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A Propensity-Matched Study of the Association of Education and Outcomes in Chronic Heart Failure

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Abstract

Background—Heart failure (HF) patients' knowledge about their disease may improve short-term outcomes and may be related to their level of education. However, the effects of patients and spousal education on long-term outcomes in ambulatory chronic HF are unknown. .

Methods—Of the 571 patients enrolled in the quality of life sub-study of the Digitalis Investigation Group trial, 159 patients or their spouses reported having higher (>12 years) education. Propensity score for higher education, calculated for each patient using a logistic regression model, was used to match 112 (70% of 159) higher education patients with 215 patients with high school (≤12 years) education. Matched Cox regression analyses were used to estimate associations of high school education with mortality and hospitalizations.

Results—All-cause hospitalizations occurred in 56% (rate, 3233/10,000 person-years) of higher education and 65% (rate, 4558/10,000 person-years) of high school education patients (hazard ratio {HR} for high school, compared with higher education=1.52; 95% confidence interval {CI}=1.06–2.16; p=0.022). Hospitalizations due to cardiovascular causes occurred in 42% (rate, 2067/10,000 person-years) of higher education and 50% (rate, 4558/10,000 person-years) of high school education patients (HR=1.55; 95% CI, 1.05–2.30; p=0.029). All-cause mortality occurred in 20% (rate, 746/10,000 person-years) of higher education and 30% (rate, 1204/10,000 person-years) of high school education patients (HR=1.52; 95% CI=0.89–2.58; p=0.124).

Conclusions—Compared with >12 years of education, lower education was associated with increased hospitalizations among ambulatory chronic HF patients. Patient and spousal education levels may be used to risk stratify HF patients at high risk for hospitalizations.

Keywords

Education; heart failure; mortality; hospitalization

1. Introduction

Systematic and tailored health education to improve heart failure (HF) patients' knowledge and understanding about their disease symptoms and treatment has been shown to improve short-term outcomes [1–5]. Patients' understanding of their chronic medical conditions and their ability to learn about them may be influenced by their education level, and that of their spouses [6]. Higher levels of education have also been shown to be associated with higher levels of disease-specific knowledge, healthy lifestyle, and improved outcomes [7–11]. However, the effects of education levels of patients and their spouses on long-term outcomes in ambulatory chronic HF have not been well studied. In the current analysis, we examined the association between education and long-term outcomes in a propensity score matched cohort of chronic HF patients enrolled in the quality of life sub-study of the Digitalis Investigation Group (DIG) trial.

2. Methods

We conducted a post-hoc propensity-matched study of a public-use version of the DIG dataset obtained from the National Heart, Lung and Blood Institute. During 1991–1993, 7788 ambulatory chronic HF patients (6800 systolic HF, with left ventricular ejection fraction $\leq 45\%$) were recruited from 302 centers in the United States and Canada, and were randomized into digoxin and placebo groups [12]. Of these, 93% patients were receiving angiotensin-converting enzyme inhibitor and 78% were receiving diuretics. The median follow-up time for DIG participants were 38 months. Vital status was collected up to December 31, 1995 and was ascertained for 99% of the patients [13].

A subgroup of 581 patients, who participated in the DIG Quality of Life sub-study, responded to questions about their and their spouses' educational background. We categorized patients into high school (≤ 12 years) and higher (>12 years) education groups based on the education of patients or their spouses. Of the 571 patients (10 patients with missing education data were excluded from this analysis), 159 (28% of 571) patients had higher education. Next, we estimated propensity scores for higher education for all 571 patients, using a non-parsimonious multivariable logistic regression model (c statistic=0.73), and used that to match 112 (70% of 159) patients with higher education and 215 patients with high school education (1 patient with higher education were matched with up to 2 patients with high school education) in order to reduce the imbalance in baseline covariates. All baseline patient characteristics displayed in Table 1 and clinically plausible interactions [14–16] were included in the model as covariates. The propensity score is the conditional probability of receiving an exposure (e.g. higher education) given a set of measured covariates, and can be used to adjust for selection bias when assessing causal effects in observational studies [17,18]. Pre-match mean propensity scores for patients with higher education and high school education were respectively 0.36765 and 0.24440 (absolute standardized difference, 83%; t-test p, <0.0001). After matching, mean propensity scores for higher and high school education were respectively 0.31797 and 0.30616 (absolute standardized difference, 8%; t-test p, 0.485). We also used Pearson chi-square and Student's t test to compare the baseline characteristics of HF patients with higher education versus high school education before and after matching.

The primary outcomes of this analysis were all-cause mortality and all-cause hospitalization. However, we also studied mortality and hospitalization due to cardiovascular causes and worsening heart failure as secondary outcomes. Kaplan-Meier and matched Cox regression analysis were used to determine the effect of baseline education level on mortality and hospitalization. All data analyses were performed using SPSS for Windows version 14 (SPSS, Chicago, Illinois). All *P* values were 2-sided and *P* < 0.05 was regarded as statistically significant.

3. Results

The mean ($\pm$ SD) age of the 327 matched patients was 64 ($\pm$ 12) years, (median 65; range 28–92), 22% were women, and 12% were non-whites. There were significant pre-match imbalances in several prognostically important covariates including age and sex that were balanced after matching (Table 1 and Figure 1). Absolute standardized differences for most baseline covariates were $<10\%$ in the post-matching cohort, suggesting substantial reduction of bias [14,19,20].

During an average 30 months of follow up (range, 0.3 to 45.4 months), hospitalizations due to all causes, cardiovascular causes and worsening HF occurred respectively in 202 (62%), 155 (47%) and 78 (24%) patients. Kaplan-Meier plots for hospitalizations are displayed in Figures 2 a–c. All-cause hospitalizations occurred in 56% (63/112) of patients in the higher education group (rate, 3233/10000 person-years) during a total of 195 person-years of follow-up and 65% (139/215) of patients in the high school education group (rate, 4558/10000 person-years) during a total of 305 years of follow-up (hazard ratio =1.52; 95% confidence interval =1.06–2.16; $p=0.022$; Table 2).

Hospitalizations due to cardiovascular causes occurred in 42% (rate, 2067/10000 person-years) of higher education and 50% (rate, 3009/10000 person-years) of high school patients (hazard ratio =1.55; 95% confidence interval =1.05–2.30; $p=0.029$; Table 2). Hospitalizations due to worsening HF occurred in 20% (rate, 826/10000 person-years) of higher education and 26% (rate, 1223/10000 person-years) of high school education patients (hazard ratio =1.63; 95% confidence interval =0.94–2.81; $p=0.082$; Table 2).

During an average 30 months of follow-up, 86 (26%) patients died from all causes, 75 (23%) due to cardiovascular causes, and 32 (10%) due to progressive HF. All-cause mortality occurred in 20% (22/112) of patients in the higher education group (rate, 746/10000 person-years) during a total of 295 person-years of follow-up and 30% (64/215) of patients in the high school education group (rate, 1204/10000 person-years) during a total of 531 years of follow-up (hazard ratio =1.52; 95% confidence interval =0.89–2.58; $p=0.124$; Table 2). Associations of education with cardiovascular and HF mortalities and hospitalizations are displayed in Table 2.

4. Discussion

We observed that compared with ≥ 12 years of education, <12 years of patient or spousal education was associated with significant increase in hospitalizations due to all causes and cardiovascular causes, with a trend toward increase in HF hospitalizations, among ambulatory chronic HF patients. However, <12 years of education was not statistically associated with significant increase in mortality, likely due to small sample size of our study. These findings are important as HF patients and their spouses' education levels can be used to identify HF patients at increased risk for hospitalizations.

As education levels correlate positively with socioeconomic status [21,22], patients with higher education may have better understanding and knowledge of their disease process and treatment thereof. They also have easier access to high quality health care [23]. Patients with lower education levels are less likely to have a regular primary care physician [24,25], to see or consult a cardiologist [26,27], or be adherent to therapeutic recommendations [28,29]. In addition, lower education level has been shown to be associated with poor quality of life [30], anxiety [30], physical and emotional distress [31], and inability to actively participate in self-care recommendations [32–34]. Non-compliance with medications and diet contributes to worsening HF symptoms, in many cases leading to HF hospitalizations [35]. Even though association of education level and hospitalization due to worsening HF did not reach statistical

significance, likely due to small number of events, the association was in the same direction as for total and cardiovascular hospitalizations, and was of borderline significance. This consistency of associations of lower education with hospitalizations due to both cardiovascular and non-cardiovascular causes adds to the internal validity of our findings. Lack of significant association between education level and mortality was likely due to small number of events. For example, among patients in the lower education group, compared with 139 events of all-cause hospitalization, there were only 64 events of all-cause mortality. However, the large increase in absolute rates in all-cause mortality (458 extra deaths in patients with <12 years of education per 10000 person-years of follow-up) and the large magnitude (52%, similar to that of all-cause hospitalization; Table 2) of relative increase in all-cause mortality suggest that our study was underpowered to detect a significant association between education and mortality.

Data from non-HF patient populations suggest that lower education levels may be associated with increased mortality [10,11,36]. Among HF patients, lower socioeconomic status has been shown to be associated with increased HF hospitalization in hospitalized acute HF patients [27]. Education has also been shown to be associated with incident HF in men [37]. However, to the best of our knowledge, this is the first study of an association of education level and long-term outcomes in a cohort of propensity matched patients with chronic HF [27,35,37].

Despite improvements in therapy, rates of hospitalization and readmission in HF patients remain high [38]. It is estimated that approximately half of all HF readmissions may be preventable [32,35]. Lack of adherence to and insufficient knowledge about diet, medication and HF symptoms may contribute to HF hospitalizations and readmissions [32,33]. Our findings suggest that HF patients with lower level patient or spousal education are at increased risk of hospitalization and that these patients might benefit from targeted intervention to improve their knowledge about their disease [1–4].

These results of our study should be interpreted in light of its limitations. We did not have data on patients' income, occupation, and insurance status. We used both patients' and their spouses' education levels; however, we had no data if spouses were living with the patients or were involved in care giving. Though propensity score matching can account for imbalances in all measured covariates, it may or may not balance unmeasured covariates. However, for any unmeasured confounder to explain away our finding it must be strongly related to both education level and outcomes, and be not strongly related to any of the many baseline covariates used in our analysis [12,14]. Patients in our study were relatively younger, predominantly white men with normal sinus rhythm, thus limiting generalizability. Further, since the conduct of the DIG trial, the treatment of HF has changed significantly, and has become more complex and poly-pharmaceutical, potentially making it more difficult for patients with lower education to comprehend and adhere to. Thus, it is likely that associations observed in our analysis will be more pronounced in contemporary HF patients. Therefore, the results of this study needs to be replicated in contemporary HF patients.

In conclusion, educational status of HF patients and their spouses may be used to risk stratify HF patients at increased risk of hospitalizations, and probably of mortality, and targeted for appropriate interventions. Future prospective studies are needed to assess the potential prognostic role of education level in contemporary HF patients, and interventions need to be developed and tested to improve outcomes in those with lower levels of education.

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Figure 1.
Absolute standardized differences for covariates between patients with high school education and higher education, before and after propensity score matching

Figure 2a

Number at risk				
High school education	215	120	71	21
Higher education	112	70	52	16

Figure 2b

Number at risk				
High school education	215	139	91	31
Higher education	112	78	66	27

Figure 2c

Number at risk				
High school education	215	168	136	49
Higher education	112	90	84	37

Figure 2. Kaplan-Meier plots for hospitalization due to (a) all-causes, (b) cardiovascular causes, and (c) worsening heart failure

Table 1
Baseline patient characteristics, before and after propensity score matching, by patient and spouse education

N (%) or mean ($\pm$ SD)	Before matching			After matching		
	High school education (≤ 12 years) (N=412)	Higher education >12 years (N=159)	P	High school education (≤ 12 years) (N=215)	Higher education (>12 years) (N=112)	P
Age (years)	65.5 (± 11.8)	62.0 (± 11.2)	0.001	63.8 (± 12.0)	63.5 (± 11.0)	0.850
Female	119 (28.9%)	33 (20.8%)	0.049	47 (21.9%)	25 (22.3%)	0.924
Non-white	61 (14.8%)	19 (11.9%)	0.378	26 (12.1%)	13 (11.6%)	0.898
Body mass index, kg/sq meter	27.8 (± 5.9)	27.6 (± 5.7)	0.787	27.8 (± 5.5)	27.7 (± 5.7)	0.834
Duration of HF (months)	21.9 (± 32.0)	25.4 (± 38.6)	0.280	22.1 (± 34.2)	22.7 (± 34.4)	0.893
Primary cause of HF						
Ischemic	279 (67.7%)	106 (66.7%)		143 (66.5%)	80 (71.4%)	
Hypertensive	52 (12.6%)	18 (11.3%)		25 (11.6%)	10 (8.9%)	
Idiopathic	60 (14.6%)	27 (17.0%)	0.892	35 (16.3%)	15 (13.4%)	0.748
Others	21 (5.1%)	8 (5.0%)		12 (5.6%)	7 (6.3%)	
Prior myocardial infarction	267 (64.8%)	102 (64.2%)	0.883	139 (64.7%)	76 (67.9%)	0.562
Current angina	128 (31.1%)	41 (25.8%)	0.215	67 (31.2%)	36 (32.1%)	0.856
Hypertension	187 (45.4%)	72 (45.3%)	0.982	103 (47.9%)	49 (43.8%)	0.474
Diabetes	107 (26.0%)	47 (29.6%)	0.386	60 (27.9%)	30 (26.8%)	0.829
Chronic kidney disease	182 (44.2%)	73 (45.9%)	0.708	97 (45.1%)	55 (49.1%)	0.492
Medications						
Pre-trial digoxin use	161 (39.1%)	58 (36.5%)	0.567	84 (39.1%)	41 (36.6%)	0.664
Trial use of digoxin	201 (48.8%)	89 (56.0%)	0.124	110 (51.2%)	57 (50.9%)	0.963
ACE inhibitors	361 (87.6%)	137 (86.2%)	0.640	184 (85.6%)	97 (86.6%)	0.800
Hydralazine & nitrates	6 (1.5%)	4 (2.5%)	0.476	5 (2.3%)	3 (2.7%)	1.000
Diuretics	303 (73.5%)	124 (78.0%)	0.273	164 (76.3%)	86 (76.8%)	0.918
PS diuretics	31 (7.5%)	6 (3.8%)	0.103	11 (5.1%)	6 (5.4%)	0.926
Potassium supplement	123 (29.9%)	61 (38.4%)	0.051	78 (36.3%)	40 (35.7%)	0.920
Symptoms and signs of HF						
Dyspnea at rest	75 (18.2%)	31 (19.5%)	0.722	42 (19.5%)	20 (17.9%)	0.713
Dyspnea on exertion	313 (76.0%)	110 (69.2%)	0.097	166 (77.2%)	82 (73.2%)	0.423
Activity limitation	335 (81.3%)	120 (75.5%)	0.120	174 (80.9%)	87 (77.7%)	0.487

N (%) or mean ($\pm$ SD)	Before matching			After matching		
	High school education (≤ 12 years) (N=412)	Higher education >12 years (N=159)	P	High school education (≤ 12 years) (N=215)	Higher education (>12 years) (N=112)	P
Jugular venous distension	35 (8.5%)	22 (13.8%)	0.056	23 (10.7%)	14 (12.5%)	0.625
Third heart sound	73 (17.7%)	37 (23.3%)	0.132	49 (22.8%)	22 (19.6%)	0.512
Pulmonary rales	63 (15.3%)	20 (12.6%)	0.410	33 (15.3%)	14 (12.5%)	0.486
Lower extremity edema	85 (20.6%)	27 (17.0%)	0.325	44 (20.5%)	22 (19.6%)	0.860
NYHA functional class						
I	52 (12.6%)	24 (15.1%)		23 (10.7%)	14 (12.5%)	
II	221 (53.6%)	88 (55.3%)	0.340	119 (55.3%)	64 (57.1%)	0.833
III	127 (30.8%)	46 (28.9%)		69 (32.1%)	33 (29.5%)	
IV	12 (2.9%)	1 (0.6%)		4 (1.9%)	1 (0.9%)	
Heart rate (/minute),	77.2 ($\pm$ 13.0)	76.6 ($\pm$ 12.6)	0.600	76.9 ($\pm$ 13.3)	76.2 ($\pm$ 12.6)	0.645
Blood pressure (mm Hg)						
Systolic	128.0 ($\pm$ 21.9)	127.6 ($\pm$ 22.4)	0.817	128.9 ($\pm$ 22.1)	128.1 ($\pm$ 21.6)	0.742
Diastolic	74.7 ($\pm$ 12.2)	75.9 ($\pm$ 12.6)	0.276	76.3 ($\pm$ 12.2)	75.7 ($\pm$ 11.7)	0.674
Pulmonary congestion	44 (10.7%)	15 (9.4%)	0.661	21 (9.8%)	13 (11.6%)	0.605
Cardiothoracic ratio >0.5	268 (65.0%)	102 (64.2%)	0.840	142 (66.0%)	69 (61.6%)	0.426
Serum concentrations						
Creatinine (mg/dL)	1.27 ($\pm$ 0.38)	1.27 ($\pm$ 0.32)	0.965	1.30 ($\pm$ 0.40)	1.27 ($\pm$ 0.30)	0.536
Potassium (mEq/L)	4.33 ($\pm$ 0.41)	4.24 ($\pm$ 0.46)	0.020	4.28 ($\pm$ 0.41)	4.28 ($\pm$ 0.46)	0.959
Estimated glomerular filtration rate (mL/min/1.73 square meter)	63.2 ($\pm$ 20.6)	62.9 ($\pm$ 16.3)	0.863	63.2 ($\pm$ 20.8)	62.1 ($\pm$ 16.2)	0.618
Ejection fraction (%)	35.0 ($\pm$ 13.5)	33.5 ($\pm$ 12.8)	0.211	34.5 ($\pm$ 13.1)	33.8 ($\pm$ 12.6)	0.640

Association of high school education (versus higher education) with cause-specific mortalities and hospitalizations in a propensity matched cohort of heart failure patients

Table 2

	Higher education(>12 years) (N=112)	High school Education (≤12 years) (N=215)	Rate, per 10000 person-years (events/total follow-up in years)	Absolute rate difference (per 10000 person-years of follow-up)	Hazard ratio(95% confidence interval)	P value
Mortality						
All-cause	746 (22/295)	1,204 (64/531)		+ 458	1.52 (0.89–2.58)	0.124
Cardiovascular	644 (19/295)	1,054 (56/531)		+ 410	1.60 (0.90–2.84)	0.110
Worsening heart failure	271 (8/295)	452 (24/531)		+ 180	1.58 (0.66–3.78)	0.308
Hospitalization **						
All-cause	3,233 (63/195)	4,558 (139/305)		+ 1,325	1.52 (1.06–2.16)	0.022
Cardiovascular	2,067 (47/227)	3,009 (108/359)		+ 942	1.55 (1.05–2.30)	0.029
Worsening heart failure	826 (22/266)	1,223 (56/458)		+ 397	1.63 (0.94–2.81)	0.082
Number of total hospitalizations	190	428		+ 238		

* Absolute differences in rates of events per 10000 person-year of follow up were calculated by subtracting the event rates in the higher education group from the event rates in the high school education group (before values were rounded)

** Data shown include the first hospitalization of each patient due to each cause.

*** Cardiovascular hospitalization included first hospitalization due to worsening heart failure, ventricular arrhythmia, cardiac arrest, supraventricular arrhythmias, suspected digoxin toxicity, myocardial infarction, unstable angina, stroke, coronary revascularization, or cardiac transplantation.