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ORIGINAL ARTICLE

Predictors of Frequent Readmissions in Patients With Heart Failure

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Background Patients with heart failure (HF) have a high incidence of hospital readmissions. However risk models that explore predictors of a single readmission may be less useful at identifying the patients with frequent readmissions who contribute to a disproportionately large proportion of morbidity and health care costs.

Methods A total of 6252 patients enrolled in the Management of Cardiac Failure Program (MACARF) in Northern Sydney Area Hospitals between 1998 and 2015 were randomly divided into derivation and validation cohorts to create and test a risk model for predictors of ≥2 readmissions or death within 1 year of initial hospitalisation for HF.

Results Multivariate predictors of frequent (≥2) readmissions or death were a history of ischaemic heart disease and chronic kidney disease, being unmarried, having anaemia, low serum albumin, elevated creatinine, prolonged hospital stay (>7 days), and not receiving beta blockers on discharge. Event rates increased with a higher risk score ($p < 0.001$) and the prediction was similar in the validation and derivation cohorts ($p = 0.588$). The C-statistic was 0.65.

Conclusions Our risk score may assist in focussing health care resources and interventions by identifying the subset of HF patients at increased risk for a disproportionately high burden of disease.

Keywords Heart failure • Risk model • Frequent admissions • Cohort study

Introduction

Heart failure (HF) is a common disease with a high mortality and morbidity, and 1-year readmission rates of over 60% [1–3]. Given this public health issue, there is an urgent need to better understand the patterns of HF hospitalisations to minimise the health burden. It is particularly important to identify the smaller proportion of HF patients with repeated hospitalisations, who contribute disproportionately to morbidity, cost and mortality [4,5], however, there has been limited study of this high risk group.

In one community study, 66.9% of patients with HF were hospitalised over a mean follow-up of 4.7 years at least twice, 53.6% at least three times, and 42.6% at least four times [6]. Over half (61.9%) of the readmissions were due to non-cardiovascular causes. Most studies that evaluated predictors of total or HF readmissions have focussed on any readmission [6–8], however one US study found that lower socioeconomic and minority race status were significant predictors of ≥2 readmissions within 1 year [9].

The development of focussed interventions for those with frequent readmissions is hindered by an inability to identify

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their clinical predictors, while the efficacy of HF disease management programs could be further enhanced by an early recognition of these high-risk patients. The present analysis aimed to develop a risk model that can be readily calculated at the time of hospital discharge to identify the predictors of multiple readmissions or death within 1 year. In addition, we evaluated whether there were any predictors of multiple versus single readmissions.

Methods

Study Design and Setting

This study was an analysis of data collected prospectively from 6252 patients hospitalised with a primary diagnosis of HF between December 1998 and April 2015. The study included seven hospitals in the Northern Sydney Area Health District, Australia, who were enrolled in the Management of Cardiac Failure (MACARF) program. Heart failure was diagnosed using the Framingham criteria for heart failure [10] and all patients >18 years were offered a referral to the program. The program aims to reduce the burden of HF by offering home visits, patient education and follow-up phone calls from HF specialists nurses. Data for the initial HF admission were entered into a database, together with readmission data.

Data Collection

All data were entered into a Microsoft Access database by the HF nurses from data collection forms within 2 weeks of patient enrolment. Data included sociodemographics, risk factors, comorbid diseases, serum electrolytes, admission heart rate and rhythm, cardiac function and discharge medication. Readmissions were differentiated based on whether the primary cause was a HF exacerbation or non-HF. All patients were followed up for subsequent readmissions and death. Ischaemic heart disease and chronic kidney disease were noted if they were mentioned as a prior diagnosis in the patient's medical records. Long length of stay was defined as >7 days, HF with preserved ejection fraction (HpEF) was defined as EF ≥50%, unmarried included single, widowed and divorced, anaemia was defined as haemoglobin <120 g/L, low serum albumin as <35 g/L, and elevated serum creatinine as >100 umol/l.

Statistical Analysis

Patient characteristics were described using frequencies and percentages and means and standard deviations. We determined the number of hospitalisations within 1 year after the index HF admission. We defined frequent readmission as two or more readmissions (equivalent to ≥3 admissions) within 1 year as has been used in previous studies [9,11]. The primary endpoint was a composite of frequent readmissions (≥2) or death within 1 year. As secondary endpoints, we also evaluated predictors of frequent readmission as a secondary endpoint, after excluding patients who died within 12 months of admission, and predictors of a single versus multiple readmission. To develop the risk scores and test their validity, all patients were randomly assigned to either a derivation cohort to develop the risk model, or a validation cohort to apply the model. Randomisation was achieved using software from Excel 2010 (Microsoft, Redmond, WA, USA).

Continuous variables were expressed as categories with appropriate cut-offs set as the lower and upper limits of normal. Among patients in the derivation subset alone, univariate analyses were conducted to determine predictors of frequent rehospitalisation using χ^2 test for categorical variables. We included risk factors, precipitants of hospitalisation, pre-admission symptoms, routine in-hospital tests and discharge medications. All predictors of frequent rehospitalisation at the univariate level ($p < 0.20$) were included in a multivariate stepwise (backward elimination) logistic regression. The goodness of fit was evaluated by calculating the Hosmer-Lemeshow statistic and C-statistic. The significant predictors in the regression were then used to create a risk prediction model to be tested on the validation cohort. The risk score was computed by adding the number of positive predictors present for each patient. Differences in event rates for increasing risk score values were assessed using the χ^2 test for trend. Differences between the derivation and validation cohort were also assessed by comparing the slope of the increase in rate of events with increasing risk score using least squares linear regression analysis. All analyses were undertaken using SPSS version 23 (IBM Chicago: SPSS Inc.).

Results

A total of 3137 patients were randomly assigned to the derivation cohort and 3115 patients to the validation cohort. The demographics and risk factors for the patients are summarised in Table 1. The admission data, including laboratory values, presenting symptoms, precipitants of hospitalisation and discharge medications are summarised in Table 2.

Table 3 shows the readmission and mortality rates of the two groups. There were no significant differences between the cohorts. The primary combined endpoint of frequent readmissions or death within 1 year occurred in 1101 (35.1%) patients in the derivation cohort and 1077 (34.6%) in the validation cohort. The 1-year single readmission rate was 42% and the multiple readmission (≥2) rate was 18%. The 1128 patients with frequent readmissions had twice the 1-year mortality of patients without frequent readmissions (26% versus 13%).

Univariate analysis identified 26 variables with $p < 0.20$, of which eight remained significant in the multivariate analysis (Table 4) and formed the final set of predictor variables. These predictors were: a history of ischaemic heart disease and chronic kidney disease, being unmarried, having anaemia, low serum albumin, elevated serum creatinine (>100 umol/l), a prolonged length of hospital stay, and not receiving beta blockers on hospital discharge (C-statistic 0.65).

Table 1 Demographic Features and Risk Factors of the Study Patients Hospitalised With Heart Failure.

	Derivation Cohort		Validation Cohort		p-value	Total
	n	%	n	%		%
Demographics						
Number	3137		3115			
Age (mean, SD)	80	11	80	11		80
Age > 80 years	1767	56	1746	56	0.81	56
HFpEF	1020	37	1007	36	0.64	
Male	1636	52	1627	53	0.98	52
Private Insurance	1552	51	1524	51	0.86	51
Unmarried	1583	53	1599	54	0.56	54
Lives Alone	1148	38	1071	36	0.07	37
Risk Factors						
Current Smoker	136	4	159	5	0.18	5
Hypertension	1785	59	1772	59	0.86	59
Diabetes Mellitus	782	26	774	26	0.91	26
Insulin	181	6	177	6	0.89	6
Ischaemic Heart Disease	1809	60	1746	58	0.15	59
Chronic Kidney Disease	490	16	522	17	0.26	17
Atrial Fibrillation	1129	39	1118	38	0.84	39
Atrial Flutter	77	3	95	3	0.18	3

Abbreviations: HFpEF, heart failure with preserved ejection fraction (EF ≥ 50%).

The Hosmer and Lemeshow test of significance was 0.206, indicating the model can be adequately fitted to the logistic function. Different cut-offs for haemoglobin, albumin and creatinine were tested and did not significantly influence the results. The odds ratio of the eight predictors were of similar magnitude, and therefore the risk score was calculated by assigning a value of 1 when a variable was present, categorising patients in each cohort by number of predictors present, as shown in Figure 1.

The predictors of frequent readmissions when patients survived beyond 1 year, were elevated creatinine, anaemia, angina as a precipitant and not having private health insurance (Table 5).

Validation of the Risk Model

Validation of the risk model for the composite endpoint of frequent readmission or death is shown in Figure 1. Binary logistic regression using the eight independent predictors was performed on the validation cohort (C-statistic 0.62). The point scoring system was then applied to both derivation and validation cohorts. There was a homogeneous pattern between the cohorts when patients were stratified by risk score since the slope of the increase in event rates with increasing number of risk factors was not statistically different ($p = 0.588$). There was a significant increase in the rate of events with increasing number of risk factors present ($p < 0.001$). We combined the cohorts, giving a total of 6252 patients with hospitalisation for heart failure.

The multivariate predictors of a single readmission within 1 year were largely similar to those for multiple readmissions, but with some differences. In common was a history of ischaemic heart disease and chronic kidney disease, being unmarried, having anaemia, elevated serum creatinine and not receiving beta blockers on hospital discharge. Differences were that low serum albumin and prolonged length of hospital stay predicted multiple but not single readmissions, while being a non-English speaker, being on insulin, and having angina or poor medication compliance as precipitants predicted single but not multiple readmissions.

Discussion

In patients with HF, the burden of frequent hospitalisations on the health care system and patient mortality is well recognised and studied [1,3–5]. However, the majority of studies have focussed on predictors of any readmission and not those with frequent readmissions who contribute disproportionately to morbidity, mortality and health care costs [12,13]. In our cohort with HF, the 18% of patients with ≥2 readmissions within 1 year of initial hospitalisation, contributed to 68% of the total hospitalisations, and had twice the mortality of those who did not. Despite this, approximately 15% of patients with no identifiable risk factors reached the composite endpoint at 1 year. Our data suggests the prognosis associated with elderly heart failure patients in the community is poor, and no truly low risk group can be defined.

Table 2 Clinical characteristics of the Study Patients Hospitalised With Heart Failure.

	Derivation Cohort		Validation Cohort		p-value	Total
	n	%	n	%		%
Admission Data						
Albumin < 35 g/l	1573	50	1609	52	0.23	51
Na < 135 mmol/l	733	23	728	23	1.00	23
K > 5 mmol/l	302	10	322	10	0.35	10
Haemoglobin < 120 g/l	1464	47	1460	47	0.87	47
Creatinine > 100 umol/l	1608	59	1617	59	0.77	59
Presenting Symptoms						
Dyspnoea	2697	92	2702	92	0.43	92
Cough	758	26	762	26	0.82	26
PND	730	25	755	26	0.42	25
Fatigue	898	31	909	31	0.68	31
Weight gain	295	10	307	10	0.57	10
Peripheral Oedema	1401	48	1390	48	0.92	48
Anorexia	398	14	373	13	0.41	13
Palpitations	304	10	321	11	0.47	11
Angina	589	20	564	19	0.45	20
Precipitants						
Recent AMI	188	6.2	215	7.2	0.16	6.7
Ischaemia	684	22.6	704	23.4	0.47	23.0
Arrhythmia	741	24.5	776	25.8	0.24	25.2
Poor Diet	175	5.8	169	5.6	0.83	5.7
Infection	890	29.4	827	27.5	0.11	28.5
Poor Compliance	170	5.6	183	6.1	0.47	5.9
Medication Side Effect	80	2.6	80	2.7	1.00	2.7
Medication Change	173	5.7	163	5.4	0.66	5.6
Discharge Details						
Beta Blocker	1610	53	1585	53	0.75	53
ACEI/ARB	2156	71	2164	72	0.47	72
Diuretics	2548	84	2561	85	0.25	85
Spironolactone	1016	34	1022	34	0.72	34
Digoxin	904	30	903	30	0.88	30
LOS > 7days	1450	46	1381	44	0.14	45

Abbreviations: ACEI/ARB, angiotensin converting enzyme or angiotensin II receptor blocker; Diuretics, not including spironolactone; LOS, length of stay; PND, paroxysmal nocturnal dyspnoea.

Although the risk model does not have strong discriminatory value, it does offer insights into risk factors that are associated with worse outcomes. In particular, the results reinforce the importance of treating anaemia, optimisation of diet to avoid hypoalbuminaemia, maintaining adequate hydration to prevent renal insufficiency and using beta blockers for suitable patients. It is also likely that the high readmissions rates associated with heart failure are largely contributed by the comorbidities. The comorbidities associated with HF patients may be driving an increase in non-HF readmissions. Wider intervention strategies that focus on treating comorbidities in addition to the traditional heart failure management model are needed to minimise readmissions and mortality.

The inclusion in the risk model of not being on beta blocker medication on discharge supports the well documented benefits of beta blockers in HF [16], although it is also possible that the patients were not commenced on beta blockers because of an adverse risk profile. A history of ischaemic heart disease in the model, reinforces the greater potential for ischaemia-related readmissions and need for preventive measures. Anaemia and chronic kidney disease have been previously identified as independent predictors of hospitalisation and death [17]. We have also previously shown in

Table 3 Rate of Frequent Readmissions (≥2) and Mortality Within 1 Year Among Heart Failure Patients.

	Derivation Cohort		Validation Cohort		p-value	Total
	N	%	n	%		%
Outcomes						
Frequent All-Cause Readmissions	570	18	558	18	0.68	18
Frequent HF Readmissions	160	5	159	5	0.40	5
Frequent Non-HF Readmissions	332	11	325	10	0.53	11
1 Year Mortality	493	17	461	16	0.32	17
≥5 Admissions	48	15	50	16	0.45	16

Abbreviation: HF, heart failure.

MACARF a higher rate of frequent readmission among anaemic patients [18], and an association between anaemia and multiple readmissions was seen in EMPHASIS-HF [19]. Treating anaemia in HF patients has been shown to improve outcomes, including reducing the rate of hospitalisations [20,21].

While many of the predictors of frequent readmissions also predicted single readmissions, there were some differences. For example, a prolonged initial length of hospital stay, which is consistent with a more complex condition, was a predictor of multiple but not single readmissions. Similarly, a low serum albumin, reflecting more advanced HF, was predictive of multiple but not single readmissions. In contrast, being a non-English speaker, being on insulin, and having poor medication compliance as a precipitant predicted single but not multiple readmissions. These factors could be identified on a first readmission, and addressed in follow-up, for example providing language specific information for non-English speakers, and with optimal medication packaging and other measures to improve medication compliance. Not having private insurance, which was a predictor of frequent readmission among those who survived at least 1 year, may be a surrogate for reduced socioeconomic level, which has previously been shown to predict frequent readmissions [10].

A recent Australian paper reported a model for predicting any readmission among HF patients using 280 patients [22]. The significant predictors included age, living alone, sedentary lifestyle and multiple comorbidities. The Enhanced Feedback for Effective Cardiac Treatment (EFFECT) study derived a risk model for predicting mortality in patients hospitalised with HF, based on an analysis of a derivation cohort of 2624 patients in 1999–2001 with a validation cohort of 1407 patients from 1997 to 1999 [23]. Our study also used two randomised cohorts, but over the same time period and additionally targeting patients with frequent readmissions. We attempted to minimise the complexity of our model by limiting it to eight easily identifiable variables. Many risk models are complicated by using a multitude of predictors, often with more than one cut-off, and are limited in their bedside application [24]. We specifically targeted frequent readmissions and death at 1 year and used a simple point scoring system that gives each patient an individual risk of event. Although using continuous variables would have given the analysis more statistical power, we elected to use categorical variables to allow for a simple 'yes' or 'no' model for clinicians to use at the bedside. The modest C-statistic of 0.65 emphasises the difficulty in predicting these particularly high-risk HF patients for frequent readmission

Table 4 Multivariate Predictors of Frequent Readmissions or Death for Development of Risk Score for Primary Composite Endpoint in Derivation Model.

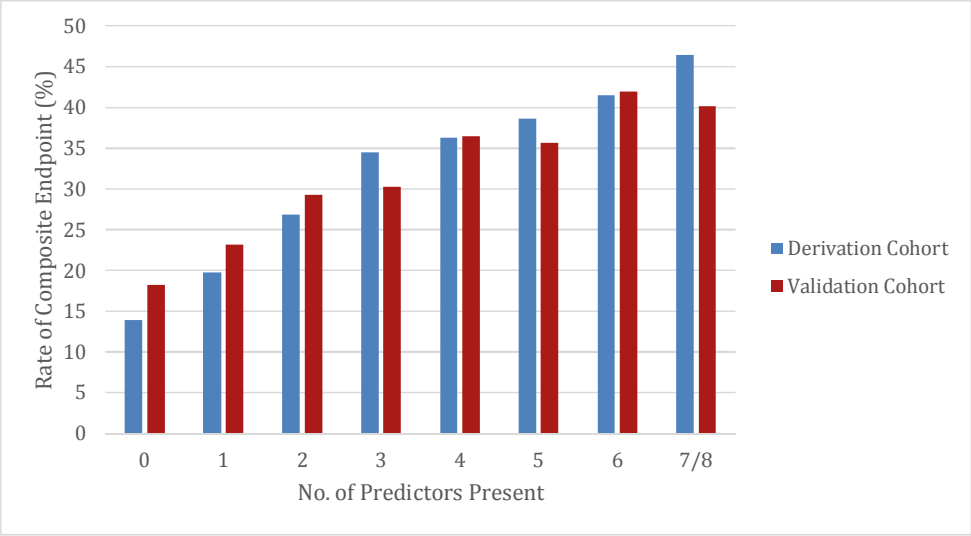
Predictor	OR	95% CI	p-value
Ischaemic Heart Disease	1.45	1.21–1.73	<0.001
Chronic Kidney Disease	1.47	1.16–1.86	0.001
Unmarried	1.22	1.03–1.46	0.024
Haemoglobin < 120 g/L	1.29	1.08–1.55	0.005
Length of hospital stay > 7 days	1.34	1.12–1.59	0.001
Albumin < 35 g/L	1.28	1.07–1.53	0.006
Creatinine > 100 umol/l	1.46	1.20–1.76	<0.001
Not on Beta blocker	1.48	1.24–1.76	<0.001

Abbreviations: OR, odds ratio.
Hosmer and Lemeshow test of significance: 0.206. C-statistic: 0.65.

Table 5 Multivatiate Predictors of Frequent Readmission Excluding Patients Who Died Within 1 Year in Derivation Cohort.

Predictor	OR	95% CI	p-value
No Private Health Insurance	1.29	1.02–1.64	0.033
Angina as a Precipitant	1.37	1.04–1.80	0.025
Haemoglobin < 120 g/L	1.32	1.04–1.67	0.022
Creatinine > 100 umol/l	1.38	1.08–1.76	0.010

Abbreviations: OR, odds ratio.
Hosmer and Lemeshow test of significance: 0.972. C-statistic: 0.593.



		Risk Score							
		0	1	2	3	4	5	6	7/8
Derivation Cohort	Endpoint (%)	14	20	27	34	36	39	41	46
	n	43	182	451	583	703	554	275	114
Validation Cohort	Endpoint (%)	18	23	29	30	36	36	42	40
	n	44	194	416	618	667	538	298	112

n, number of patients at risk of composite endpoint

The 8 predictors were being unmarried, ischaemic heart disease, chronic kidney disease, haemoglobin <120 g/l, hospital length of stay >7 days, albumin <35 g/l, creatinine>100 umol/l and discharge without beta blocker. The number of event rates increased significantly with increasing risk score ($p<0.001$). C-statistic for derivation and validation cohort, 0.65 and 0.62 respectively. The slope of the increase in event rates with increasing risk score was not significantly different between derivation and validation cohorts ($p=0.588$).

Figure 1 Rates of frequent readmissions (≥2) or death within 1 year of initial HF presentation, calculated for the derivation and validation cohort.

and death. Besides HF variables, readmission is influenced by patient and physician factors, psychosocial and health care system issues.

In our analysis, there were no low risk HF patients, since even those with no risk predictors still had a 15% chance of frequent admissions or death at 1 year. However the model can still assist clinicians and HF management programs in targeting the modifiable risk factors identified in our study. Heart failure management programs like MACARF, from which these data were derived, aim to reduce hospitalisations, burden of disease and mortality of HF. Our analysis provides data for clinicians and nurses on the importance of maintaining optimal medical therapy, adequate hydration and diet and treating anaemia in order to prevent readmissions or death.

Our study has several limitations. Our patient population is not a random sample of HF patients and it was not possible to estimate what proportion of admitted patients were accepted into the program. Nevertheless, all patients with HF admitted to hospital were screened for enrolment and patients were excluded only if they refused. Our patients were part of a cardiac management program and may have higher rates of readmission than individuals not enrolled on such a program. Some of the patients may have been readmitted to a hospital outside of the Northern Sydney district and thus not be recorded in our dataset. The modest C-statistic of 0.63–0.65 offers limited discriminatory value and likely reflects the poor prognosis associated with all HF patients. Our prediction model was for combined readmissions due to HF and non-HF although it is possible that the risk factors differ between causes of readmission. It is also possible that changes in the cohort over the time period may have contributed to some heterogeneity. We chose not to separate the derivation and validation groups chronologically as this may have reduced the predictive power of the model. We note that the current model would need to be

updated as trends in HF continue to evolve. Chronic kidney disease was identified if it was mentioned as a prior diagnosis in the medical records. It is possible that differences in definitions of chronic kidney disease may exist and could explain some of the differences with elevated serum creatinine. Other variables such as frailty, cognitive impairment, Charlson comorbidity profile and BNP levels were not routinely recorded in our study, and will need to be explored in future models of frequent readmission. Although measures were made to minimise missing data, some incomplete data may also be a limiting factor.

Conclusion

The present study has identified independent risk factors of frequent readmissions or death and offers insights into areas of focus for prevention. It is important that clinicians and HF management programs focus on treating anaemia, maintaining adequate hydration and diet to minimise kidney disease and hypoalbuminaemia and ensure adherence with beta blockers in suitable patients. The model's modest discriminatory ability emphasises the poor prognosis associated with all HF patients.

Disclosures

We have nothing to disclose.

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