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EDITORIAL

The continued value of risk scores in advanced heart failure

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Article Szczurek et al., see p. 1320

Heart failure (HF) is a global pandemic associated with poor quality of life, high risk of hospitalisation and death, and rapidly growing costs to society [1, 2]. Advanced HF affects between 1% and 10% of patients with HF, as recently defined in detail in a European Society of Cardiology position statement [3]. Briefly, advanced HF is characterised by: (1) severe symptoms; (2) severely reduced cardiac function (generally left ventricular ejection fraction ≤ 30%, but other severe structural or functional abnormalities also qualify); (3) episodes of HF exacerbation; and (4) severe impairment of functional and exercise capacity, and it is also often but not always associated with extracardiac organ dysfunction such as renal or liver dysfunction. A key feature of advanced HF is progression toward death despite the use of maximally tolerated conventional therapy, and the only treatment options for patients with advanced HF are heart transplantation (HTx), durable mechanical circulatory support (MCS), and structured palliative care. Selecting patients for these options is difficult and requires consideration of multiple factors and, importantly, the use of composite risk scores [4–7].

In this issue of the Journal, Szczurek et al. [8] assess three different risk scores and their ability to predict all-cause death in 370 patients listed for HTx at a single centre (median age 54 years, 87% men). The participants appear to have been stable because patients on MCS were excluded and there is no mention of inotropes or unavailable data for the peak VO_2. This is also consistent with the relatively good survival of 72% at the end of the one-year follow-up. Unusually, the authors excluded patients who were removed from the transplant list due to clinical improvement or deterioration (presumably making them ineligible for HTx) and those who underwent HTx. Although the authors were right to exclude the patients with MCS if they did not fit the study aims, the exclusion of patients who had events during follow-up may introduce bias. If the reader uses this work to assess the risk of patients listed for HTx, they cannot know in advance who will improve, deteriorate, or undergo HTx. These patients should instead have been censored alive or counted as part of a composite event (e.g. death or urgent HTx).

The Heart Failure Survival Score (HFSS) was originally derived to aid HTx listing among ambulatory patients referred for HTx evaluation. It includes the best single selection criterion, the peak VO_2 [9], as well as other relevant factors representing different dimensions of HF severity. The model for end-stage liver disease (MELD) was derived to assess the severity of chronic liver disease and excludes international normalised ratio (MELD-XI) for use in patients on anticoagulation. The Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) score (www.heartfailurerisk.org) was derived in multiple general HF cohorts and trials. The areas under the receiver operating characteristic curve (AUCs) for all-cause death at one year, representing the ability to discriminate death vs. non-death at one year, were 0.781 for the HFSS, 0.812 for the MELD-XI, and 0.771 for the MAGGIC score. These AUCs are consistent with or higher than those previously reported in the literature [10–12].

These findings are important because they confirm the utility of these three risk scores in assessing the prognosis in patients considered or listed for HTx, and thus further strengthen the evidence for using risk scores in HTx or durable MCS (generally left ventricular assist devices [LVADs]) selection. However, the authors did not assess other important risk scores such as the Seattle Heart Failure Model (SHFM) [11] or the Metabolic Exercise Test data combined with Cardiac and Kidney Indexes (MECKI) score [13], nor any of the multiple existing and emerging HF biomarkers [14]. There are also two important limitations applying to this work and to the previous literature on HF risk scores: lack of prediction of the cause-specific risk that HTx or LVAD addresses, namely

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HF hospitalisation and death; and lack of prediction of the outcome *after* HTx or LVAD.

The MELD and MELD-XI scores do not consider any cardiac-specific factors, and even HF-specific risk scores have generally been derived using all-cause death outcomes. Thus, they do not distinguish between HF-related events (death, hospitalisation or progressive symptoms), which can be prevented by HTx or LVAD, and other events, which cannot. Therefore, these and other authors with the access to large cohorts should be encouraged to validate the existing risk scores for HF-specific events. Furthermore, these scores predict who is at high risk without HTx or LVAD, and not who does well after HTx or LVAD [5, 15]. In HF with reduced ejection fraction, drug and device therapies improve outcomes and are cost-effective; indications and contraindications are clear, and selection is straightforward. In contrast, selecting patients for HTx or LVAD, which are of limited availability and/or expensive, requires assessment of the prognosis both without intervention (how much the patient needs HTx or LVAD) and with intervention (the risk for complications and poor outcomes). The ideal candidate is not the one with a worse prognosis before or a better prognosis after HTx or LVAD, but the patient who stands to gain the most, i.e. with the greatest difference in the prognosis with vs. without intervention.

The central clinical take-home message from the work of Szczurek et al. [8], taken in the context of other literature on advanced HF and HTx or LVAD selection, is that we can be further reassured that clinical risk scores are useful, and as stated by guidelines and consensus documents [3, 4], they should be used in selecting patients for HTx and LVAD. However, it should also be emphasised that HTx and LVAD selection is complex and difficult and best performed at HF referral centres. Therefore, we need a confirmation not only of HTx and LVAD selection tools, as provided by Szczurek et al. [8], but also of simplified tools and criteria to help general cardiologists and physicians recognise when to refer patients to HF centres before it is too late [3, 16].

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