LETTER

Latest British Society of Echocardiography recommendations for left ventricular ejection fraction categorisation: potential implications and relevance to contemporary heart failure management

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Letter to the Editor

We read with interest the recent guideline publication from the British Society of Echocardiography (BSE) relating to normal reference intervals for cardiac dimensions and function for use in echocardiographic practice (1). We commend the authors and the Education Committee for attempting to produce updated guidance taking into account contemporary, prospective data to determine new reference ranges for echocardiographic parameters. However, we suggest the newly proposed categories for left ventricular ejection fraction (LVEF) derangements from the BSE may contribute to diagnostic and therapeutic uncertainty and create new challenges for the management of heart failure (HF) patients in the United Kingdom (UK).

It is well recognised that HF transitions across the spectrum of LVEF and irrespective of LVEF, and that the prognosis for patients with HF is worse than in those without this diagnosis. Moreover, recent evidence points to adverse outcomes even in the setting of 'supra-normal' LVEF (2). As addressed in the recent publication (1), the latest BSE guidance for LV function categorisation ('severely impaired', LVEF ≤35%; 'impaired', LVEF 36–49%; 'borderline low', LVEF 50–54%; and 'normal', LVEF ≥55%) is clearly out of keeping with current guideline documents from international echocardiographic societies (American Society of Echocardiography (3), European Association of Cardiovascular Imaging (4)) and with those from international cardiology societies in Europe (European Society of Cardiology (ESC) (5)) and North America (American College of Cardiology/American Heart Association (6)). Both the ESC and the AHA define (heart failure with reduced ejection fraction) HFrEF at, or below, 40%. The ESC and AHA HF diagnostic thresholds have been reached not just on the basis of prognosis alone. Both heart failure with mid-range ejection fraction (HFmrEF) and heart failure with preserved ejection fraction (HFpEF) groups are characterised by marked heterogeneity and display differing epidemiological and pathophysiological profiles compared to HfrEF (7, 8, 9, 10). While the BSE document suggests that LVEF displays a continuous relation to prognosis 'i.e. as the LVEF gets progressively lower, survival is progressively poorer', LVEF exhibits a U-shaped, rather than a linear, relation to mortality (2). Both HFrEF and those with supra-normal LVEF are associated with the highest degrees of mortality, albeit HFmREF and HFpEF patients have poor prognosis relative to those without HF (11).

Current ESC HF diagnostic thresholds have been conceived on the basis of evidence-based treatment response, with the demonstration in multiple clinical

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trials of clear benefit from various classes of medication and device therapy for patients with HFrEF (defined as LVEF ≤40%), unlike HFmrEF and HFpEF. While the BSE document cites beneficial impacts upon mortality for angiotensin converting enzyme-inhibitors (ACEi), angiotensin receptor blockers (ARB), betablockers, mineralocorticoid receptor antagonists (MRA), I_f channel inhibitors, angiotensin receptor neprilysin inhibitors (ARNI) and device therapies for those with 'severely impaired' systolic function, that is, LVEF ≤35% (1, 12, 13, 14, 15, 16, 17, 18, 19, 20), some of these same classes of pharmacotherapy also (and importantly) have a well-established and evidence-based extended survival benefit in those HF patients with LVEF <40% (e.g. ACEi (21), ARBs (22), MRAs (23), ARNI (17)). The results of the BLOCK HF trial (mean LVEF 40%) support the use of cardiac resynchronisation therapy in HF patients in whom there is conventional pacing indication and with LVEF up to 50% (24). In addition to the aforementioned medications, newer classes of drugs have also recently shown prognostic benefit in large-scale multi-centre HFrEF trials with inclusion of patients with LVEF up to 40%: sodium-glucose cotransporter 2 inhibitors (dapaglifozin) (25) in the DAPA-HF study (study inclusion LVEF <40%) and soluble guanylate cyclase stimulators (vericiguat) in VICTORIA (26) (93% of patients had LVEF <40%). On this background, the apparent distinction in the BSE document of patients with LVEF ≤35% from those with LVEF 35–40% is not based upon the totality of evidence from randomised, controlled trials and carries the risk of some patients being deemed ineligible for specific interventions for which there is evidence of therapeutic benefit.

To suggest, as proposed by the latest BSE guidelines, that a LVEF of 36% equates to a comparable degree of systolic derangement as a LVEF of 49% (both classed as 'impaired' in the recent BSE guideline document) is striking and is not based upon the totality of evidence from large-scale clinical trials. The BSE guidance potentially encompasses both HFrEF and HFmrEF subsets under the umbrella of the newly proposed 'impaired' LVEF range raising the following scenarios: (1) a significant proportion of HFrEF patients are denied evidence-based HF therapies and (2) inappropriate and potentially harmful prescription of therapies in those with HFmrEF, for whom there is no evidence of clinical benefit. Additionally, historical data show that a proportion of HFrEF (nearly one in four) demonstrates improved (or recovered) LV function over time (27). Such patients may have inappropriate cessation of prescribed pharmacotherapies by non-HF specialists with potential deleterious consequences (28). Furthermore, in the setting of an individual patient LVEF improving from 36% to 48 or 49% over time, the suggested BSH guideline that this patient's status would be unchanged, appears illogical.

While we agree that LVEF calculation should not be used as a standalone metric of LV systolic function, it continues to be an extremely important imaging biomarker which not only provides both diagnostic and prognostic information but forms the basis of pharmacological and device management of patients and of enrolment into the majority of HF clinical trials (historical and current). The dichotomisation of reduced LV systolic function into a 'severely impaired' and 'impaired' range may further impact upon research settings in HF. In the clinical setting, community HF clinics which are predominantly nurse-led could be overwhelmed, since the majority of these services are commissioned by clinical commissioning groups and acceptance criteria often stipulates a diagnosis of HFrEF. However, as we have noted, the basis for inclusion of patients with LVEF >40% in this category is unclear and specific and evidence-based interventions for such patients are lacking.

We do applaud the BSE for recommending that LVEF should be quoted in all patients with 'impaired' LV function. However, in typically elderly HF populations with concomitant co-morbidity, endocardial border definition is sub-optimal in nearly one-third, precluding calculation of LVEF using the biplane Simpson's method (29), and may add to the uncertainty in the 'impaired' LV range. We suggest that patients with LVEF in the range of 36–49% in this situation fail to guide management.

The management of patients with heart failure is largely based upon evidence gained from multiple clinical trials performed across three or more decades; these trials have, for the most part, defined HFrEF in the range of LVEF 35–40%. It is our view that to diverge from this classification is unlikely to address the BSE-stated aim of enabling 'appropriate interpretation of values into a clinically relevant report' for HF patients. We do, however, welcome the view advocated by the BSE in their latest guidance and supported by British Society for Heart Failure that all echo reports should ideally provide an actual value for LVEF, thereby enabling individualised treatment plans in HF patients (30).

Declaration of interest

The authors declare that there is no conflict of interest that could be perceived as prejudicing the impartiality of this letter.

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