaneously.

Disease screening is a difficult topic and with a number of controversies including costs, false-positive and false-negative results. An effective screening of a disease is dependent on high pre-test probability, and has so far been limited to patients with risk of oncological diseases. However, cardiovascular diseases are the most

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common causes of death in Western societies, and screening for early cardiovascular diseases seems reasonable. Clearly, a single, easily available, non-expensive blood sample biomarker would be the most desirable screening method, but this blood marker is yet to be found and still multimarker samples are considered the best approach so far.[13] The obvious disadvantage of echocardiographic screening for HF is the availability and the costs of an echocardiographic examination. An eventual echo screening should clearly be restricted to high-risk patients and there is currently no reason to screen patients for HF other than those described in the paper of Yang *et al.*[4] Furthermore, screening should only be performed if there is available treatment for the screened condition and effective HF treatment is well established.

The diagnostic tool and treatment regimen are already available. So, what are we waiting for before we can recommend the cardiology community to start large-scale echocardiographic screening programmes of patients at high risk of developing HF? The answer is quite easy and straightforward, together with its complexity: we will need a carefully performed cost-effectiveness study that demonstrates improved survival and morbidity when treating patients with reduced GLS and preserved EF.

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