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Referral for Specialist Follow-Up and its Association with Post-Discharge Mortality among Patients with Systolic Heart Failure (From the National Heart Failure Audit for England & Wales)

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Abstract

For patients admitted with worsening heart failure, early follow-up after discharge is recommended. Whether outcomes can be improved when follow-up is done by cardiologists is uncertain. We aimed to determine the association between cardiology follow-up and risk of death for patients with heart failure discharged from hospital. Using data from the National Heart Failure Audit (England & Wales), we investigated the effect of referral to cardiology follow-up on 30-day and one-year mortality in 68 772 patients with heart failure and a reduced left ventricular ejection fraction (HFREF) discharged from 185 hospitals between 2007 to 2013. The primary analyses used instrumental variable analysis complemented by hierarchical logistic and propensity matched models. At the hospital level, rates of referral to cardiologists varied from 6% to 96%. The median odds ratio (OR) for referral to cardiologist was 2.3 (95% confidence interval [CI] 2.1, 2.5), suggesting that, on average, the odds of a patient being referred for cardiologist follow-up after discharge differed approximately 2.3 times from one randomly selected hospital to another one. Based on the proportion of patients (per region) referred for cardiology follow-up, referral for cardiology follow-up was associated with lower 30-day (OR 0.70; CI 0.55, 0.89) and one-year mortality (OR 0.81; CI 0.68, 0.95) compared with no plans for cardiology follow-up (i.e., standard follow-up done by family doctors). Results from hierarchical logistic models and propensity matched models were consistent (30-day mortality OR 0.66; CI 0.61, 0.72 and 0.66; CI 0.58, 0.76 for hierarchical and propensity matched models, respectively). For patients with HFREF admitted to hospital with worsening symptoms, referral to cardiology services for follow-up after discharge is strongly associated with reduced mortality, both early and late.

Key Words: Heart failure, follow up, specialist, instrumental variables, health services

Introduction

In the United Kingdom's healthcare system, cardiology care is generally provided by the hospitals and, hence, any policy recommendation for routine cardiology follow-up would have major resource and organisational implications for those hospital staff and payers not currently providing this component. We sought to assess this policy recommendation by investigating the effect of referral to cardiology follow-up on the risk of 30-day and one-year mortality in a large cohort of patients admitted for HFREF in England and Wales.

Methods

This study is a part of the UNVEIL-CHF study (Understanding National Variation and Effects of Interventions at different Levels of Care for Heart Failure), which aims to characterize variation in care and outcomes for patients hospitalized for heart failure between 2007 and 2013 and enrolled in the National Heart Failure Audit for England & Wales.[1] Only hospital admissions in which the patient survived to discharge were eligible for inclusion in the study. We restricted our analysis to patients with HFREF (an ejection fraction <40% or evidence of left ventricular systolic dysfunction) because clearly defined and evidence-based treatment recommendations exist only for this subgroup of heart failure patients. For patients with more than one hospital admission (10280, 14.4%), we randomly selected one admission. Our exposure was referral for cardiology follow-up after discharge from the hospital. Follow-up started from the date of discharge and was censored at death or the end of follow-up (March 2013). Two primary outcomes, 30-day and one-year mortality, were used. As longer term (>6 months) follow-up was not available for individuals admitted in 2012/13, the analyses of one year mortality was restricted to 2007-2011. The analyses of 30-day mortality was from 2007 until March 2013.

Since findings from non-randomised comparisons are commonly subject to confounding, our primary analysis was based on a quasi-randomised design with the use of an instrumental variable approach.[2] A valid instrument is correlated with the treatment of interest (referral to cardiology follow-up) but is not correlated with the outcome of interest (30-day and one year mortality), except through the treatment of interest. [3] We thus used regional variation in referral to cardiology follow-up, that is, the proportion of patients referred for cardiology follow-up in a given region, as our instrumental variable. The instrument was validated by classifying regions into fifths, to examine whether prognostic factors related to mortality are similar across regions and to demonstrate that it is unlikely that regional variation in cardiology referral would impact mortality other than through difference in rates of referral to cardiology follow-up.[2] Two-stage least squares logistic regression with robust standard errors was then used to estimate the causal effect of referral for cardiology follow-up on 30-day and one-year mortality.

In addition, we conducted two complementary statistical techniques to ensure that findings from our main analysis are robust to our design and modelling assumptions.[4] First, hierarchical logistic models were used to examine the association between referral to cardiology follow-up and risk of 30-day and one-year mortality, adjusting for thirty four covariates: age, sex, NYHA class I, II, III or IV, peripheral oedema (none, mild, moderate or severe), history of diabetes, history of ischemic heart disease, history of hypertension, history of valve disease, atrial fibrillation, left bundle branch block, previous myocardial infarction, diastolic dysfunction, left ventricular hypertrophy and valve disease, prescription of ACE-inhibitors/ARBs, aldosterone receptor antagonists, loop diuretics, thiazide diuretics, beta-blockers, digoxin, referral for heart failure specialist nurse follow up, referral for palliative care

follow up, referral for geriatric follow up, treatment on a cardiology ward as well as dummy variables for year of admission (2007, 2008, 2009, 2010, 2011, 2012, 2013). Second, propensity score matching was used to restrict any analysis to patients who were similarly likely to be referred to cardiology follow-up. Logistic regression was used to generate a propensity score for each patient being referred for cardiology follow-up. In total, one hundred covariates were included in the logistic regression model: the same thirty-four baseline covariates as above, as well as interaction terms between age, sex and all covariates excluding age and sex. Patients referred for cardiology follow-up were then matched one to one without replacement with individuals who were not referred for cardiology follow-up. The effectiveness of the matching process was gauged by examining the post-matching balance on covariates. Hierarchical logistic regression was performed on the matched sample, adjusting for all thirty-four covariates. Multiple imputation with chained equations was used to impute missing data; five imputations were generated. No covariate or outcome was missing at a rate exceeding 15%.

Study findings are reported in accordance with the STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) recommendations.[5] No ethics approval was needed for this analysis; the National Heart Failure Audit was conducted with the approval of the NHS Information Centre.

Results

Overall, 68 772 patients with HFREF discharged from 185 hospitals were included in the analyses. At the hospital level, rates of referral to cardiologists varied from 6% to 96%. The median odds ratio (OR) for referral to cardiologist was 2.3 (95% confidence interval [CI] 2.1, 2.5), suggesting that, on average, the odds of a patient being referred for cardiologist follow-up after discharge differed

approximately 2.3 times from one randomly selected hospital to another one. Hospitals which were tertiary hospitals and which had greater numbers of consultant cardiologists had higher rates of referral to cardiology follow up (Supp. Table).

The predicted mortality for patients referred for cardiology follow-up was lower than those not referred for follow-up (26% vs. 32%, Table 1). Patients referred for cardiology follow-up tended to be younger, and more likely to be prescribed ACE-inhibitors/angiotensin receptor blockers and beta-blockers at discharge (Table 1). Furthermore, patients referred for cardiology follow-up were more likely to be treated on a cardiology ward (70% of those referred for follow-up vs. 38% of those not referred) (Table 1).

For the instrumental variable analysis, we first tested the validity of the instrument. The proportion of patients referred for cardiology follow-up varied significantly across regions, from 5% to 100% of patients. When regions were divided into fifths by proportion of patients referred for cardiology follow-up, patient characteristics were broadly similar (Table 2). Predicted one year mortality varied slightly across regions, ranging from 29% to 27% from the lowest to highest quintile of referral, although this difference was similar to previous analyses which utilized regional variation.[2]

When regional proportion of patients referred for cardiology follow-up was used as an instrument, referral for cardiology follow-up was significantly associated with lower thirty-day (OR 0.70 CI 0.55, 0.89) and reduced one-year mortality (OR 0.81 CI 0.68, 0.95, Table 3).

In hierarchical analysis, after adjustment, referral for cardiology follow-up was associated with a substantially lower risk of thirty-day mortality (OR 0.66 CI 0.61, 0.72) and one-year mortality (OR 0.74 CI 0.70, 0.78, Figure 1). After

propensity score matching, 11 571 heart failure patients referred for cardiology follow-up were matched to 11 571 heart failure patients not referred for cardiology follow-up; 45 630 patients were excluded. Predicted one-year mortality was very similar between patients who were or were not referred for cardiology follow-up (28% vs 28%, standardized difference of 0.8%), as was age, gender, breathlessness and medical history (all standardized differences <2%, Table 1). After adjustment for thirty-four covariates on the matched sample, referral for cardiology follow-up was still associated with a substantially lower thirty-day (OR 0.66 CI 0.58, 0.76) and one-year mortality (OR 0.74 CI 0.67, 0.82). Estimates were similar when propensity score was also included in the model (data not shown).

Instrumental variable estimation of the association between referral for cardiology follow-up and one-year mortality was not substantially different if early deaths were excluded (OR 0.84 CI 0.71, 0.99), although this did attenuate the effect on 30-day mortality (OR 0.84 CI 0.64, 1.11) suggesting a very early impact of specialist care.

Discussion

We investigated the effect of the policy recommendation that patients with HFREF should have care by specialist cardiology services after discharge from hospital. With the use of instrumental variable method, which exploits natural random allocation of patients to a certain exposure variable (in this case referral for cardiology follow-up by small geographic regions), we show that referral to specialist cardiology services is strongly associated with lower risk of death after discharge. In this large national linked database, arrangement of a follow-up appointment after discharge with a cardiologist was associated with a 30% lower odds of death at 30 days post discharge (OR 0.70, CI 0.55, 0.89) and a 19% lower odds at one year post discharge

(OR 0.81, CI 0.68, 0.95). These findings were robust to alternative statistical modeling techniques and assumptions.

To our knowledge, this is the first study to demonstrate that referral for cardiology follow-up soon after discharge with heart failure is associated with a substantial reduction in mortality. This has important implications for policy and practice to improve outcomes. As suggested in an earlier report, interventions to tackle the low referral rates after discharge could also contribute to reductions in between-hospital variation in quality of care.[6]

However, there are several potential limitations to our findings. First, we only examined the association of cardiology follow-up with mortality in heart failure with reduced ejection fraction as there are few recommended therapeutic interventions for heart failure with preserved ejection. Second, our analysis relied upon retrospective registry data, which may contain recording errors of patients' diagnoses. Third, our instrumental variables analysis was not powered to examine the association of referral to cardiology follow-up with mortality in subgroups. Consequently the effect of cardiology follow-up on outcomes in certain subgroups of HF patients, such as those who are NYHA class I, may differ from the effect of cardiology follow up in the overall HFREF population. Despite our rigorous design and analytical approach, we cannot entirely rule out that some of the association observed is due to unmeasured confounding factors. Policy interventions can be costly and a formal cost-effectiveness analysis might also be needed to guide decision makers about the costs and consequences of cardiology follow-up. In this context, future studies should also address the impact of the intervention on other important outcomes such as re-hospitalization.

Conflicts of interest

MW reports consultancy fees from Amgen and Novartis.

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Figure Legend

Figure 1.

Risk of death adjusted for thirty four covariates and stratified by referral to cardiology follow-up.

Table 1. Selected baseline characteristics by referral for cardiologist follow-up.

	Overall Cohort			Propensity Matched Cohort		
	Follow Up (n=40769)	**No Follow Up (n=28003)**	**Standardised Difference**	**Follow Up (n=11571)**	**No Follow Up (n=11571)**	**Standardised Difference**
Predicted one year mortality (HF severity)[1]	25.5%	32.0%	52.7%	28.2%	28.3%	0.8%
Age (years)						
<60	17.9%	6.5%	35.5%	10.8%	11.0%	0.7%
60-80	52.9%	39.3%	27.6%	51.4%	50.5%	1.7%
>80	29.2%	54.2%	52.6%	37.8%	38.4%	1.3%
Women	32.4%	42.5%	21.0%	64.3%	64.4%	0.1%
NYHA Class						
I	6.3%	6.6%	1.2%	6.5%	6.6%	0.2%
II	19.3%	16.8%	6.5%	18.4%	18.3%	0.2%
III	45.9%	44.5%	2.8%	45.2%	45.5%	0.6%
IV	28.6%	32.2%	7.9%	29.9%	29.7%	0.6%
Peripheral Oedema						
None	31.1%	24.9%	13.7%	28.3%	28.1%	0.4%
Mild	26.3%	25.6%	1.6%	26.2%	25.9%	0.7%
Moderate	28.7%	32.5%	8.3%	30.2%	30.5%	0.7%
Severe	14.0%	17.0%	8.2%	15.3%	15.4%	0.4%
Diabetes mellitus	30.0%	29.4%	1.2%	31.0%	30.9%	0.1%
Hypertension	50.6%	51.8%	2.4%	51.3%	51.0%	0.7%
Coronary Heart Disease	51.4%	51.3%	0.4%	52.8%	52.6%	0.3%
Valve Disease	19.7%	18.4%	3.3%	18.9%	19.0%	0.3%
Baseline ECG						
Atrial fibrillation	36.9%	44.3%	15.3%	39.5%	39.9%	0.6%
Left bundle branch block	12.8%	11.5%	4.0%	12.2%	12.2%	0.1%
Previous Myocardial Infarction	2.2%	1.7%	4.1%	1.9%	2.0%	0.3%
Baseline ECHO						
Diastolic dysfunction	1.1%	1.0%	0.6%	1.0%	1.0%	0.5%
Left ventricular hypertrophy	0.9%	1.3%	4.2%	1.0%	1.0%	0.4%
Valve disease	5.4%	6.1%	2.9%	5.7%	5.4%	1.0%
Treated on Cardiology Ward	70.4%	38.2%	68.3%	59.0%	59.0%	0.1%
Therapies						
ACE/ARB	84.6%	73.6%	27.3%	81.2%	81.2%	0.2%
Beta-blocker	77.6%	64.2%	30%	73.1%	73.3%	0.6%

HF= heart failure; NYHA=New York Heart Association; ECG=electrocardiogram; ECHO=echocardiogram; ACEI/ARB = Angiotensin-converting enzyme inhibitor/Angiotensin-receptor blocker

[1]Logistic regression, adjusted for age, sex, breathlessness, peripheral oedema, history of diabetes, history of ischemic heart disease, history of hypertension, history of valve disease, atrial fibrillation, left bundle branch block, previous myocardial infarction, diastolic dysfunction, left ventricular hypertrophy and valve disease, used to predict the likelihood of death within one year.

Table 2. Selected patient characteristics across the fifths of cardiology referral for follow-up at regional levels.

	Quintile of Regional Referral to Cardiology Follow Up Rates				
	Q1 (4.6-43.7)	Q2 (43.7-54.3)	Q3 (54.7-63.7)	Q4 (64.2-74.0)	Q5 (75.0-100)
Number of patients[1]	13539	13444	13977	13351	14461
Cardiology Referral Rate	34.4%	49.2%	59.1%	69.2%	83.0%
Predicted one year mortality (HF severity)	29.4%	28.7%	28.1%	27.5%	26.8%
Age (years)					
<60	10.4%	12.0%	13.4%	14.5%	15.9%
60-80	45.4%	45.8%	47.0%	48.1%	50.3%
>80	44.2%	42.2%	39.6%	37.4%	33.8%
Women	39.1%	37.1%	36.9%	35.5%	34.0%
NYHA Class					
I	8.1%	7.0%	6.2%	5.5%	5.2%
II	16.4%	17.4%	18.0%	19.1%	20.3%
III	42.6%	44.3%	46.5%	47.8%	45.5%
IV	32.9%	31.3%	29.3%	27.6%	29.0%
Peripheral Edema					
None	28.8%	29.3%	28.3%	27.9%	28.6%
Mild	24.1%	25.4%	26.2%	27.2%	26.9%
Moderate	30.6%	29.9%	30.2%	30.1%	30.2%
Severe	16.5%	15.4%	15.3%	14.8%	14.3%
Diabetes mellitus	27.6%	29.2%	29.8%	30.7%	31.3%
Hypertension	48.2%	50.1%	51.5%	53.2%	52.5%
Coronary heart disease	48.9%	50.7%	51.2%	52.8%	53.1%
Valve disease	18.8%	19.6%	18.8%	19.0%	19.8%
Baseline ECG					
Atrial fibrillation	41.5%	40.5%	40.3%	39.4%	38.0%
Left bundle branch block	12.0%	12.9%	12.7%	12.4%	11.6%
Previous myocardial infarction	1.7%	1.7%	1.9%	2.3%	2.5%
Baseline ECHO					
Diastolic dysfunction	0.7%	1.1%	1.1%	1.2%	1.1%
Left ventricular hypertrophy	1.0%	1.3%	1.1%	1.0%	0.8%
Valve disease	5.9%	6.6%	5.9%	5.6%	4.6%
Treated on Cardiology Ward	49.8%	54.2%	56.1%	56.1%	66.9%
Therapies					
ACE-I/ARB	78.6%	79.4%	79.9%	81.1%	81.8%
Beta-blocker	69.7%	70.7%	71.4%	73.2%	75.5%

HF= heart failure; NYHA=New York Heart Association; ECG=electrocardiogram; ECHO=echocardiogram; ACEI/ARB = Angiotensin-converting enzyme inhibitor/Angiotensin-receptor blocker

[1.] Rounded to nearest number from multiply imputed estimates.

Table 3. Association between type of follow up and thirty day and one year mortality.

	30-day Mortality Odds Ratio (95% CI)	p-value	One Year Mortality Odds Ratio (95% CI)	p-value
Cardiology Follow Up vs. No Cardiology Follow Up				
Multivariable adjusted	0.66 (CI 0.61, 0.72)	p<0.001	0.74 (CI 0.70, 0.78)	p<0.001
Propensity score matched	0.66 (CI 0.58, 0.76)	p<0.001	0.74 (CI 0.67, 0.82	p=0.002
Instrumental variable estimated	0.70 (CI 0.55, 0.89)	p=0.005	0.81 (CI 0.68, 0.95)	p=0.012

All models adjusted for 34 demographic, clinical and therapy variables. age, gender, NYHA breathlessness, level of peripheral oedema, history of diabetes, history of hypertension, history of ischemic heart disease, history of valve disease, atrial fibrillation, left bundle branch block, evidence of myocardial infarction on baseline ecg, treatment in cardiology ward, treatment with aldosterone receptor antagonists, treatment with ACE inhibitors or ARB, treatment with beta blockers, treatment with digoxin, treatment with thiazide diuretics, treatment with loop diuretics, referral for specialist HF nurse follow up, referral for care of the elderly follow up, referral for palliative care follow up and baseline year of discharge. Propensity matched estimate is adjusted for the same variables, but matched on the interaction of all thirty variables with sex and age, in addition to the thirty covariates adjusted for.

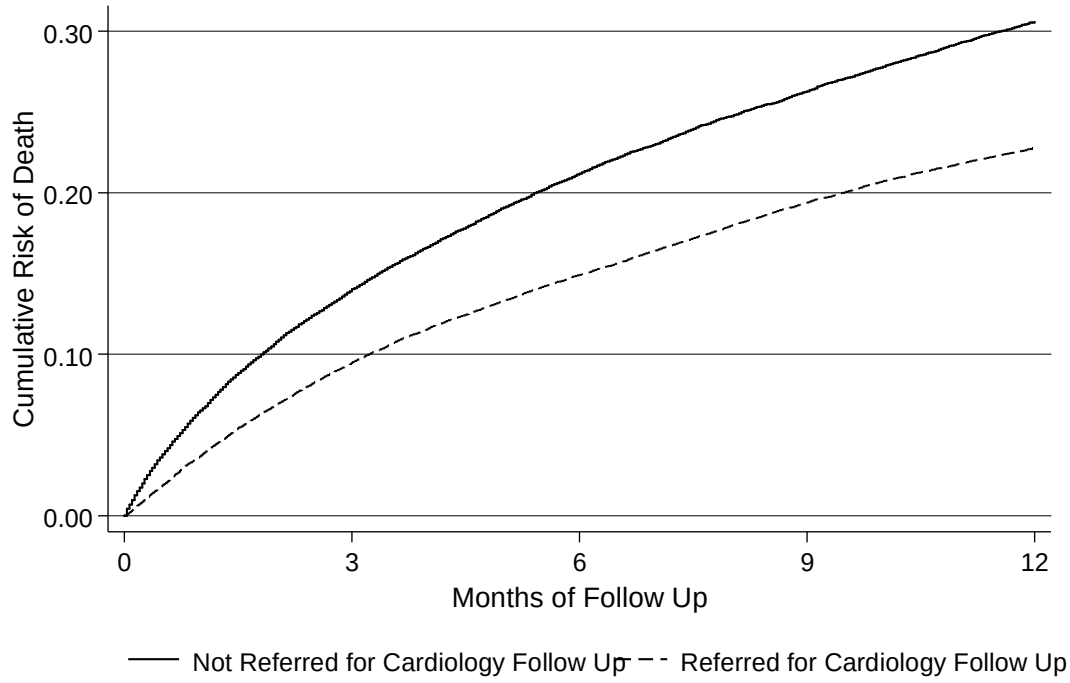
Table 4. Association between type of follow up and thirty day and one year mortality after exclusion of deaths in the first seven days.

	30-day Mortality		One Year Mortality	
Cardiology Follow Up vs. No Cardiology Follow Up	Odds Ratio	p-value	Odds Ratio	p-value
Multivariable adjusted	0.70 (CI 0.63, 0.77)	p<0.001	0.75 (CI 0.71, 0.79)	p<0.001
Propensity score matched[1]	0.69 (CI 0.60, 0.81)	p<0.001	0.76 (CI 0.68, 0.85)	p<0.001
Instrumental variable estimated	0.84 (CI 0.64, 1.11)	p=0.226	0.84 (CI 0.71, 0.99)	0.034

All models adjusted for 34 demographic, clinical and therapy variables. age, gender, NYHA breathlessness, level of peripheral oedema, history of diabetes, history of hypertension, history of ischemic heart disease, history of valve disease, atrial fibrillation, left bundle blockers, evidence of myocardial infarction on baseline ecg, treatment in cardiology ward, treatment with aldosterone receptor antagonists, treatment with ACE inhibitors or ARB, treatment with beta blockers, treatment with digoxin, treatment with thiazide diuretics, treatment with loop diuretics, referral for specialist HF nurse follow up, referral for care of the elderly follow up, referral for palliative care follow up and baseline year of discharge. Propensity matched estimate is adjusted for the same variables, but matched on the interaction of all thirty variables with sex and age, in addition to the thirty covariates adjusted for. Instrumental variable estimate utilizes proportion of patients referred for cardiology follow up in 3360 regions.

[1]Non hierarchical logistic model used due to a lack of convergence with the hierarchical model. Standard errors instead adjusted for clustering at the hospital level.

Figure 1. Risk of death adjusted[1] for thirty four covariates and stratified by referral to cardiology follow-up.



[1]Survival curves are plotted at the mean of each covariate using Cox regression.