Original Article

# The Singapore Heart Failure Risk Score: Prediction of Survival in Southeast Asian Patients

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## Abstract

**Introduction: Numerous heart failure risk scores have been developed but there is none for Asians. We aimed to develop a risk calculator, the Singapore Heart Failure Risk Score, to predict 1- and 2-year survival in Southeast Asian patients hospitalised for heart failure. Materials and Methods: Consecutive patients admitted for heart failure were identified from the Singapore Cardiac Databank Heart Failure registry. The follow-up was 2 to 4 years and mortality was obtained from national registries. Results: The derivation (2008-2009) and 2 validation cohorts (2008-2009, 2013) included 1392, 729 and 804 patients, respectively. Ten variables were ultimately included in the risk model: age, prior myocardial infarction, prior stroke, atrial fibrillation, peripheral vascular disease, systolic blood pressure, QRS duration, ejection fraction and creatinine and sodium levels. In the derivation cohort, predicted 1- and 2-year survival was 79.1% and 68.1% compared to actual 1- and 2-year survival of 78.2% and 67.9%. There was good agreement between the predicted and observed mortality rates (Hosmer-Lemeshow statistic = 14.36, *P* = 0.073). C-statistics for 2-year mortality in the derivation and validation cohorts were 0.73 (95% CI, 0.70-0.75) and 0.68 (95% CI, 0.64-0.72), respectively. Conclusion: We provided a risk score based on readily available clinical characteristics to predict 1- and 2-year survival in Southeast Asian patients hospitalised for heart failure via a simple online risk calculator, the Singapore Heart Failure Risk Score.**

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**Key words: Asia, Heart failure, Mortality**

## Introduction

Heart failure is a growing public health problem with a significant disease burden worldwide.[1,2] Given the substantial uncertainty associated with disease outcomes,[3] risk scores play an important role in prognosticating survival and aiding the clinician to identify and counsel at-risk patients.

Mortality outcomes in heart failure have been shown to be affected by ethnicity.[4-6] In Western cohorts, mortality among African American heart failure patients was found to be higher than in whites. In Asian patients with heart failure, there have been greater adverse outcomes in Malays compared to the Chinese.[4,5] Asian cohorts present and fare differently from their Western counterparts. In the Acute Decompensated Heart Failure Registry (ADHERE), patients from the Asia Pacific presented much younger than those from America and had more severe clinical features with higher rates of mechanical ventilation and in-hospital mortality.[7-9] To date, the vast majority of risk scores were designed and validated in Western populations. None of them were validated in Asian patients. In a recently published risk score incorporating 40,000 patients from 30 studies, only 1 study was from Asia.[10]

Reviews of existing risk scores have highlighted their potential limitations. The predictive accuracy of earlier models, such as the Heart Failure Survival Score (HFSS),

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have been shown to be suboptimal.[11] Some models look primarily at in-hospital mortality.[12-16] Yet others incorporate subjective variables that may compromise prognostic utility[17-19] or more complex variables—peak oxygen consumption ($pVO_2$) or other measurements obtained through invasive cardiac procedures[20-23]—which may not be readily available in clinical practice.

Our aim was to develop a simple online risk calculator to predict 1- and 2-year survival in Southeast Asian heart failure patients based on readily available clinical and laboratory parameters.

## Materials and Methods

### *Study Population*

Singapore is a multi-ethnic Southeast Asian city-state with a population of 5.31 million people (74% Chinese, 13% Malay and 9% Indian).[24] Tertiary healthcare in Singapore is provided predominantly by a network of public hospitals that account for about 80% of all hospital admissions.[25] The Singapore Cardiac Databank (SCDB) is the national registry that collects data on cardiovascular diseases.[18,19] Information from all heart failure admissions to all the public hospitals in Singapore are prospectively collected as part of the SCDB Heart Failure (SCDB-HF) registry. The SCDB-HF registry commenced on 1 January 2008 and collates data on demographics, comorbidities, medical history, clinical characteristics, initial evaluations, laboratory and imaging results and treatment and discharge outcomes. All consecutive patients ≥21 years and admitted with the DRG code 252 (Heart Failure) are included in the registry. Trained coordinators use a standardised case report form to collect data which is then entered into an electronic database following internal and external validation. Registry participation does not alter any treatment or medical care and is not linked to specific therapy or medication. Ethical approval for this study was obtained from the institutional review board.

Consecutive patients admitted with heart failure to 2 institutions in the SCDB-HF registry from 1 January 2008 to 31 December 2009 were included in the study. Both institutions are representative of Singapore hospitals that see a large number of public hospital admissions since they accounted for about 40% of admissions in the SCDB-HF registry. Repeat admissions and patients who were foreigners (due to inadequate follow-up) were excluded. The derivation cohort was derived from the first institution and an initial validation cohort was provided by the second institution (validation cohort 1). A second validation cohort was obtained from patients in the SCDB-HF registry who were admitted to the second institution between 1 January 2013 and 31 December 2013 (validation cohort 2).

### *Outcomes*

The primary outcome measure was all-cause mortality. In Singapore, all mortality data are maintained by the National Registry of Diseases Office (NRDO). All study patients were followed up for 2 to 4 years. Mortality data and cause of death were obtained from the NRDO.

### *Statistical Analysis*

The baseline characteristics of study patients were summarised as frequencies and percentages for categorical variables and as mean ± standard deviation (SD) for continuous variables. The demographic, clinical and laboratory variables available from the registry are listed in Table 1. Univariate analysis was performed on all these

Table 1. Demographics and Clinical Characteristics of Study Population

| | Derivation Cohort (n = 1392) | Validation Cohort 1 (n = 729) | Validation Cohort 2 (n = 804) |
|---|---|---|---|
| Demographics | | | |
| Mean age (SD) | 68.2 (12.4) | 71.4 (11.6) | 70.9 (13.5) |
| Male (%) | 789 (56.7) | 317 (43.5) | 406 (50.5) |
| Race (%) | | | |
| Chinese | 976 (70.1) | 530 (72.7) | 589 (73.3) |
| Indian | 162 (11.6) | 88 (12.1) | 74 (9.2) |
| Malay | 223 (16.0) | 103 (14.1) | 122 (15.2) |
| Others | 31 (2.2) | 8 (1.1) | 19 (2.4) |
| Clinical characteristics (%) | | | |
| Prior coronary artery disease | 515 (37.0) | 453 (62.1) | 381 (47.4) |
| Prior myocardial infarction | 435 (31.3) | 171 (23.5) | 146 (18.2) |
| Atrial fibrillation | 409 (29.4) | 149 (20.4) | 183 (22.8) |
| Diabetes mellitus | 707 (50.8) | 391 (53.6) | 398 (49.5) |
| Hypertension | 986 (70.8) | 577 (79.1) | 603 (75.0) |
| Hyperlipidaemia | 894 (64.2) | 418 (57.3) | 447 (55.6) |
| Stroke | 207 (14.9) | 136 (18.7) | 108 (13.4) |
| Peripheral vascular disease | 82 (5.9) | 61 (8.4) | 55 (6.8) |
| COPD | 165 (11.9) | 105 (14.4) | 84 (10.4) |
| Ever smoker | 583 (41.9) | 212 (29.1) | 225 (28.0) |
| Implantable cardioverter-defibrillator | 89 (6.4) | 5 (0.7) | 8 (1.0) |
| Left ventricular ejection fraction | | | |
| ≥50% | 464 (33.3) | 381 (52.3) | 446 (55.5) |
| 30% – 49% | 417 (30.0) | 190 (26.1) | 225 (28.0) |
| <30% | 511 (36.7) | 158 (21.7) | 133 (16.5) |
| Systolic blood pressure (SD) (mmHg) | 137.0 (30.1) | 141.9 (29.8) | 141.4 (28.3) |
| Diastolic blood pressure (SD) (mmHg) | 76.5 (18.2) | 73.6 (18.0) | 73.8 (15.5) |

ACE: Angiotensin-converting-enzyme; COPD: Chronic obstructive pulmonary disease; NT proBNP: N-terminal pro b-type natriuretic peptide; SD: Standard deviation
*There were 312 patients with missing data.

Table 1. Demographics and Clinical Characteristics of Study Population (Cont'd)

| | Derivation Cohort (n = 1392) | Validation Cohort 1 (n = 729) | Validation Cohort 2 (n = 804) |
|---|---|---|---|
| Heart rate (SD) | 88.9 (23.4) | 85.1 (19.9) | 87.1 (20.3) |
| QRS duration (SD) | 103.3 (25.6) | 97.0 (23.1) | 97.1 (21.1) |
| NT proBNP (SD) (pg/mL)* | 9737.3 (13202.7) | 9869.8 (15635.9) | 10529.6 (16022.9) |
| Creatinine (SD) (μmol/L) | 128.8 (79.9) | 155.1 (138.4) | 170.9 (172.9) |
| Sodium (SD) (mmol/L) | 136.2 (8.0) | 135.9 (5.0) | 134.9 (5.4) |
| Potassium (SD) (mmol/L) | 4.4 (3.8) | 4.2 (0.8) | 4.3 (0.8) |
| Haemoglobin (SD) (g/dL) | 12.5 (4.0) | 11.6 (2.2) | 11.4 (2.4) |
| Discharge medications (%) | | | |
| ACE inhibitor (ACEI) | 753 (54.1) | 297 (40.7) | 216 (26.9) |
| Angiotensin receptor blocker (ARB) | 279 (20.0) | 150 (20.6) | 184 (22.9) |
| ACEI/ARB | 1016 (73.0) | 429 (58.8) | 390 (48.5) |
| Beta-blocker | 890 (63.9) | 359 (49.2) | 490 (60.9) |
| Spironolactone/ aldosterone antagonist | 274 (19.7) | 78 (10.7) | 86 (10.7) |
| Nitrate | 741 (53.2) | 272 (37.3) | 182 (22.6) |
| Diuretic | 1210 (86.9) | 553 (75.9) | 485 (60.3) |
| Digoxin | 406 (29.2) | 83 (11.4) | 76 (9.5) |
| Aspirin | 759 (54.5) | 313 (42.9) | 428 (53.2) |
| Clopidogrel | 233 (16.7) | 63 (8.6) | 428 (53.2) |
| Warfarin | 249 (17.9) | 46 (6.3) | 71 (8.8) |
| Statins | 1006 (72.3) | 426 (58.4) | 459 (57.1) |

ACE: Angiotensin-converting-enzyme COPD: Chronic obstructive pulmonary disease; NT proBNP: N-terminal pro b-type natriuretic peptide; SD: Standard deviation
*There were 312 patients with missing data.

variables for the derivation cohort to identify predictors of mortality. The significant variables on univariate analysis are shown in Table 2. Following univariate analysis, stepwise Cox multiple regression analysis was performed on the significant univariate variables to obtain the candidate variables for the Singapore Heart Failure Risk Score (SHFRS). The significance level for entry and retention in the model was $P$ <0.05. After multivariable analysis, the significant candidate variables in the selection pool were prior myocardial infarction (MI), atrial fibrillation (AF), hyperlipidaemia, stroke, diabetes mellitus, peripheral vascular disease (PVD) and left ventricular ejection fraction (LVEF). The continuous candidate variables were age, systolic blood pressure (SBP), diastolic blood pressure (DBP), QRS duration, sodium, creatinine and haemoglobin. LVEF was analysed in 3 categories (≥50%, 30-49% and ≤30%) as collected by the registry.

In the derivation cohort, survival at time $t$ was estimated by the fitted equation

$$\hat{S}(t|\boldsymbol{X}\hat{\boldsymbol{\beta}}) = [\hat{S}_0(t)]^{exp\{\sum_{i=1}^{p}\hat{\beta}_i X_i\}}, \quad 0 < t \leq 2 \qquad (1)$$

where time is expressed in years, $\hat{S}_0(t)$ is the baseline survival function—purely a function of time—and $\hat{l} = \sum_{i=1}^{p}\hat{\beta}_i X_i$ is the estimated linear predictor which is a linear combination of the independent predictor variables $X_1, X_2, \ldots, X_p$ and the corresponding parameter estimates $\hat{\beta}_1, \hat{\beta}_2, \ldots, \hat{\beta}_p$.

Based on the derivation data and use of the selected independent variables, the fitted linear predictor was

$$\hat{l} = 0.023 \cdot Age + 0.437 \cdot Prior\ MI + 0.221 \cdot AF + 0.245 \cdot Stroke - 0.009 \cdot SBP + 0.004 \cdot QRS - 0.007 \cdot Sodium + 0.003 \cdot Creatinine + 0.456 \cdot PVD + 0.118 \cdot LVEF_1 + 0.301 \cdot LVEF_2$$

The categorical variables—prior MI, AF, stroke, PVD, $LVEF_1$ (EF 30-49%) and $LVEF_2$ (EF <30%)—were coded as 1 for "yes" and 0 for "no".

An equation that approximated the estimated baseline survival function was obtained in the following manner: 1) coordinates $[t_i, \hat{S}_0(t_i)]$ $i = 1, \ldots, n$ were obtained as output from the Cox regression analysis (SAS PROC PHREG) and then transformed into $x_t = ln(t)$ , $y_t = ln(-ln(\hat{S}_0(t))$ using Weibull coordinates; 2) a fifth-degree polynomial, $y = P_0^5(x)$, was fitted to the $(x_i, y_i)$ coordinate pairs over the range of the observed data; 3) $\hat{S}_0(t)$ was approximated as $\check{S}_0(t) = exp\{-exp(y_t)\}$. The derived survival predictor equation is restricted to 0 <$t$ ≤2 and is expressed as

$$\check{S}(t|\boldsymbol{X}\hat{\boldsymbol{\beta}}) = [\check{S}_0(t)]^{exp\{\sum_{i=1}^{p}\hat{\beta}_i X_i\}}, \quad 0 < t \leq 2 \qquad (2)$$

Derived from the derivation cohort, equation 2 was then prospectively applied to each patient in the validation cohorts to provide individual estimates of survival at 1 and 2 years. In both cohorts, predicted survival was compared against actual survival. Using the predictive model, mean survival for each cohort was compared to actual mean survival. Model discriminant ability was assessed by the 1-year and 2-year receiver operating characteristics (ROC) area under the curve (AUC) for both data sets. A similar model was analysed that included medication data in addition to demographic, clinical and laboratory variables. The interaction between ejection fraction (EF) and individual predictors with the overall model for outcomes was also tested. The Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) risk score10 was also validated in the derivation cohort.

All significance tests were two-sided and conducted at $P$ <0.05. All analyses were performed using SAS© software

Table 2. Significant Univariate and Multivariate Predictors of Mortality in the Derivation Cohort

| | Univariate Hazard Ratio (95% CI) | *P* Value | Multivariate Hazard Ratio (95% CI)* | *P* Value |
|---|---|---|---|---|
| Age | 1.021 (1.014 – 1.028) | <0.001 | 1.024 (1.016 – 1.032) | <0.001 |
| Implantable cardioverter-defibrillator | 0.664 (0.457 – 0.965) | 0.032 | | |
| Prior myocardial infarction | 1.664 (1.412 – 1.961) | <0.001 | 1.548 (1.295 – 1.850) | <0.001 |
| Atrial fibrillation | 1.199 (1.011 – 1.422) | 0.037 | 1.248 (1.032 – 1.508) | 0.022 |
| Hyperlipidaemia | 1.209 (1.019 – 1.435) | 0.030 | | |
| Stroke | 1.502 (1.223 – 1.844) | <0.001 | 1.278 (1.027 – 1.589) | 0.028 |
| Diabetes mellitus | 1.240 (1.056 – 1.456) | 0.009 | | |
| Peripheral vascular disease | 2.114 (1.609 – 2.779) | <0.001 | 1.578 (1.188 – 2.096) | 0.002 |
| Left ventricular ejection fraction | | | | |
| ≥50% (ref) | - | - | - | - |
| 30% – 49% | 1.234 (1.002 – 1.520) | 0.048 | 1.125 (0.899 – 1.408) | 0.303 |
| <30% | 1.409 (1.161 – 1.711) | 0.001 | 1.351 (1.077 – 1.694) | 0.009 |
| Systolic blood pressure (mmHg) | 0.992 (0.989 – 0.995) | <0.001 | 0.991 (0.988 – 0.994) | <0.001 |
| Diastolic blood pressure (mmHg) | 0.984 (0.979 – 0.989) | <0.001 | | |
| QRS duration (ms) | 1.007 (1.004 – 1.010) | <0.001 | 1.004 (1.001 – 1.007) | 0.019 |
| NT proBNP (pg/mL)† | 1.000 (1.000 – 1.000) | <0.001 | | |
| Sodium (mmol/L) | 0.990 (0.984 – 0.997) | 0.003 | 0.993 (0.986 – 0.999) | 0.030 |
| Creatinine (μmol/L) | 1.003 (1.002 – 1.003) | <0.001 | 1.003 (1.002 – 1.004) | <0.001 |
| Haemoglobin (g/dL) | 0.922 (0.883 – 0.962) | <0.001 | | |
| ACE inhibitor/angiotensin receptor blocker | 0.699 (0.589 – 0.831) | <0.001 | | |
| Nitrate | 1.240 (1.054 – 1.458) | 0.009 | | |
| Beta-blocker | 0.791 (0.672 – 0.932) | 0.005 | | |
| Warfarin | 0.715 (0.571 – 0.897) | 0.004 | | |
| Aspirin | 0.848 (0.723 – 0.996) | 0.044 | | |

ACE: Angiotensin-converting-enzyme; NT proBNP: N-terminal pro b-type natriuretic peptide; ref: Reference
*Excludes NT proBNP and medications.
†There were 312 patients with missing data.

version 9.3 (SAS Institute, Cary, NC) and SPSS software version 22.0 (SPSS Inc., Chicago, IL). The SHFRS calculator can be accessed online via the homepage of Duke-NUS Medical School (https://webapps.duke-nus.edu.sg/tools/SHFRiskScore) (shown in Figure 1).

## Results

A total of 1392 patients were included in the derivation cohort, 729 patients in validation cohort 1 and 804 patients in validation cohort 2. The demographics and clinical characteristics of the patients are described in Table 1.

### *Predictors of Mortality*

The overall 2-year mortality was 32.1% (n = 447), 35.9% (n = 262) and 34.8% (n = 280) in the derivation and validation cohorts, respectively. The univariate and multivariate predictors of mortality in the derivation cohort are shown in Table 2. The findings of the multivariable analysis showed that older age (HR 1.024, 95% CI, 1.016-1.032, *P* <0.001), prior MI (HR 1.548, 95% CI, 1.295-1.850, *P* <0.001), AF (HR 1.248, 95% CI, 1.032-1.508, *P* = 0.022), prior stroke (HR 1.278, 95% CI, 1.027-1.589, *P* = 0.028), PVD (HR 1.578, 95% CI, 1.188-2.096, *P* = 0.002), lower EF (HR 1.351, 95% CI, 1.077-1.694, *P* = 0.009, EF ≥50% vs <30%), longer QRS duration (HR 1.004, 95% CI, 1.001-1.007, *P* = 0.019) and higher creatinine levels (HR 1.003, 95% CI, 1.002-1.004, *P* <0.001) were associated with significantly increased mortality. Higher SBP (HR 0.991, 95% CI, 0.988-0.994, *P* <0.001) and higher sodium levels (HR 0.993, 95% CI, 0.986-0.999, *P* = 0.03) were associated with decreased mortality. Ethnicity was not a significant predictor of mortality.

We tested the interaction between EF and individual predictors with the overall model for outcomes. With the

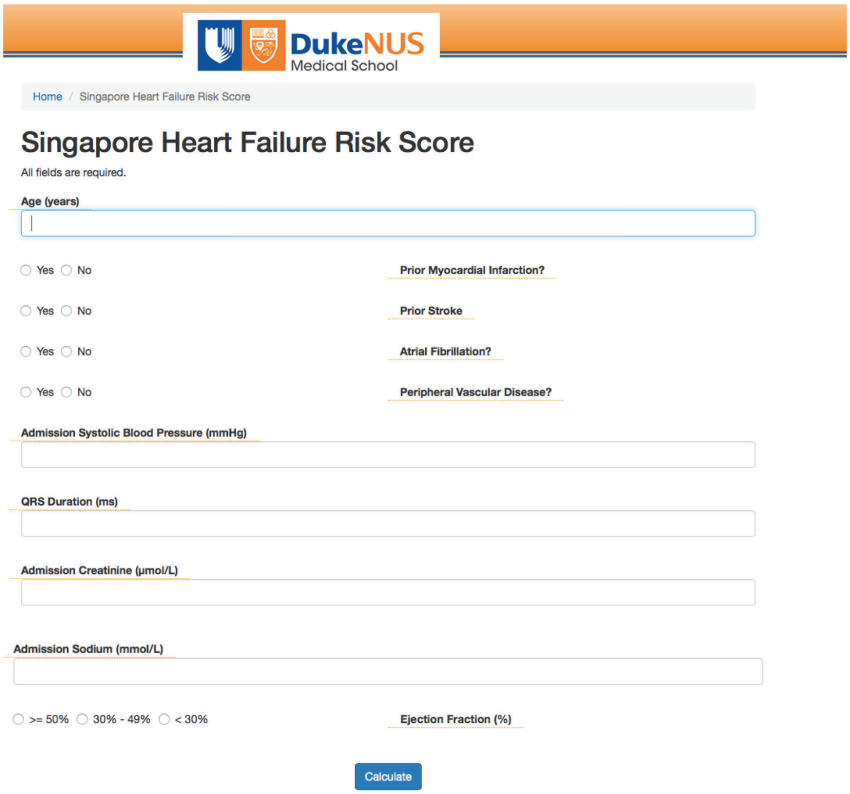


Fig. 1. The Singapore Heart Failure Risk Score (SHFRS) calculator found on the homepage of Duke-NUS Medical School. Reprinted with permission from Duke-NUS Medical School.

exception of PVD (its inclusion did not change the variables in the model), there was no significant interaction with the remaining 8 clinical predictors. Thus, a combined risk score for heart failure was proposed.

*Performance of Model in Derivation and Validation Cohorts*

The overall model performed well. In the derivation cohort, the predicted 1- and 2-year survival was 79.1% and 68.1%, respectively, compared to the actual 1- and 2-year survival of 78.2% and 67.9%, respectively. There was a good match between predicted and observed mortality rates (Hosmer-Lemeshow statistic = 14.36, $P = 0.073$ for 2-year survival). In validation cohort 1, the predicted 1- and 2-year survival was 78.8% and 67.9%, respectively, compared to the actual 1- and 2-year survival of 75.2% and 64.1%, respectively. There was a good match between predicted and observed mortality rates (Hosmer-Lemeshow statistic = 8.35, $P = 0.400$ for 2-year survival). In validation cohort 2, the predicted 1- and 2-year survival was 78.2% and 67.7%, respectively, compared to actual 1- and 2-year survival of 75.7% and 65.2%, respectively. There was good agreement between the predicted and observed mortality rates (Hosmer-Lemeshow statistic = 6.33, $P = 0.610$). C-statistics for 2-year mortality in the derivation cohort, validation cohort 1 and validation cohort 2 were 0.726 (95% CI, 0.697-0.754), 0.681 (95% CI, 0.640-0.722) and 0.648 (95% CI, 0.606-0.690), respectively (Fig. 2 and Table 3).

When medication data was included in the analysis, no improvement in the predictive accuracy of the model was seen. The C-statistics for 2-year mortality in the derivation cohort and validation cohort 1 were 0.723 (95% CI, 0.694-0.752) and 0.686 (95% CI, 0.646-0.727), respectively.

We compared the performance of our model against the MAGGIC risk score in the derivation cohort. The C-statistic for 1-year mortality in our model was 0.731 (95% CI, 0.699-0.764) against 0.620 (95% CI, 0.583-0.658) for the MAGGIC risk score.

## Discussion

We report a new risk model, the SHFRS, that accurately predicted 1- and 2-year survival in patients hospitalised with heart failure. The SHFRS uses readily available clinical and laboratory variables on heart failure patients in Southeast Asia. It accurately predicted 1- and 2-year survival in these patients with AUC values of 0.731 and 0.726, respectively. These findings are comparable to the Seattle Heart Failure Model (SHFM) which had a 1-year AUC of 0.729 in the derivation cohort and an AUC of 0.679 in one of its validation cohorts.[11] Our score prognosticates longer-term mortality and expands on previous models such as the Organized Program to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure (OPTIMIZE-HF) which looked primarily at inpatient mortality.[12-16]

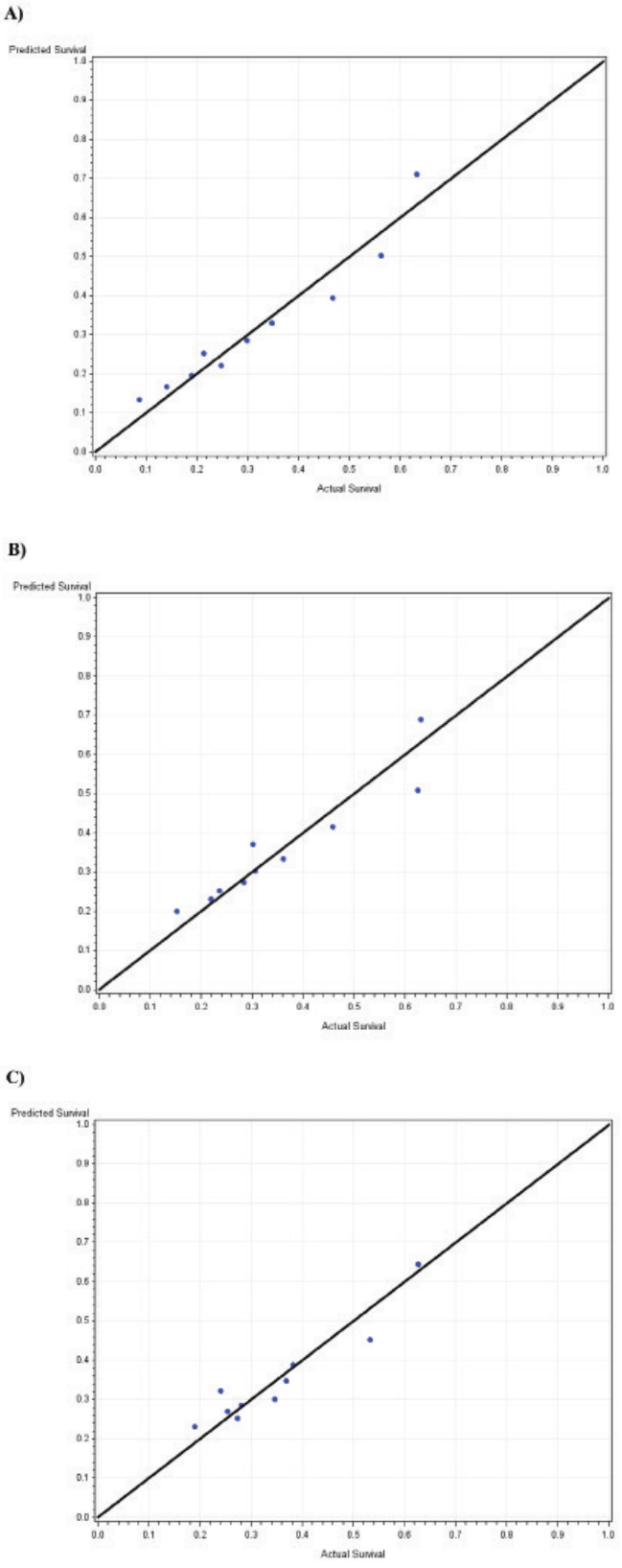


Fig. 2. Predicted vs actual 2-year survival in A) derivation cohort, B) validation cohort 1 and C) validation cohort 2.

Table 3. Survival in the Derivation and Validation Cohorts

| | Derivation Cohort (n = 1392) | Validation Cohort 1 (n = 729) | Validation Cohort 2 (n = 804) |
|---|---|---|---|
| Death (n) | 601 | 353 | 386 |
| 1-year survival (95% CI) | | | |
| Actual | 0.782 (0.760 – 0.804) | 0.752 (0.720 – 0.783) | 0.757 (0.728 – 0.787) |
| Predicted | 0.791 (0.785 – 0.798) | 0.788 (0.778 – 0.798) | 0.782 (0.771 – 0.794) |
| 2-year survival (95% CI) | | | |
| Actual | 0.679 (0.655 – 0.704) | 0.641 (0.606 – 0.676) | 0.652 (0.619 – 0.685) |
| Predicted | 0.681 (0.673 – 0.690) | 0.679 (0.667 – 0.692) | 0.677 (0.663 – 0.690) |
| 1-year AUC (95% CI) | 0.731 (0.699 – 0.764) | 0.670 (0.623 – 0.716) | 0.630 (0.583 – 0.677) |
| 2-year AUC (95% CI) | 0.726 (0.697 – 0.754) | 0.681 (0.640 – 0.722) | 0.648 (0.606 – 0.690) |

AUC: Area under the curve; CI: Confidence interval

Most risk scores were derived and validated in Western patients. To date, none has been validated in Asian patients. Among the 30 studies used for the risk model by the MAGGIC investigators, only 1 study originated from Asia (Japan).[10] Ethnic differences in heart failure outcomes have previously been demonstrated. African American patients had higher mortality than white patients in the Studies of Left Ventricular Dysfunction (SOLVD).[6] In the Multi-Ethnic Study of Atherosclerosis (MESA),[26] African Americans had the highest incidence of heart failure followed by Hispanics and whites. One local study found that mortality in elderly Malay heart failure patients was 3.5 times higher than their Chinese and Indian counterparts.[4] This finding was similar to that of all-comers in a smaller study by Lee and colleagues.[5] In this study, ethnicity did not impact mortality after careful multivariable adjustment was made for baseline differences. Our study did not focus exclusively on the elderly and had a much larger cohort than Lee and colleagues. Our findings are similar to another local study[27] which did not find any ethnic differences in patients with reduced EF. We also did not report any significant ethnic differences in mortality in Asian patients with preserved EF in a previous study.[28] Although no significant differences were found among the Chinese, Indians and Malays, SHFRS nonetheless provides the first risk score that was developed for Asians.

Asian heart failure cohorts have been shown to present and fare differently from Western cohorts. In the Acute Decompensated Heart Failure Registry (ADHERE), patients from the Asia Pacific presented at younger ages (67

years vs 75 years) than those from America and had more severe clinical features, longer hospital stay, higher rates of mechanical ventilation and higher in-hospital mortality.[7-9] In particular, Southeast Asian patients in the ADHERE-Asia Pacific registry presented even younger at 54 years.[29]

The SHFRS comprises 10 readily available clinical and objective parameters. It contrasts with more complex models such as SHFM and CHARM (Candesartan in Heart Failure – Assessment of Mortality and Morbidity) which require a total of 24 variables each.[11,19] The variables in our model were also objective and did not include subjective factors found in other models such as the New York Heart Association (NYHA) Functional Classification.[10,17-19] The NYHA model may vary over different time points and studies have found significant differences in physician-rated and patient-rated classifications[30] as well as significant inter-observer assessment of NYHA class.[31] The clinical parameters used in the SHFRS are readily available to the clinician and do not require further exercise test or any invasive cardiac test like in the HFSS[20] and other risk models,[21-23] thereby improving its ease of use.

Gorodeski and associates reported that $pVO_2$ improved discrimination beyond the SHFM but it did not significantly improve reclassification of risk.[32] Aaronson and colleagues observed that there was no added benefit in including Pulmonary Capillary Wedge Pressure in risk models.[20] In comparison, the MUerte Súbita en Insuficiencia Cardiaca (MUSIC) risk score—which also used 10 objective clinical variables—was based on a cohort of less than 1000 patients without a validation group.[3] It required both troponin and N-terminal pro b-type natriuretic peptide (NT proBNP) levels and 24-hour Holter monitor results which may not be readily available to all heart failure patients. Several of the published risk models also require manual calculation.[3,13,20,23,33-35] We compared the SHFRS to the MAGGIC model in our derivation cohort and it was shown that SHFRS performed better (C-statistic of 0.731 vs 0.620). The availability of the SHFRS as an online calculator also ensures its easy access. It allows scores to be easily applied in clinical practice for risk stratification and in prognostication to guide patient management.

The clinical variables selected by the stepwise multivariable analysis were all supported by a strong body of evidence. In many previous studies, age,[2,12,16,17,19,33,34,36,37] prior MI,[37] prior stroke,[12] prior PVD,[38] lower EF,[16,17,19] AF,[39] longer QRS duration,[40,41] lower SBP,[12,16,17,42-44] lower haemoglobin[45,46] and lower sodium levels[2,12,13,16,36,44,47] have all been shown to be independent predictors of increased mortality. Higher creatinine levels[2,13,16,17,36,37,42] have also previously been shown to be a significant risk factor for mortality in heart failure patients. Creatinine levels have been included in our score as a surrogate for renal function. This is especially pertinent since impaired renal function is commonly associated with heart failure and patients with cardio-renal syndrome often have a poorer prognosis.[48-50] In contrast, SHFM[11] and MAGGIC[10] did not include any markers of renal function to aid prognostication.

Medications were excluded from our risk model for several important reasons. First, the beneficial effects of medications in the treatment of patients with preserved EF have not been established.[28,51-55] The inclusion of medications may affect the predictive accuracy of the model in patients with preserved EF. Second, differences in the dosage of medications administered affect mortality and morbidity outcomes.[56,57] Very often, exact dosing is not readily available. To account for the potential impact of medications, a separate analysis that included the effects of medications was performed. The result did not show any significant change in the predictive accuracy of the model. The exclusion of medications is commonly found in many risk scores.[3,11-13,15,20,23,33,35,36,58]

The strengths of our study include a large cohort size, the ease of use of the SHFRS and its ability to provide accurate and reliable mortality estimates. It is also the first heart failure risk score developed in Southeast Asia. It has the potential to provide the clinician with a means to better risk-stratify heart failure patients in order to guide management and to allocate resources more equitably. This helps to identify high-risk heart failure patients who may need more intensive therapy and follow-up. Additionally, the SHFRS may provide valuable prognostic information in the conversation with the patient and family regarding possible end-of-life care.

## Limitations

Our study has several limitations. Similar to other registry studies, bias may have arisen from missing data but this was kept to a minimum (<3%) for all data fields except NT proBNP. Due to about 15% of missing data, NT proBNP was excluded from our model. We were unable to compare the performance of some of the existing risk models in our cohort due to differences in the variables collected by the various registries. Second, our cohort was based on hospitalised patients with a DRG code of 252. Patients in the outpatient setting may have different outcomes and the restriction of the DRG code may give rise to the possibility of misclassification. Third, our study included mainly Chinese, Indian and Malay ethnicities and will need to be validated in similar Asian cohorts, other Asian ethnicities and Western cohorts. Fourth, the exact EF was not available in the registry as such data was coded into the above categories. Within limitations, the categories provide good differentiation among patients with preserved, impaired and severely impaired EFs. Last, with constant

improvements in heart failure management,[59,60] the SHFRS will need to be validated in future patient cohorts.

## Conclusion

We provide a risk score based on readily available clinical characteristics to predict 1- and 2-year survival in Southeast Asian patients hospitalised for heart failure. This was done using a simple online risk calculator.

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