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EDITORIAL

Efficiency is key

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This editorial refers to 'Regional myocardial work by cardiac magnetic resonance and non-invasive left ventricular pressure: a feasibility study in left bundle branch block', by C.K. Larsen *et al.*, pp. 143–153.[1]

Several decades after the introduction of cardiac resynchronization therapy (CRT) in clinical practice, one-third of patients continue to fail to respond favourably to the therapy. Cardiac imaging techniques have been proposed to improve patient selection and reduce non-response. A large randomized trial, however, failed to demonstrate a benefit (PROSPECT).[2] Over the past years, a variety of new imaging markers of CRT response have been proposed, with strain parameters showing particularly promising results. Despite these efforts, subsequent randomized trials evaluating these parameters have not been performed, and current guidelines on CRT justify the use of cardiac imaging only to estimate left ventricular (LV) ejection fraction.

Left bundle branch block (LBBB) leads to septal-to-lateral activation delay. The ensuing uncoordinated contraction results in reduced LV pump function efficiency, further reducing LV function in patients with underlying heart failure (HF) leading to clinical deterioration and premature death.[3] Biventricular stimulation reduces septal-to-lateral activation delay and re-coordinated contraction subsequently improves LV pump function as well as LV efficiency.[4] Recently, we showed that conventional CRT increased mechanical efficiency by 29%, which can be further increased to 39% using haemodynamic optimization strategies.[5] These changes are important since therapeutic interventions that enhance mechanical efficiency have proven to be beneficial with respect to outcome.[6]

Myocardial strain imaging enables quantification of the mechanical consequences of LBBB. In LBBB, the septum typically demonstrates a paradoxical outward motion during contraction of the late-activated LV lateral wall. Septal dis-coordination measured by end-systolic strain showed to be a robust predictor of CRT response.[7] From a theoretical point of view, however, myocardial motion parameters do not fully describe myocardial function since the stress at which a particular motion is accomplished is lacking. Russell *et al.*[8] elegantly showed the consequences of including stress in calculating wasted myocardial work. Regional differences in work between the septal and lateral wall were found to increase substantially when LV pressure was incorporated, providing a more adequate representation of LV dysfunction in LBBB than assessment of deformation indices only. Myocardial work and efficiency can be determined by combining regional fibre strain with instantaneous LV pressure as first shown by Delhaas *et al.*[9] and Urheim *et al.*[10] This method measures regional work in terms of LV pressure-strain loop areas, which may serve as an index of regional myocardial work and metabolism when segments within a given ventricle are compared. In LBBB, myocardial work generated in late-activated regions (by contraction of the lateral wall) is wasted in early-activated regions (systolic stretching of the septum) compromising LV pump function efficiency and leading to an inhomogeneous work distribution as illustrated in *Figure 1*. In a previous study, we showed that (i) the contribution of the septum to LV work varies widely in CRT candidates with LBBB and (ii) the lower the septal contribution to myocardial work at baseline, the higher the acute pump function improvement that can be achieved during CRT.[11] These results were confirmed in a subsequent study by Vecera *et al.*[12] who showed that wasted septal work strongly predicted CRT response after one year. During CRT, recruitment of myocardial work in the septum leads to a more balanced work distribution over the LV. A more homogenous work distribution increases LV pump function efficiency and improves patient outcome. LV pressure–strain analysis, therefore, provides an insight in the negative effect of LBBB on myocardial work and energy utilization and reflects the potential benefit that can be achieved by CRT. Russell *et al.*[13] introduced a fully non-invasive approach by combining estimated LV pressure curves with strain measurements. Left ventricular pressure was estimated by utilizing an empiric, normalized reference curve which was adjusted according to the duration of LV isovolumic and ejection phases, as defined by timing of aortic and mitral valve events by echocardiography. The area of calculated LV pressure–strain loops was shown to reflect regional myocardial metabolism as measured by positron emission tomography (PET). Russell used speckle tracking echocardiography (STE) for myocardial strain assessment. STE, however, is highly dependent on the quality of the available acoustic windows. In contrast, cardiovascular magnetic resonance imaging (CMR) imaging offers high image quality in all patients. CMR

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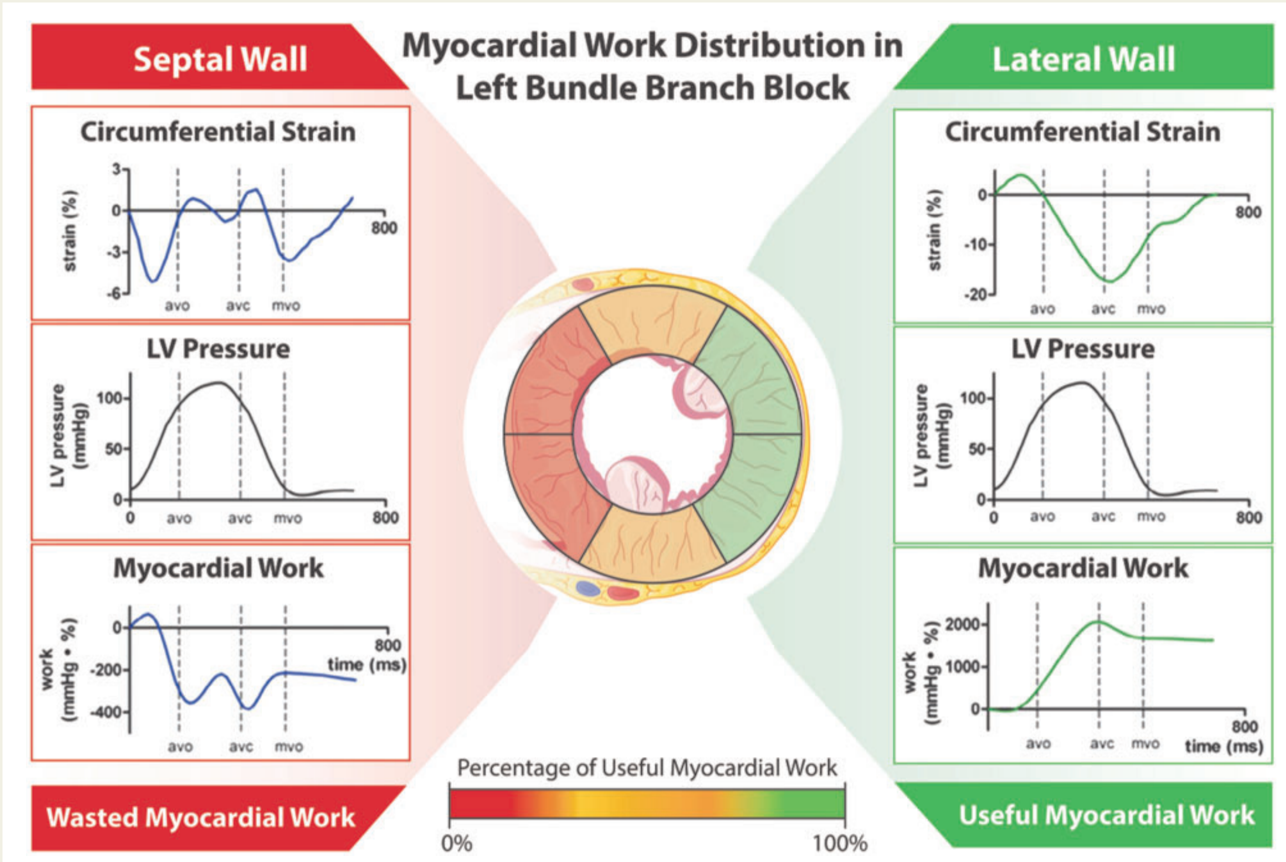

Figure 1 Myocardial work distribution in left bundle branch block. In patients with left bundle branch block myocardial work generated by the lateral wall is wasted in the septum compromising LV pump function efficiency and leading to an inhomogeneous work distribution.

feature tracking (CMR-FT) recently emerged as a post-processing strain technique on standard CMR cine images and showed good agreement with gold standard CMR myocardial tagging.[14] Applying a method similar to Russell's, the present proof-of-concept study aimed to assess feasibility of calculating regional myocardial work from strain by FT-CMR and non-invasively estimated LV pressure. Kjellstad Larsen *et al.*[1] included 37 CRT candidates and nine controls who underwent CMR-FT and STE for strain analysis. Furthermore, a subgroup of 25 patients underwent additional fluorodeoxyglucose (FDG) PET imaging to assess energy utilization. Regional strain curves were combined with estimated LV pressure curves to calculate regional work distribution. In LBBB, a typical pattern was observed with reduced myocardial work in the septum relative to the lateral wall. Work distribution showed good agreement between CMR-FT and STE techniques and energy demand as reflected by FDG uptake.

Although the concept that myocardial work wasted by LBBB activation forms the substrate for LV pump function improvement during CRT is not new, a single-modality approach by CMR for strain assessment and non-invasive blood pressure estimates provides novelty and the authors should be commended for their work. Performing CMR imaging in the work-up of CRT candidates already provides information on global LV function (LV ejection fraction) and is often combined with scar visualization to target LV lead placement.[15] Additional LV pressure–strain analysis could potentially expand diagnostic yield of this comprehensive imaging technique. Future clinical studies that investigate the value of myocardial efficiency estimation in the prediction of response to CRT are greatly encouraged.

Conflict of interest: none declared.

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