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EDITORIAL

Predicting Events in Heart Failure Patients: An Ongoing Challenge

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Heart failure (HF) is a worldwide health problem, with an estimated 37.7 million people affected in 2010 [1]. HF carries a heavy burden on both patients and health systems due to high mortality rates and frequent hospitalisations [2,3]. HF is associated with substantial in-hospital and post-discharge mortality, as well as high rates of readmission [4]. In a recent systematic review on HF in Australia [5], 1-year mortality rate was 25% and 1-year readmission rate was 56%. Therefore, identifying a risk model could be a useful tool to target this high-risk population.

In this issue, Wang et al. [6] report a risk scoring system for HF patients by including 6,252 patients from the Management of Cardiac Failure Program (MACARF) in Northern Sydney Area Hospitals between 1998 and 2015 who were randomly divided into two halves for derivation and validation. These patients were part of one of the biggest HF programs. The authors came up with a relatively simple tool to predict 1-year two or more all-cause readmissions and/or 1-year all-cause mortality (primary outcome). The mean age of the patients was 80 years, and more than half were males. Ischaemic heart disease and hypertension were reported in 60% of the patients. Despite the reported age in Europe and USA being slightly younger [7,8], this is similar to the NSW HF snapshot study. Around one-third of the patients in this MACARF cohort had HF with preserved ejection fraction (HFpEF), which is again close to the 42% reported in the NSW HF snapshot study [9]. Thus, in terms of demographics and co-morbidities, these patients were representative of Australian HF patients. Ischaemic heart disease, chronic kidney disease, being unmarried, prolonged hospitalisation (>7 days), anaemia, hypoalbuminaemia, creatinine >100 μmol/L and lack of β-blocker therapy were predictors of primary outcomes. The odds ratios were similar between the predictors; therefore, 1 point was given for each predictor for a maximum score of 8. The authors validated the risk score and the C-statistic value was only 0.65, which means a modest prediction. Interestingly, the rate of primary outcome increased with an increasing number of predictors and where the risk score was 4 or more, the rate of the primary outcome was similar for derivation and validation. However, when the score was 7 or 8, the tool was less predictive [6]. Surprisingly, age was not included in the prediction model, and we know from other studies that HF increases with age and age is an important independent predictor of HF outcomes [10]. In addition, HF carries a significant burden in the Indigenous population which is also not reported in this study [11]. Iron deficiency is common in HF patients and has a known association with worse prognosis and it is recommended to be treated with iron infusion depending on ferritin level, even if the patient is not anaemic [12]. On the other hand, anaemia is also common in hospitalised HF patients and is more common in females, the elderly and those with renal impairment. Anaemia is associated with more advanced HF and with poor outcome [12]; however, while anaemia was one of the predictive parameters, the cause of anaemia was not reported.

It is worth mentioning that, during the study period, significant changes in medical and device management of HF have occurred. For example, β-blocker and aldosterone receptor antagonist studies were published between 1999–2005 and subsequently became part of the guidelines. Moreover, studies of device management in HF with implantable defibrillators and cardiac resynchronisation were published during a similar period [13,14] and, once again, have changed our best practice. All these may have introduced significant heterogeneity into the collected data and may

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explain some of the differences between this and other published cohorts.

In terms of guideline-directed medical treatment, Wang et al. report that 53% of the patients were on β-blockers, 72% were on angiotensin converting enzyme inhibitors or angiotensin II receptors blockers and 34% were on aldosterone receptor antagonists [6]. HFpEF patients accounted for 42% of this cohort and we know that, in this type of HF, there is no guideline-directed medical therapy apart from treating fluid congestion. Therefore, not being on a β-blocker in this cohort might also be a reflection of this cohort's composition and be one of the factors that affected the predictability of the model. In addition, as mentioned above, β-blockers were still not used for HF management during the first few years of the study. The 1-year mortality in this cohort was 17%, which is slightly less than reported in the systematic review (1-year mortality 25%, 95% confidence interval 22–29%) [5]. However, the rate of readmission was similar.

In Australia, several studies reported risk factors of HF mortality and readmission. Robertson et al. reported major risk factors for all-cause readmission which were increasing age, increasing Charlson score, and male gender [15]. In addition, Teng et al. reported age, gender, length of stay, Charlson co-morbidity index, renal failure, hypertension, peripheral vascular disease and cerebrovascular disease were predictors of 5-year mortality [16]. We published HF outcomes after index HF hospitalisation and reported that age, socio-economic disadvantage, ischaemic heart disease, renal failure and chronic lower respiratory disease were predictors of the 1-year all-cause mortality and/or readmission [17]. Interestingly, diabetes is known to be associated with worse outcomes and none of the above studies showed diabetes to be a predictor of hospitalisation or mortality [12]. However, we need to interpret this with caution because all of the above studies are observational studies. We also need to be mindful that the patients within this study were enrolled in a multi-disciplinary HF service which we know has a significant impact on HF mortality and readmission [18].

Many multivariable risk scores are available to predict HF death/hospitalisation. Of the scores recommended by American Heart Association/American College of Cardiology Foundation (AHA/ACCF) HF guidelines are the Seattle Heart Failure model [19] for ambulatory patients and the Acute Decompensated Heart Failure National Registry (ADHERE) score for hospitalised patients [20]. However, HF prediction models usually have moderate prediction of mortality and poor prediction of readmission [21,22]. In addition, Heart Failure Survival Score, American Heart Association Get With The Guidelines Score, Enhanced Feedback for Effective Cardiac Treatment (EFFECT) Risk Score are other tools that are available online. In the Seattle model, New York Heart Association (NYHA) class, ischaemic aetiology, diuretic dose, ejection fraction, systolic blood pressure, sodium, haemoglobin, percentage of lymphocytes, uric acid, and cholesterol showed independent predictive power. The model was validated in five prospective cohorts and showed great accuracy in prediction of 1-year, 2-year and 3-year survival [19]. The ADHERE model predicted in-hospital mortality and found systolic blood pressure, urea and creatinine values were independent predictors [20]. The development of a model using demographic features, biomarkers and response to treatment is suggested [21]. Age, sex, renal and cardiovascular diseases were independent predictors of rehospitalisation [22]. Indeed, HF hospitalisation by itself is an important risk factor for rehospitalisation [10]. There are many risk factors that can lead to these two outcomes and several risk assessment tools were used. Because co-morbidities are common in HF patients and can affect treatment, prognosis and outcomes, the predictors for mortality are more accurate than the predictors for readmission [10,23]. In addition, readmission for HF can be for multiple reasons not necessarily clinical; individual patient factors like health literacy [24] or limited access to HF specialists [25] can impact on readmission rates. In this study, individual patient factors were not reviewed, and all patients had access to HF specialists who may have different thresholds for readmitting patients when compared to other centres, especially those in rural/remote areas.

In summary, HF is a heterogeneous syndrome and that is likely to be one reason for modest correlation of different prediction tools. Increasing age, unplanned HF hospitalisation and presence of comorbidities, especially ischaemic heart disease and renal impairment, are usually good predictors of poor outcomes in HF patients. Management of HF has changed dramatically over the past 20 years with new medical and device management strategies, including those for comorbidities, showing improvements in morbidity, mortality and readmissions for patients with HF. Emergence and greater prevalence of new subtypes of HF, such as HFpEF, cardiomyopathy secondary to cancer therapies, or use of illicit drugs further alters the HF landscape in Australia and around the world. Thus, with an ever-changing field, we need to continue to test and re-test our predictive tools in contemporary cohorts, ideally in a prospective manner, to develop the best possible diagnostic and prognostic algorithms and hence improve outcomes for our HF patients.

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