Letters

RESEARCH LETTER

Predictive Score for 30-Day Readmission or Death in Heart Failure

Readmissions shortly after heart failure (HF) are common, expensive, and usually considered preventable.[1] However, despite the use of several interventions, rates of readmission after HF remain stable.[2] An effective risk score might permit the targeting of resource-intensive interventions (such as disease-management programs) specifically on high-risk patients. We sought to determine the combination of clinical and nonclinical factors that would have the best discriminatory power in predicting 30-day readmission or death in HF.

Table. Prediction of 30-day Readmission or Death in Heart Failure

Predictors	Description, No. (%)[a]	Univariable Logistic Regression		Final Prediction Model,
		OR (95% CI)	G	OR (95% CI)
Social history				
Completed education (high school or college)	220 (52)	0.69 (0.53-0.89)	8.05	
Living alone (yes vs no)	129 (30)	2.29 (1.48-3.55)	13.62	2.05 (1.12-3.76)
Remoteness index (outside major city)	172 (40)	1.41 (0.93-2.15)	2.59	
Medical				
Smoking (ever vs never)	301 (70)	1.85 (1.14-3.01)	6.48	
Solid organ tumor (yes vs no)	30 (7)	0.39 (0.13-1.14)	3.59	
Diabetes mellitus, No.	254 (59)	1.38 (1.04-1.83)	4.80	
Mild, without complications	125 (29)			
Complications/end-organ damage	51 (12)			
Life-threatening arrhythmia (yes vs no)	39 (9)	2.04 (1.04-4.02)	4.27	2.92 (1.20-7.13)
Cerebrovascular disease or stroke (yes vs no)	51 (12)	1.80 (1.00-3.25)	3.69	
Discharge during winter (yes vs no)	116 (27)	2.65 (1.57-4.48)	12.97	1.61 (1.00-3.31)
Heart rate, per 5 bpm	75 (68-86)	1.12 (1.04-1.21)	9.98	1.12 (1.01-1.24)
Charlson Comorbidity Index	7 (5-9)	1.15 (1.04-1.27)	7.08	
Chronic kidney disease (yes vs no)	155 (36)	1.76 (1.15-2.70)	6.70	
Cardiac catheterization	172 (40)	0.64 (0.44-0.93)	5.82	
NYHA classification		2.25 (1.70-2.98)	35.91	1.95 (1.35-2.84)
Class II or under	241 (56)			
Class III	150 (35)			
Class IV	39 (9)			
Questionnaires				
MoCA score	23 (18-26)	0.89 (0.86-0.93)	34.56	0.90 (0.86-0.95)
GAD-7 score	4 (1-10)	1.05 (1.01-1.08)	7.32	
PHQ-9 score	9 (4-15)	1.06 (1.02-1.09)	12.34	1.04 (1.00-1.08)
Physiology				
Right atrial pressure, mm Hg	8 (3-15)	1.11 (1.06-1.16)	21.47	1.06 (1.01-1.12)
Left atrial volume index, mL/m^2	42 (30-60)	1.02 (1.01-1.03)	16.30	1.02 (1.01-1.03)
Pulmonary systolic pressure, mm Hg	38 (30-48)	1.03 (1.01-1.05)	13.71	
Left ventricular volume index, mL/m^2	56 (43-80)	1.01 (1.00-1.02)	5.26	
Biochemistry				
Blood urea nitrogen, mg/dL	10.5 (7.6-16.1)	1.05 (1.02-1.08)	12.47	1.04 (1.01-1.08)
Serum albumin, g/dL	35 (31-38)	0.94 (0.91-0.98)	7.98	0.95 (0.91-0.99)
Medical therapy				
Aldosterone use (yes vs no)	202 (47)	0.66 (0.43-1.01)	3.65	
Beta-blocker use (yes vs no)	327 (76)	0.64 (0.41-1.02)	3.42	
Antiarrhythmic medication use (yes vs no)	73 (17)	1.60 (0.95-2.69)	3.04	
ACE inhibitor/ARB use (yes vs no)	348 (81)	0.64 (0.39-1.06)	2.95	
C-reactive protein, mg/L	10.5 (5.0-25.4)	1.01 (1.00-1.01)	2.91	
Serum creatinine, μmol/L	116 (90-153)	1.00 (1.00-1.01)	2.90	

Abbreviations: ACE, angiotensin converting enzyme; ARB, angiotensin II receptor blocker; G, change in deviance; GAD-7, Generalized Anxiety Disorder; MoCA, Montreal Cognitive Assessment; NYHA, New York Heart Association; OR, odds ratio; PHQ-9, Patient Health Questionnaire.

[a] Data are presented as No. (%) or Median (interquartile range).

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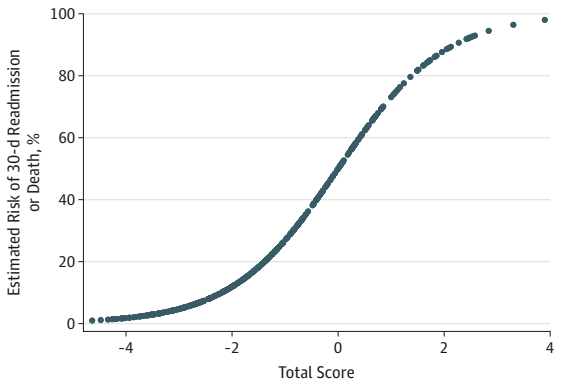
Figure. Final Risk Score for Prediction of 30-Day Readmission or Death Among Heart Failure Patients



Methods | *Study Design*. We developed a score for likelihood of readmission or death from HF from a prospective Australia-wide study of 430 HF patients (median age 74 years), of which 275 patients (64%) were male, and validated it in a group of 161 HF patients (median age 78 years), of which 89 patients (55%) were male.

The primary outcome measure in the study was 30-day all-cause readmission or death. Data on readmission and death were collected from medical records. All patients provided written informed consent for participation in the study, which was approved by the Tasmanian Health and Medical Human Research Ethics Committee.

Potential Predictors. Clinical data included patient history, medications, physical measurements, blood tests, and findings on echocardiography. Nonclinical data included age, sex, language background, marital status, living alone or with others, education, socioeconomic status, remoteness index (differentiating residence in a metropolitan, rural, or remote area of Australia), medical insurance, and any home health care services provided. Questionnaires used for data collection included the Montreal Cognitive Assessment (MoCA), Patient Health Questionnaire (PHQ-9), and Generalized Anxiety Disorder (GAD-7).

Statistical Analyses. Logistic regression was used to determine the variables that served as the best predictors of readmission or death. Predictors were ranked by the change of deviance (G, the difference between null and residual deviance) that reflected the improvement in predictability provided by the univariable model as compared with the null model for each predictor.[3] A predictor was included in the multivariable model if it contributed by 0.01 or more units to the area under the curve.[4] Changes in standard errors when new variables were added were small (<10%), implying limited variance inflation in our models and no overfitting. The final model was internally validated through the use of 500 bootstrapped samples[3] and externally validated by applying the intercept and regression coefficients to a cohort of 161 HF patients from Tasmania, Australia. Patients without any admissions for HF in the previous 6 months were recruited in the 2 largest public hospitals in Tasmania. Within 30 days of discharge, 44 of the 161 patients (27%) in the cohort either died or were readmitted. The claims-based prediction model developed by Keenan et al was applied to our study population by using the intercept and coefficients described in the original study.[5]

Results | The **Table** shows the patients' characteristics that were typical of HF in Australia. Within 30 days of discharge, 38 of the 430 HF patients (9%) in the study cohort died and 92 of the 430 patients (21%) were readmitted. The univariable associations are shown in the Table, with predictors ranked by their predictability of the outcome. The final prediction model (C statistic = 0.82; 95% CI, 0.77-0.87) (Table) had very good discrimination when predicting 30-day death (C statistic = 0.83; 95% CI, 0.73-0.93) or readmission (C statistic = 0.80; 95% CI, 0.74-0.85). The **Figure** shows the association between score and outcome. The discriminatory power of the model was much higher than that of the claims-based model (C statistic = 0.56; 95% CI, 0.50-0.61).

The internal (C statistic = 0.82; 95% CI, 0.76-0.87) and external (C statistic = 0.80; 95% CI, 0.69-0.91) validation values demonstrated great stability and generalizability of our final prediction model. The model calibration across different risk categories showed a close association of predicted and observed outcomes.

Discussion | The short-term risks of death or readmission after HF remain very high. Effective targeting of disease management programs for HF is likely to reduce readmissions and save money. However, a systematic review of readmission risk scores showed that the strongest prediction models provided only poor discrimination (C statistic <0.6) in predicting readmissions among HF patients.[6] This study optimized the predictive score of 30-day readmission or death by adding important determinants not included in previous models, including echocardiography, mental health, cognitive function, and individual socioeconomic status. The model developed in the study has excellent internal and external validation and calibration, and might be used to predict both short-term mortality and readmission for HF with very good discrimination. Further validation of the model in a larger sample of HF patients that can be generalized to other health systems is needed.

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Correction: This article was corrected on May 18, 2016, to fix errors in the Table and text.

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Association of a Family History of Coronary Heart Disease With Initiation of Statin Therapy in Individuals at Intermediate Risk: Post Hoc Analysis of a Randomized Clinical Trial

A family history of coronary heart disease (CHD) is associated with an approximately 1.5- to 2.0-fold higher risk of CHD independent of conventional risk factors,[1] highlighting the contribution of genetic factors to disease susceptibility. Whether discussion of risk associated with a family history of CHD influences shared decision making regarding statin initiation is unknown. The Myocardial Infarction-GENES (MI-GENES) study[2-4] tested the hypothesis that incorporating a multilocus genetic risk score (GRS) into CHD risk estimates would be associated with lower low-density lipoprotein cholesterol levels. We conducted a post hoc analysis to assess whether disclosure of risk associated with a family history of CHD was associated with initiation of statin therapy.

Methods | Between October 9, 2013, and April 28, 2014, residents of Olmsted County, Minnesota, at intermediate risk for CHD and not receiving statin therapy were randomized 1:1 to either a conventional (Framingham) risk score (FRS)[5] alone or FRS supplemented with a GRS. Family history was defined as the presence of CHD (ie, angina, myocardial infarction, or myocardial revascularization) in a first-degree male or female relative (ie, parents, siblings, and children) before age 55 or 65 years, respectively. A GRS was calculated based on genotypes at 28 CHD susceptibility loci.[6] The 10-year risk of CHD was disclosed by a genetic counselor informing participants of a 1.5- to 2.0-fold higher risk in the presence of family history, followed by shared decision making regarding statin therapy with a physician. The study protocol was approved by the Mayo Clinic institutional review board. All participants gave written informed consent; financial compensation was provided.

Participants returned at 3 and 6 months after risk disclosure for measurement of low-density lipoprotein cholesterol levels and assessment of statin use, dietary fat consumption (scores ranged between 0 [no fat intake] to 110 indicative of very high dietary fat intake as measured by the fat screener[7]), and physical activity levels (scores ranged between 7 [active] and 1 [sedentary] based on the adapted version of telephonic assessment of a physical activity questionnaire).[8] Continuous or dichotomous variables were compared between groups using a 2-sample *t* test or a χ^2 test, respectively. We compared the rate of statin initiation between participants with and those without a family history of CHD using logistic regression, also adjusting for allocation to GRS. We tested the association of GRS with family history, using *t* tests with significance set at $P < .05$. A paired difference test was used to assess changes over time within each group. A comparison between the groups was performed using an unpaired *t* test. All analyses were performed in JMP Pro, version 10.0.0 (SAS Institute Inc). Data analysis was conducted from September 26, 2015, to January 10, 2016.

Results | Participant characteristics did not differ significantly between groups (**Table 1**). Both the GRS and FRS tended to be higher in participants with a family history of CHD but the 2 measures were not correlated ($r = 0.01$; $P = .85$). No difference in self-reported fat intake and physical activity was noted between participants with and those without a family history of CHD.

Of individuals with a family history of CHD, 26 (47.3%) began statin therapy compared with 42 (28.4%) of those without a family history ($\chi^2 = 6.43$; $P = .01$). Among participants who received a GRS, statin therapy was also more frequent in those with than in those without a family history of CHD (16 [64.0%] vs 26 [33.3%], $P = .007$). Disclosure of a GRS resulted in a higher rate of statin prescriptions (16 [64.0%] vs 10 [33.3%]; $P = .02$) among individuals with a family history of CHD than in those who received only an FRS (**Table 2**). In a 2-variable model (odds ratio [95% CI]), both family history (2.46 [1.28-4.76]; $P < .01$) and allocation to GRS (2.13 [1.16-3.97]; $P = .01$) were associated with greater frequency of statin initiation.

Discussion | To our knowledge, this study is the first to demonstrate that discussion of risk associated with a family history of CHD influences shared decision making regarding statin treatment in intermediate-risk individuals. Among participants with a family history of CHD, disclosure of a GRS was associated with a greater initiation of statins than was disclosure of an FRS alone, suggesting that quantitative genetic risk information additionally influences shared

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