# Prognostic risk scores for patients with heart failure


## Abstract

Heart failure has many causes. Although new drugs, devices and technologies are available, the survival rate and prognosis of patients with heart failure remain poor, placing a significant burden on individuals and society. Attempts to improve outcomes for patients with heart failure include developing prognostic risk scores. With medical advances, however, previous heart failure risk scores are not fully applicable to current practice, particularly because of the classification as heart failure with reduced ejection fraction, heart failure with mildly reduced ejection fraction, and heart failure with preserved ejection fraction. This article describes the use of risk prediction scores for heart failure patients with different clinical status and discusses their clinical applicability.



Key words: Heart failure; Prediction; Prognosis; Risk score

Submitted: 9 November 2021; accepted following double-blind peer review: 17 January 2022



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## Introduction

From 2012 to 2030, the prevalence of heart failure is predicted to increase by 46% (Virani et al, 2020). Although therapeutic progress is remarkable, heart failure remains a serious public health issue with high morbidity and economic burden. It is the common final stage for many cardiac diseases, usually with adverse outcomes. In the past decade, the overall risk-adjusted 30-day readmission rate has been above 20% and mortality greater than 6% (Ko et al, 2020), so reducing readmission rates and mortality for patients with heart failure is a global priority.

It is important to identify high-risk patients to allow early prediction of adverse events and future outcomes. This can help to optimise drug treatment programmes, help in the selection of patients for heart transplantation and assist in formulating more targeted follow up.

Researchers have established numerous heart failure risk scores to estimate a patient's prognosis. However, many of these are not fully applicable to current clinical practice, especially because heart failure has been classified into heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmrEF), and heart failure with preserved ejection fraction (HFpEF) (McDonagh et al, 2021). This article reviews heart failure risk scores and their use and value in clinical settings.

## Literature search

PubMed and ScienceDirect databases were searched for full texts published in English using the keywords 'heart failure' and 'risk score', focusing on research studies referring to HFrEF, HFmrEF and/or HFpEF. If articles did not explicitly mention the heart failure classification by ejection fraction, then heart failure was stratified by the authors based on the specific content description. All eligible articles reported the prognosis of heart failure and described the methodology for quantifiable risk scores. Studies dealing only with risk factors and risk models were excluded. The literature search and selection process are shown in Figure 1.

To facilitate clinical selection, the authors grouped heart failure risk scores based on the specific status of patients with heart failure:

1. Heart failure in the emergency department
2. Outpatients (defined as ambulatory, community and discharged patients)
3. Inpatients
4. Others.


How to cite this article:
Zhao H-L, Cui W. Prognostic risk scores for patients with heart failure. Br J Hosp Med. 2022. https://doi.org/10.12968/hmed.2021.0594

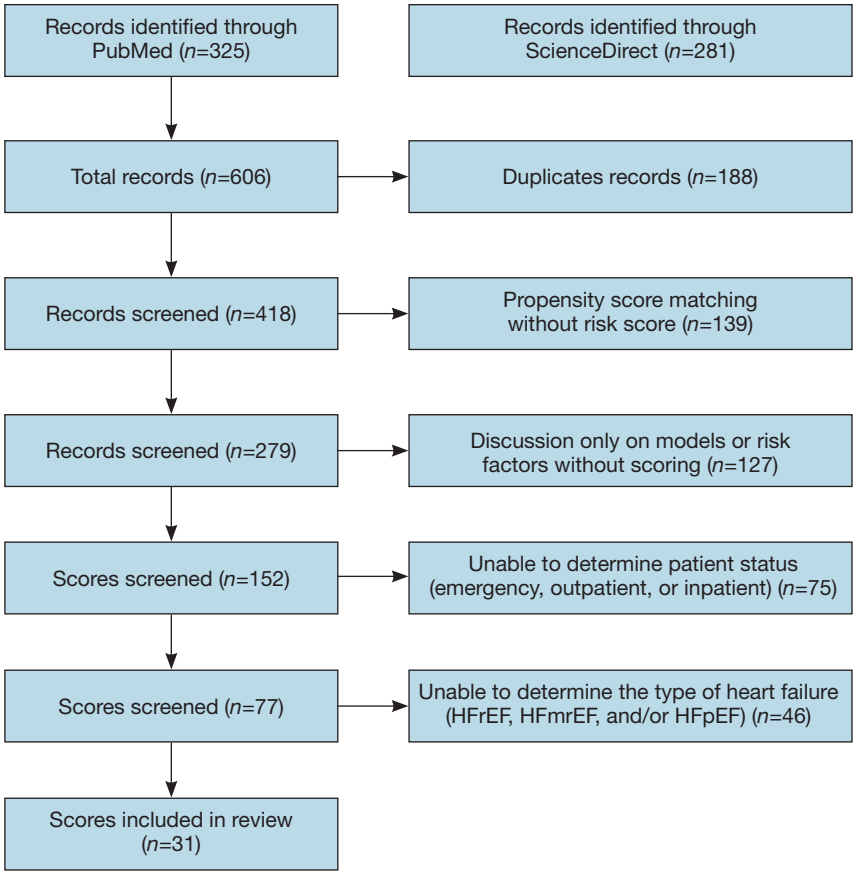


**Figure 1.** Flow chart describing the literature search and selection process.
HFmrEF= heart failure with mildly reduced ejection fraction; HFpEF= heart failure with preserved ejection fraction; HFrEF= heart failure with reduced ejection fraction.

The period of risk assessment was defined as short-term (≤30 days), mid-term (between 30 days and 1 year) or long-term (≥1 year).

A total of 77 scores were retrieved and more than half were excluded for lacking valid data to distinguish between HFrEF, HFmrEF or HFpEF, leaving 31 scores to be evaluated (Figure 1). Measures of score discrimination included hazard ratio, the area under the curve from the receiver-operating characteristic (AUC) and C-statistic.

## Risk scores for patients with heart failure presenting to the emergency department

In general, patients with heart failure presenting to the emergency department are critically ill, with acute heart failure, acute decompensated heart failure or even cardiogenic shock. Accordingly, heart failure risk scores for this group cover this range of critical clinical conditions (Appendix 1).

The Acute Decompensated Heart Failure National Registry (ADHERE) score is the first and most important score for patients with acute decompensated heart failure in this context, although it does not meet the inclusion criteria for the current article. Fonarow et al (2005) believed that in-hospital mortality risk levels in patients with acute decompensated heart failure could be easily identified using clinical and laboratory variables obtained at admission. The Larissa Heart Failure Risk Score (LHFRS) was initially developed to stratify risk for patients admitted with acute heart failure (Xanthopoulos et al, 2017). Kitai et al (2020) performed an external validation of the LHFRS for emergency department patients with HFrEF, HFmrEF and HFpEF and demonstrated that a higher LHFRS (≥2) is strongly related to a higher risk of 1-year all-cause mortality and readmission as a result of heart failure. However, all variables were collected during hospitalisation and confounding factors at admission and after discharge, which could affect the outcome, were not included.

Heart failure risk scores for use in the emergency department should be as brief, quick and efficient as possible. Containing only three variables (hypertension, myocardial infarction and red cell distribution width), the LHFRS accurately predict risk for patients with acute or chronic heart failure (Xanthopoulos et al, 2018; Kitai et al, 2020).

There are other heart failure risk scores for use with patients in the emergency department, such as the Ottawa HF Risk Scale (Stiell et al, 2013) and the Acute Heart Failure Risk Score (AHFRS) (Garcia-Gutierrez et al, 2017). However, these made no distinction between HFrEF, HFmrEF and HFpEF, possibly because patients were critically ill and the priority was to treat them rather than distinguish between types of heart failure. These issues require attention in future research.

## Risk scores for outpatients with heart failure

For relatively stable outpatients, the main challenge is to prevent hospitalisation and reduce mortality. Heart failure risk scores can effectively predict risk, guide treatment and improve prognosis at different stages. **Appendix 2** presents the heart failure risk scores for outpatients, including ambulatory, community and discharged patients.

### Short-term prognostic risk score

The HOSPITAL (Haemoglobin level at discharge, Oncology at discharge, Sodium level at discharge, Procedure during hospitalisation, Index admission, number of hospital admissions, Length of stay) score, the LACE (length of stay in hospital, acuity of admission, comorbidity and emergency department utilisation within the 6 months before admission) index and the LACE+ index are all validated tools for predicting readmission in a multidisciplinary population (van Walraven et al, 2010; 2012; Donzé et al, 2013). Ibrahim et al (2020) tried to use these scores to predict 30-day readmission for outpatients with HFpEF, but the results were not satisfactory.

### Long-term prognostic risk score

Jones et al (2004) used data from the Digitalis Investigation Group (DIG) trial to create a risk score for patients with HFpEF to determine predictors of mortality. They found that ageing, male sex, renal insufficiency and poor exercise ability were associated with a high mortality rate. The DIG trial data set was well-validated, but the definition of HFpEF used was different from the current definition and some key information was not collected. The Redin-SCORE used routinely collected, proven variables to predict early and late readmission of outpatients with chronic deterioration of HFpEF and HFrEF (Álvarez-García et al, 2015). However, the score did not collect information on comorbidities or psychosocial factors, and the capacity for early prediction was low.

The HF-ACTION risk score is based on stable outpatients with chronic HFrEF, the mortality discrimination of which was modest (C-statistic=0.63). This score can help clinicians better understand the importance of enhanced surveillance to monitor high-risk patients (O'Connor et al, 2012). Collier et al (2013) created a simple risk score derived from the EMPHASIS-HF (the Eplerenone in Mild Patients Hospitalisation and Survival Study in Heart Failure) trial. They believed that the EMPHASIS-HF score had a powerful ability to discriminate low- and high-risk patients with HFrEF and mild symptoms, but categorising continuous variables and converting model coefficients into integer points caused a loss of predictive accuracy.

Using widely available clinical variables, Peterson et al (2010) derived and validated the GWTG-HF (American Heart Association Get with the Guidelines–Heart Failure) risk score for predicting in-hospital mortality. The GWTG-HF risk score was also used to evaluate the prognosis after discharge. Suzuki et al (2018) confirmed that the GWTG-HF risk score was a useful predictor of prognosis for patients with chronic HFrEF or HFpEF following hospitalisation in a Japanese population. The $H_2$FPEF score (obesity, two or more hypertensive drugs, atrial fibrillation, pulmonary hypertension, older age >60 years, elevated filling pressure) is used to assess the probability of a diagnosis of HFpEF in clinical settings (Reddy et al, 2018). Segar et al (2019) found that a high $H_2$FPEF score may identify a higher risk of adverse clinical events in patients with HFpEF.

The MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) risk score was constructed as an online calculator to predict 1- and 3-year mortality in patients with heart failure (Pocock et al, 2013). Sartipy et al (2014) evaluated the MAGGIC risk score in a Swedish registry large-scale study including patients with HFrEF, HFmrEF and HFpEF. The score showed good discrimination (C-statistic=0.741) for the prediction of 3-year death in patients with heart failure with different risk strata. Rich et al (2018) validated the MAGGIC score in predicting the morbidity and mortality of patients with HFpEF in a prospective registry.

The Heart Failure Survival Score (HFSS) is the first decision-making model to predict survival in outpatients with end-stage congestive heart failure, and could be used to allocate scarce donor hearts more effectively for patients with HFrEF (Aaronson et al, 1997). Agostoni et al (2013) built the MECKI (Metabolic Exercise Cardiac Kidney Indexes) score for patients with HFrEF, which could identify the long-term risk of cardiovascular death for patients with ambulatory heart failure. However, Agostoni et al (2013) highlighted that the selection of population and variables and the therapy upgrading might impact the results. The Seattle Heart Failure Score (SHFS) is one of the best known multivariate risk models for estimating the survival of patients with HFrEF, which has been used worldwide (Levy et al, 2006). Using readily obtained clinical, pharmacological, device and laboratory characteristics, it provided an accurate estimate of 1-, 2- and 3-year survival rates for clinic and community patients. However, the SHFS was based on earlier studies that omitted some important variables such as whether or not a patient was taking an angiotensin-converting enzyme inhibitor, level of B-type natriuretic peptide and presence or not of an implantable cardioverter defibrillator. Agostoni et al (2018) compared these in 6112 patients, and showed that the prognostic accuracy of the MECKI score was superior to that of HFSS and SHFS in stable patients with HFrEF at 2- and 4-year follow up, but prospective evaluation is still needed.

In the absence of invasive measures, these scores are usually derived from routine information and auxiliary examination results. Some scores have not been externally validated in independent cohorts (Jones et al, 2004) and some were modified from scoring systems for other diseases (Kim et al, 2013). For outpatients with heart failure, heart failure risk scores should be simple, accurate and convenient to use. Further studies are needed to support these scores as generalisable clinical prediction tools, especially for heart failure patients with different ejection fractions.

## Risk scores for inpatients with heart failure

Since variables used in heart failure risk scores can be collected comprehensively during hospitalisation, there are more risk scores based on inpatient rather than emergency department patient or outpatient data (**Appendix 3**).

### Short-term prognostic risk score

The GWTG-HF risk score is widely applied to patients with heart failure, including those with HFpEF, but has not been validated in an external population (Peterson et al, 2010). By combining levels of N-terminal pro-brain natriuretic peptide (NT-proBNP) with other clinical factors, Huang et al (2016) created a novel NT-proBNP-based score that accurately predicted in-hospital mortality in patients with HFrEF or HFpEF. Compared to SHFS (Levy et al, 2006), the MAGGIC score incorporating B-type natriuretic peptide showed better predictive accuracy for hospitalisation outcomes (Allen et al, 2017). The OPTIMIZE-HF (Organized Programme to Initiate Lifesaving Treatment in Hospitalised Patients with Heart Failure) clinical model reliably identified high risk of mortality in patients with heart failure (Abraham et al, 2008). However, because there are fewer events in these patients, the modified OPTIMIZE-HF risk score may underestimate the extreme (lowest and highest) risk for inpatients with HFrEF, HFmrEF or HFpEF (Yap et al, 2019a).

### Mid-term prognostic risk score

Some studies have discussed the mid-term prognostic value of heart failure risk scores. The OPTIME-CHF (Outcomes of a Prospective Trial of Intravenous Milrinone for Exacerbations of Chronic Heart Failure) score is designed to predict the prognosis for patients with

decompensated HFrEF. Using easily evaluated clinical variables, the OPTIME-CHF score can assess the risk of 60-day death in inpatients with decompensated heart failure, although it needs prospective external validation before it can be used in clinical practice (Felker et al, 2004). The APACHE-HF (Acute Physiology and Chronic Health Evaluation) scoring system makes it possible to estimate the adverse outcomes of acute HFmrEF and HFrEF. The score showed significantly higher sensitivity and specificity than the APACHE II score and could predict adverse mid-term results for patients with acute heart failure (Okazaki et al, 2014). However, only patients admitted to intensive care units were assessed by this system. New scoring systems are needed to evaluate a wider range of factors.

### Long-term prognostic risk score

Based on routine clinical information, the 3C-HF (Cardiac and Comorbid Conditions HF) score is a simple and valuable tool to evaluate all-cause 1-year mortality in patients with HFrEF or HFpEF (Senni et al, 2013). The Singapore Heart Failure Risk Score is a calculator used to predict 1- and 2-year mortality from HFrEF, HFmrEF or HFpEF in south-east Asian inpatients (Yap et al, 2019b). However, neither of these distinguish between acute and chronic heart failure and were not validated in other cohorts.

### Mixed-term prognostic risk score

Some risk scores explored the prognostic stratification of heart failure among inpatients at different stages. Using multi-parametric variables, the ACUTE HF score assessed the prognosis of coronary care unit patients with acute HFrEF for 30-day, 6-month and 5-year all-cause death, and the duration of hospitalisation was analysed using the univariate model. While data gaps limited the analysis, the predictive capacity of the score was outstanding (Cameli et al, 2019). Researchers updated the ADHF/NT-proBNP score, in which study 5.2% of HFrEF patients received a ventricular assist device implant or urgent heart transplantation, and this risk score could predict in-hospital and 90-day post-discharge mortality for severe acute decompensated heart failure (Scrutinio et al, 2015).

Several studies on heart failure risk scores included both inpatients and outpatients, such as the ST2-R2 score. This was first applied to predict reverse remodelling in patients heart failure (Lupón et al, 2015). Using the biomarker interleukin-1 receptor-like 1 (ST2) and five clinical parameters, the score could effectively predict reverse left ventricle remodelling and mortality up to 4 years in patients with heart failure. However, three different cohorts were included in this study (Lupón et al, 2016), making the data heterogeneous.

Compared to emergency department patients and outpatients with heart failure, heart failure risk scores for inpatients can serve as a bridge to guide treatment of patients admitted to the emergency department and to evaluate their prognosis after discharge.

## Other risk scores for patients with heart failure

In addition to the above heart failure risk scores, other heart failure risk scores are used for clinical and research purposes (**Appendix 4**).

The genetic risk score (GRS) is a special scoring system, based on genomic information from eight single nucleotide polymorphisms, that was used to assess the prognosis of chronic heart failure in a Chinese population. Li et al (2020) demonstrated that GRS is strongly associated with the prognosis of heart failure (heart transplantation, cardiovascular death, heart failure readmission, discharge composites, or all-cause mortality), which might help to stratify the risk of heart transplantation or cardiovascular death for the individual prognosis of HFrEF and HFpEF as a supplement to conventional risks. However, the results should be verified in other populations.

Yamauchi et al (2017) investigated 5382 patients from the CHART-2 (Chronic Heart Failure Analysis and Registry in the Tohoku District-2) study. They developed the New-Onset AF score to estimate the risk of onset of atrial fibrillation in patients with heart failure. Also derived from the CHART-2 study, the 3A3B score was designed to predict all-cause mortality in patients with HFpEF. Comprising six commonly available factors, this simple score has a high discriminatory capacity to manage and predict the long-term prognosis of patients with HFpEF (Kasahara et al, 2019).

Both the $CHADS_2$ score and $CHA_2DS_2$-VASc score are globally recognised for predicting the risk of ischaemic stroke in patients with non-valvular atrial fibrillation. Studies have tried to use them to assess the prognosis of patients with heart failure. Kondo et al (2017) found that the $CHADS_2$ score could predict the risk of ischaemic stroke in patients with chronic HFrEF without atrial fibrillation, although their study was limited by heterogeneity of anticoagulant therapy and sample size. Based on a large registered population, Melgaard et al (2015) found a correlation between the $CHA_2DS_2$-VASc score and ischaemic stroke risk, thromboembolism and mortality in heart failure patients with or without atrial fibrillation, but the score had poor predictive power for these events. Likewise, Ye et al (2016) did not get a good prediction accuracy with the $CHA_2DS_2$-VASc score. The clinical application of these scores remains unclear.

## Discussion

Heart failure risk scores help to inform clinical management and prognosis. Various prognostic risk scores have been created for patients with heart failure, but so far none is better than the others. Few of the scores are universally accepted and clinically applicable. No score captures all critical information for patients with heart failure, and there is an inherent contradiction between simplicity and accuracy. Using comprehensive scores can be cumbersome while using simple scores may miss important information and affect the predictive ability.

How should doctors choose which risk score to use clinically? Considering the specific condition of the patient and the category of heart failure (acute or chronic heart failure, and having HFrEF, HFmrEF or HFpEF) allows selection of the appropriate heart failure risk score for the patient (Table 1).

Since heart failure is a dynamic syndrome, it is not possible to use only one or two scores to predict the outcomes of all patients with heart failure. Heart failure risk scores should be carefully selected, matching the patient's characteristics with those used by the risk score. Fewer heart failure risk scores correlate with the new classification of heart failure (HFrEF, HFmrEF or HFpEF), especially HFmrEF. New risk predictors should be included in new heart failure risk scores, such as novel biomarkers (adiponectin and mi-RNA) (Pourafkari et al, 2019) and new therapeutic agents (sacubitril-valsartan and sodium-glucose cotransporter 2 inhibitors) (Sauer et al, 2019; Zelniker and Braunwald, 2020). Future heart failure risk score studies should be simpler, more practical and more accurate, with additional clinical validation.

## Conclusions

The prognostic risk scores of heart failure are useful tools for clinicians, which can refine management strategies for patients with heart failure and even improve the outcomes. Application of different scores should be based on the different clinical status of patients (patients in the emergency department, outpatients, inpatients, or others). The previously established risk scores need to be further improved, while new individualised risk scores need to be developed in the future.

**Table 1. Choosing which heart failure risk score to use**

| Patient status | Type of heart failure* | Recommended heart failure risk score |
|---|---|---|
| Emergency department | Acute heart failure | Larissa Heart Failure Risk Score (LHFRS) (Xanthopoulos et al, 2017) |
| Outpatient | Chronic heart failure | Meta-Analysis Global Group in Chronic Heart Failure (MAGGIC) (Sartipy et al, 2014) |
| Inpatient | Acute heart failure or chronic heart failure | Get With the Guidelines-Heart Failure (GWTG-HF) (Peterson et al, 2010) |
| Other | No single score can be recommended, further study is needed for these patients | |

**This includes patients with heart failure with reduced ejection fraction, heart failure with mildly reduced ejection fraction or heart failure with preserved ejection fraction*

## Key points

- Heart failure risk scores can be grouped based on the specific status of patients that they are for use in (emergency department, outpatients, inpatients, and others).
- The applicability of risk scores needs to be expanded to include heart failure with reduced ejection fraction, heart failure with mildly reduced ejection fraction and heart failure with preserved ejection fraction.
- It is important to select the appropriate risk score for use in each area of clinical practice.

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**Conflicts of interest**

The authors declare that they have no conflicts of interest.

**Funding**

This work was supported by the S&T Program of Hebei, China (grant number 16277738D).

**Acknowledgements**

The authors would like to thank Na Jin, MD, for English language editing, the authors of the original studies selected in this work, and the peer reviewers for their suggestions.

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**Appendix 1. Risk scores for patients with heart failure presenting to the emergency department**

| Risk score (reference) | Heart failure criteria | Data source | Setting | Study type | Derivation size (*n*) | Validation size (*n*) | Score variables | Model development | Primary endpoint | Discrimination |
|---|---|---|---|---|---|---|---|---|---|---|
| LHFRS (Kitai et al, 2020) | Acute heart failure, HFrEF, HFmrEF, and HFpEF | Registry | Multicentre, multinational | Retrospective | Not involved | 694 | Hypertension, myocardial infarction and red cell distribution width | Cox proportional hazards model | 1-year all-cause mortality and/or heart failure readmission | Hazard ratio=1.27 |
| AHFRS (Garcia-Gutierrez et al, 2017) | Acute heart failure, without distinction of HFrEF, HFmrEF and HFpEF | Clinical trial | Multicentre, Spain | Prospective | 912 | 912 | Comorbidities, glycaemia, blood urea nitrogen, potassium, pH, troponin, N-terminal prohormone B-type natriuretic peptide, pulmonary oedema, respiratory rate, visits to emergency department and/or admission during the past 2 years | Logistic regression model | In-hospital mortality for hospitalised patients and 7-day mortality after emergency department discharge; admission to an intensive care unit or mechanical ventilation needed during time in emergency department | Area under the curve from the receiver-operating characteristic =0.84 |

*HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; HFrEF = heart failure with reduced ejection fraction.*

**Appendix 2. Risk scores for outpatients with heart failure**

| Risk score (reference) | Heart failure criteria | Data source | Setting | Study type | Derivation size (n) | Valid-ation size (n) | Score variables | Model development | Primary endpoint | Discrimination |
|---|---|---|---|---|---|---|---|---|---|---|
| HOSPITAL (Ibrahim et al, 2020) | HFpEF | Clinical trial | Single centre, USA | Retrospective | Not involved | 692 | Haemoglobin and sodium at discharge, discharge from an oncology service, procedure during the index admission, index type of admission, number of admissions during the last year, and hospital duration | Logistic regression model | 30-day all-cause readmission | C-statistic =0.595 |
| LACE index and LACE+ (Ibrahim et al, 2020) | HFpEF | Clinical trial | Single centre, USA | Retrospective | Not involved | 692 | LACE: hospital duration, acuity of the admission, comorbidity, emergency department use; LACE+: LACE, age, sex, teaching status of the discharge hospital, acute diagnoses and procedures performed during the index admission, number of days on alternative level of care during the index admission, and number of elective and urgent admissions to hospital in the year before the index admission | Logistic regression model | 30-day all-cause readmission | C-statistic =0.551 (LACE index) and 0.568 (LACE+ index), respectively |
| DIG score (Jones et al, 2004) | HFpEF | Registry | Multicentre, USA | Randomised controlled trial | 988 | No | Cardiothoracic ratio, estimated glomerular filtration rate, NYHA class, diuretics, age, gender, vasodilators, diabetes mellitus, body mass index | Cox regression model | 3.1-year mortality | Not reported |

| Appendix 2. Risk scores for outpatients with heart failure (continued) | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| Redin-SCORE (Álvarez-García et al, 2015) | HFrEF and HFpEF | Registry | Multicentre, Spain | Prospective | 2507 | 992 | Left ventricular heart failure signs, heart rate, BNP/NT-proBNP, estimated glomerular filtration rate, left atrial size | Logistic regression model | 1-month and 1-year readmission | C-statistic=0.72 and 0.66 respectively |
| HF-ACTION (O'Connor et al, 2012) | Chronic heart failure, HFrEF | Registry | Multicentre, Multination | Randomised controlled trial | 2331 | No | Sex, cardiopulmonary exercise test, body mass index, blood urea nitrogen | Cox proportional hazard model | 2.5-year all-cause mortality or all-cause admission | C-statistic=0.63 |
| EMPHASIS-HF (Collier et al, 2013) | Chronic heart failure, HFrEF | Registry | Multicentre, multinational | Randomised controlled trial | 2737 | 342 | Age, sex, body mass index, heart rate, systolic blood pressure, estimated glomerular filtration rate, haemoglobin, diabetes mellitus, prior admission for heart failure, and prior myocardial infarction/ coronary artery bypass grafting | Cox proportional hazard model | 2.1-year cardio-vascular mortality or admission for heart failure | C-statistic= 0.685 |
| HFSS (Aaronson et al, 1997) | Chronic congestive heart failure, HFrEF | Clinical trial | Multicentre, USA | Prospective | 268 | 199 | Ischaemic cardiomyopathy, LVEF, heart rate, mean arterial blood pressure, peak $VO_2$, intraventricular conduction defects, and serum sodium | Cox proportional hazards model | 1-year death without transplant | C-statistic=0.74 |
| MECKI (Agostoni et al, 2013) | HFrEF | Registry | Multicentre, Italy | Prospective | 2716 | No | Haemoglobin, sodium, kidney function by the modification of diet in renal disease equation, LVEF, $ppVO_2$ and $VE/VCO_2$ slope | Cox proportional hazard regression model | 1-, 2-, 3- and 4-year cardio-vascular death | AUC=0.804, 0.789, 0.762 and 0.760 respectively |

**Appendix 2. Risk scores for outpatients with heart failure (continued)**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| GWTG-HF (Suzuki et al, 2018) | Chronic heart failure, HFrEF and HFpEF | Clinical trial | Single centre, Japan | Prospective | 1452 | No | Age, systolic blood pressure, blood urea nitrogen, heart rate, sodium, chronic obstructive pulmonary disease, and race | Cox proportional hazard regression model | 965.8-day all-cause mortality and cardiac events | Hazard ratio=1.537 and 1.584 respectively |
| $H_2$FPEF (Segar et al, 2019) | HFpEF | Registry | Single centre, USA | Retrospective | Not involved | 360 | Body mass index, antihypertensive medications, atrial fibrillation, pulmonary artery systolic pressure, age, and doppler echocardiography E/e' | Cox model | 3.1-year cardio-vascular death, aborted cardiac arrest, or heart failure admission | Hazard ratio=1.18 |
| MAGGIC (Sartipy et al, 2014) | Chronic heart failure, HFrEF, HFmrEF, and HFpEF | Registry | Multicentre, Swedish | Not reported | Not involved | 51 043 | Age, sex, NYHA, serum creatinine, diabetes mellitus, β-blocker, LVEF, systolic blood pressure, smoke, body mass index, heart failure duration, chronic obstructive pulmonary disease, and ACEI/ARB | Cox model | 3-year mortality | C-statistic= 0.741 |
| SHFS (Levy et al, 2006) | HFrEF | Registry | Multicentre, USA | Retrospective | 1125 | 9942 | Age, diuretic, aetiology, gender, systolic blood pressure, haemoglobin, sodium, lymphocytes (%), LVEF, uric acid, cholesterol, allopurinol, statin | Cox proportional hazards model | 1-, 2-, and 3-year survival | AUC=0.729 |

*ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin-2 receptor blocker; AUC = area under the curve from the receiver-operating characteristic; BNP = B-type natriuretic peptide; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; $ppVO_2$ = percentage of predicted peak oxygen consumption; $VE/VCO_2$ = minute ventilation-carbon dioxide production*

**Appendix 3. Risk scores for inpatients with heart failure**

| Risk score (reference) | Heart failure criteria | Data source | Setting | Study type | Derivation cohort (*n*) | Validation cohort (*n*) | Score variables | Model development | Primary endpoint | Discrimination |
|---|---|---|---|---|---|---|---|---|---|---|
| GWTG-HF (Peterson et al, 2010) | HFrEF, HFmrEF and HFpEF | Registry | Multicentre, USA | Not reported | 27 850 | 11 933 | Age, race, heart rate, systolic blood pressure, blood urea nitrogen, sodium and chronic obstructive pulmonary disease | Logistic regression model | In-hospital mortality | C-statistic= 0.75 |
| NT-pro-BNP-based score (Huang et al, 2016) | HFrEF and HFpEF | Clinical trial | Taiwan, China | Retrospective | 269 | No | NT-pro-BNP, age, cardiopulmonary resuscitation, ACEI/ARB, beta blocker, loop diuretics, mechanical ventilator, non-invasive ventilator, vasopressors, and experience of cardiopulmonary resuscitation | Logistic regression model | In-hospital mortality | AUC=0.96 |
| Modified OPTIMIZE-HF (Yap et al, 2019a) | HFpEF | Registry | Multicentre, Singapore | Prospective | 15 219 | No | Age, heart rate, systolic blood pressure, sodium, serum creatinine, primary cause of admission (heart failure vs others), LVEF, and coefficients | Logistic regression model | In-hospital mortality | C-statistic= 0.741 |
| OPTIME-CHF (Felker et al, 2004) | HFrEF | Registry | Multicentre, USA | Randomised clinical trial | 949 | Bootstrap (200 samples) | Age, sodium, NYHA class, systolic blood pressure, blood urea nitrogen | Cox proportional hazards model | 60-day mortality | C-statistic= 0.77 |
| 3C-HF (Senni et al, 2013) | HFrEF and HFpEF | Registry | Multicentre, multi-national | Prospective | 2016 | 4258 | Age, NYHA class, LVEF, RASI, valve heart disease, atrial fibrillation, beta blocker, chronic kidney disease, diabetes mellitus with target organ damage, anaemia, hypertension | Logistic regression model | 1-year all-cause mortality | C-statistic= 0.87 |

**Appendix 3. Risk scores for inpatients with heart failure (continued)**

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| APACHE-HF (Okazaki et al, 2014) | HFrEF and HFmrEF | Clinical trial | Single centre, Japan | Not reported | 824 | No | Age, haematocrit, mean arterial pressure, pulse, potassium, sodium, serum creatinine and Glasgow Coma Scale | Cox regression model | 90-day mortality and heart failure events | AUC=0.779 |
| SHFRS (Yap et al, 2019b) | HFrEF, HFmrEF and HFpEF | Registry | Multicentre, Singapore | Prospective | 1392 | 729/804 (cohort 1/ cohort 2) | Age, myocardial infarction, stroke, atrial fibrillation, peripheral vascular disease, systolic blood pressure, QRS duration, LVEF, serum creatinine, and sodium | Cox multiple regression model | 1- and 2-year all-cause mortality | AUC=0.731 and 0.726 respectively |
| ACUTE HF (Cameli et al, 2019) | Acute heart failure, HFrEF | Clinical trial | Single centre, Italy | Retrospective | 771 | No | Age, serum creatinine, non-invasive ventilation, transient ischaemic attack or stroke, LVEF, prior hospitalisation for acute heart failure, mitral valve dysfunction | Generalized linear mode | 30-day, 6-month and 5-year all-cause mortality | AUC=0.78, 0.79 and 0.76 respectively |
| Updated acute decompensated heart failure/ NT-proBNP score (Scrutinio et al, 2015) | Acute decompen-sated heart failure, HFrEF | Registry | Multicentre, Italy | Not reported | 701 | No | Age, sodium, haemoglobin, chronic obstructive pulmonary disease, estimated glomerular filtration rate, NT-proBNP, LVEF, systolic blood pressure, tricuspid regurgitation, prior admission for heart failure | Logistic regression model | In-hospital and 90-day mortality | C-statistic =0.851 and 0.810 respectively |
| ST2-R2 (Lupón et al, 2016) | HFrEF | Registry | Multicentre, multi-national | Prospective | Not involved | 569 | Soluble ST2, ischaemic aetiology, left bundle–branch block, heart failure duration, LVEF and beta blocker | Cox regression model | 4-year mortality | Hazard ratio=0.87 |

*ACEI = angiotensin-converting enzyme inhibitors; ARB = angiotensin receptor blocker; AUC = area under the curve from the receiver-operating characteristic; HFrEF = heart failure with reduced ejection fraction; HFmrEF = heart failure with mildly reduced ejection fraction; HFpEF = heart failure with preserved ejection fraction; LVEF = left ventricular ejection fraction; NT-proBNP = N-terminal pro-B-type natriuretic peptide; NYHA = New York Heart Association; RASI =renin–angiotensin system inhibitor; ST2 = interleukin-1 receptor-like 1.*

**Appendix 4. Other risk scores for patients with heart failure**

| Risk score (reference) | The patient | Data source | Setting | Study type | Derivation size (*n*) | Validation size (*n*) | Score variables | Model development | Study endpoint | Discrimination |
|---|---|---|---|---|---|---|---|---|---|---|
| GRS (Li et al, 2020) | Chronic heart failure, HFrEF and HFpEF | Clinical trial | Single centre, China | Not reported | 319 genes | No | Single nucleotide polymorphisms: genes AGT, SLC25A13, HRG, APOB, SOD3, SYNM and TLN2 | Cox proportional hazard model | Heart transplantation or cardiovascular mortality | Hazard ratio=1.28 |
| New-Onset AF score (Yamauchi et al, 2017) | Chronic heart failure | Registry | Multi-centre, Japan | Prospective | 2766 | 1389 | Age, smoke, pulse pressure, estimated glomerular filtration rate, B-type natriuretic peptide, aortic valvular regurgitation, left ventricular hypertrophy, and left atrial and left ventricle dilatation on echocardiography | Logistic regression model | New-onset atrial fibrillation | AUC=0.76 |
| 3A3B score (Kasahara et al, 2019) | HFpEF | Registry | Multi-centre, Japan | Prospective | 1277 | 835/170 (cohort 1/ cohort 2) | Ages, anaemia, albumin, blood urea nitrogen, body mass index and B-type natriuretic peptide | Cox proportional hazard models and random survival forests | 5.7-year all-cause mortality | C-statistic =0.708 |
| $CHADS_2$ (Kondo et al, 2017) | Chronic heart failure (HFrEF) without atrial fibrillation | Clinical trial | Single centre, Japan | Prospective | Not involved | 127 | Chronic heart failure, hypertension, age, diabetes mellitus, and prior stroke or transient ischaemic attack | Cox proportional hazards regression model | 8.4-year ischaemic stroke or transient ischaemic attack | AUC=0.805 |
| $CHA_2DS_2$-VASc (Ye et al, 2016) | HFrEF, with sinus rhythm | Registry | Multi-centre, multi-national | Prospective | Not involved | 2224 | Chronic congestive heart failure, hypertension, age ≥75 years or age 65–75 years, diabetes mellitus, stroke, transient ischaemic attack or thromboembolism, vascular disease, and female | Cox proportional hazard model | Mortality, ischaemic stroke and major haemorrhage | C-statistic =0.57, 0.58, 0.64 and 0.68 respectively |

*AUC = area under the curve from the receiver-operating characteristic; HFpEF=heart failure with preserved ejection fraction, HFrEF=heart failure with reduced ejection fraction*