A Study of Heart failure events of survival as a Composite of Heart Failure, Physical and Depressive Symptoms

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Introduction

Heart failure (HF) is a growing health care concern associated with adverse issues and stunning health care expenditures. In addition to traditional threat factors (e.g., age and comorbidities), cerebral status is honored as a significant predictor of issues. Depressive symptoms are related to poor prognostic and quality of life in cases with HF. therefore, it's important for health care providers to fete and manage depressive symptoms meetly in the HF population.

Depressive symptoms are common in cases with HF, with a frequency from 30 to 51. This large variability might be related to the selection of instruments to measure depressive symptoms and their cut points for defining varying situations of depressive symptoms. Instruments used to measure the situations of depressive symptoms frequently include physical depressive symptoms, similar as changes in appetite, sleep disturbances, or fatigue. still, these symptoms are constantly reported by cases with HF. This poses a challenge for health care providers to directly screen and cover depressive symptoms because these physical depressive symptoms may reflect the inflexibility of HF rather than depressive symptom status.

Cases in more advanced stages of HF have lesser physical symptom frequency and burden than those in less advanced stage of HF. Cases with depressive symptoms witness further physical symptoms of HF (dyspnea, fatigue, sleep disturbance, and loss of appetite) than cases without depressive symptoms. therefore, the addition of physical symptoms might reflect HF inflexibility, inflate the inflexibility of depressive symptoms, and in turn, instinctively increase their impact on issues in HF.

Experimenters have expressed concern about measuring depressive symptoms in cases with HF using instruments that include physical symptoms. One way to address this concern is to use an established depressive symptom instrument similar as the Patient Health Questionnaire (PHQ- 9) that includes physical and affective depressive symptoms to compare the prophetic capability between performances of the instrument with and without physical depressive symptoms. The purpose of this

study was to determine whether the presence of physical depressive symptoms on the PHQ- 9over-estimates the relationship of depressive symptoms to cardiac event-free survival. The specific end was to compare the prophetic capability for cardiac event-free survival of the full PHQ- 9 with performances that contain just the physical and just the affective depressive symptoms after conforming for health status and clinical and socio- demographic variables.

Methods

Design, Setting, and Procedure

This study was a prospective, longitudinal disquisition. Cases with HF were signed from inpatient conventions associated with two academic medical centers in Georgia and Kentucky from August 2004 to March 2009. This study was approved by the Institutional Review Boards at each study point. Cases with HF were linked by referral from their nursers and croakers, and their eligibility was verified by trained exploration nursers. inked, informed concurrence was attained from cases who agreed to share in the study during a visit to the General Clinical Research Center (GCRC).

Cases were canvassed to collect demographic and clinical data and completed questionnaire packets during the visit to the GCRC. Cases were followed up over a standard of 360 days (2 – 1826 days) to determine cardiac events.

Participants

Cases who met the following criteria were eligible for this study (1) opinion of HF by a cardiologist using the Framingham criteria;(2) no myocardial infarction within the former three months;(3) taking harmonious boluses of HF specifics at the time of study participation; and (4) suitable to read and speak English. Cases who had valvular heart complaint as an etiology of their HF, were appertained for heart transplantation, had egregious cognitive impairments, or had major life-changing comorbidities (e.g., end- stage renal or liver complaint or cancer other than skin cancer) were barred.

Measurement

Depressive symptoms. Depressive symptoms were assessed using the PHQ- 9, which consists of nine particulars. Each item corresponds to one of the nine symptoms of the major depressive

complaint criteria of the Diagnostic and Statistical Manual of Mental diseases- IV (DSM- IV). Cases rate particulars grounded on how frequently they witness these symptoms over two weeks on a 4-point Likert scale ranging from 0 (not at each) to 3(nearly every day). The scores were added and ranged from 0 to 27, with scores of ≥ 5, ≥ 10, ≥ 15, and ≥ 20, representing mild, moderate, relatively severe, and severe situations of depression symptoms, independently. The validity of the PHQ- 9 has been demonstrated to screen for depression in cases with cardiac complaint with high particularity and prophetic value. Its brevity makes its use in clinical settings or exploration desirable.

Three particulars related to sleep disturbance, fatigue, and appetite change were classified as comprising the PHQ- 9 physical depressive symptom dimension in this study because these are frequently endured by cases with HF. The remaining six particulars of anhedonia, depressed mood, negative passions about oneself, attention problems, psychomotor agitation/ deceleration, and suicidal creativity were classified as comprising the PHQ- 9 affective depressive symptom dimension. The trustability of the scores for the two confines of depressive symptoms in this study was measured using Cronbach's α0.764 for physical depressive symptom and0.814 for affective depressive symptom confines.

Health status and Clinical, socio- demographic characteristics. Health status in this study was operationally defined as comorbidity burden measured with the Charlson Comorbidity Index and functional status measured with New York Heart Association (NYHA) functional bracket. The Charlson Comorbidity Index was used to measure comorbidity burden which is ladened by taking into account comorbid ails (i.e., the number and soberness). New York Heart Association functional bracket was determined to assess limitations of physical conditioning performing from symptoms by in- depth structured interviews by a trained exploration nanny. Clinical and socio- demographic characteristics (e.g., drug and connubial status) were collected via case interviews and medical record reviews.

Cardiac events. Cardiac events were defined as the compound end point of cardiac-affiliated death, cardiac-affiliated hospitalization, or exigency department (ED) visit attributable to cardiac reasons (e.g., worsening HF symptoms). The data were attained by yearly follow- up calls to cases and their families and verified by reviewing medical records and public death records.

Statistical Analyses

Data were anatomized using SAS software interpretation (SAS Institute Inc, Cary, North Carolina). Unacclimated Cox commensurable hazards retrogressions were performed independently for physical and affective depressive symptom confines of the PHQ- 9 in order to examine prophetic capability for time to first cardiac event. Two series of multivariable analyses were done. Health status (the Charlson Comorbidity Index and NYHA class) was entered as covariates in the first model and health status and clinical, socio- demographic variables (age, gender, etiology of HF, body mass indicator (BMI), and anti-depressant drug remedy) were entered together in the alternate model.

Covariates included in the models were named a priori grounded on former studies.

The seven covariates included in our survival analysis models redounded in a rate of seven events per predictors, which is lower than the recommended 10 events per predictor for survival analysis. To determine whether models with seven covariates handed dependable vaticination, we ran progressive models in which the least significant predictors were removed one by one and compared information criteria values (e.g., Akaike's information criterion) among the models. The information criteria values in the reduced models were analogous to the full model with seven covariates. thus, given that all covariates were linked as important in previous exploration we included all seven covariates in the analyses.

The commensurable hazards hypotheticals were estimated with graphical displays of diversions between the observed accretive martingale residuals and the values of each explicatory variable from 20 arbitrary simulations. The Kolmogorov- type supremum tests from 1000 simulated patterns also were used. Both styles indicated that there wasn't a gross violation of the model supposition.

Results

Sample Characteristics

An aggregate of 210 cases with HF shared in the study**.** The maturity of cases was manly, Caucasian, and wedded or cohabitating. Ischemia was the most common HF etiology. The median score of the PHQ- 9 was 4 (the first and third quartiles 1 and 9, independently). Cases having moderate to severe depressive symptoms (PHQ- 9 scores ≥ 10) were 23(49/210) of total actors. Of these cases having moderate to severe depressive symptoms, 41(20/49) were specified anti-depressants.

Cases were grouped by the median split of PHQ- 9 scores for physical depressive symptom and affective depressive symptom confines. The high PHQ- 9 physical depressive symptom group (scores> 3) had a lesser proportion in NYHA functional classes III and IV, advanced comorbidity burden scores, and a lesser number of specified anti-depressants than the low PHQ- 9 physical depressive symptom group (scores ≤ 3). The high PHQ- 9 affective depressive symptom group (scores> 1) were youngish and had a lesser proportion in NYHA functional classes III and IV, advanced comorbidity burden scores, and a lesser number of specifiedanti-depressants compared to the low PHQ- 9 affective depressive symptom group (scores ≤ 1).

Cardiac Events

During the follow-up period, 59 cardiac events passed 2(4/210) were cardiac death, 23(48/210) were cardiac-affiliated hospitalizations, and 3(7/210) were ED visits due to cardiac causes.

Vaticination of Cardiac Event-free Survival

Full interpretation of the PHQ- 9. The total scores of the PHQ- 9 prognosticated cardiac event-free survival in the unacclimated and acclimated analyses. The association between total scores of the PHQ- 9 and time to first cardiac event remained significant after conforming for the covariates (unacclimated hazard rate (HR) = 1.08, 95 confidence intervals (CI) = 1.03 –1.13; acclimated HR for health status (the Charlson Comorbidity Index and NYHA functional class) = 1.07, 95 CI = 1.03 – 1.13). Every one-point increase in total PHQ- 9 score was associated with a 6 increase in the threat for a cardiac event after controlling for all covariates (acclimated HR for all covariates = 1.06, 95 CI = 1.01 –1.12).

PHQ- 9 physical depressive symptom dimension. In the unacclimated Cox retrogression analysis scores of the PHQ- 9 physical depressive symptom dimension were a predictor for cardiac event (unacclimated HR = 1.11, 95 CI = 1.02 –1.21). Scores of the PHQ- 9 physical depressive symptom dimension didn't prognosticate cardiac event-free survival after conforming for health status. Neither the Charlson Comorbidity Index nor NYHA functional class prognosticated cardiac event-free survival.

After entering all covariates, the association between scores of the PHQ- 9 physical depressive symptom dimension and cardiac event-free survival wasn't significant (Table). Only anti-depressant

drug remedy was an independent predictor of cardiac event-free survival (acclimated HR = 1.98, 95 CI = 1.06 –3.71). Cases specified anti-depressants had nearly double the threat for a cardiac event than cases not specified anti-depressants.

Table : Multivariable Cox retrogression analysis using scores of PHQ- 9 physical depressive symptoms (N = 210)

	Hazard Ratio	*p*-value	95% Confidence Interval
Age	0.99	.21	0.96-1.01
Female	0.80	.48	0.42-1.50
Charlson Comorbidity Index	1.06	.49	0.93-1.22
Ischemic etiology	2.09	.08	0.93-4.71
NYHA Class (I/II vs. III/IV)	0.96	.88	0.53-1.72
Body mass index (kg/m^2)	0.96	.06	0.92-1.00
Anti-depressant use	**1.98**	**.033**	**1.06-3.71**
PHQ-9 physical scores	1.07	.18	0.97-1.19

Total model *p*-value =.007

Note. NYHA: New York Heart Association functional class; PHQ-9: the Patient Health

PHQ- 9 affective depressive symptom dimension. The scores of the PHQ- 9 affective depressive symptom dimension prognosticated cardiac event-free survival in both unacclimated and acclimated models (unacclimated HR = 1.14, 95 CI = 1.06 –1.22). In the two series of multivariable analyses the association between scores of the PHQ- 9 affective depressive symptom dimension and cardiac event-free survival remained significant. In the first model conforming for health status, scores of the PHQ- 9 affective depressive symptom dimension were the only predictor of cardiac event-free survival (acclimated HR for health status = 1.13, 95 CI = 1.05 –1.21). In the alternate model conforming for all covariates, scores of the PHQ- 9 affective depressive symptom dimension singly prognosticated cardiac event-free survival. Every one-point increase in the scores of the PHQ- 9 affective depressive symptom dimension was associated with a 12 increase in the threat for a cardiac event (acclimated HR for all covariates = 1.12, 95 CI = 1.03 –1.22).

Discussion

We set up different prophetic issues for the PHQ- 9 physical and affective depressive symptom

confines in cases with HF. Both affective and physical depressive symptom confines were prophetic of a cardiac event in unacclimated models. However, affective depressive symptoms, but not physical depressive symptoms, persistently prognosticated time to cardiac event in acclimated models controlling for health status (the Charlson Comorbidity Index and NYHA functional class) and clinical, socio ¬ demographic factors. These results suggest that physical depressive symptoms may largely reflect health status, and the relationship between depressive symptoms and threat for a cardiac event is limited to affective depressive symptoms.

There's substantiation that affective depressive symptoms may be a useful index to descry situations of depressive symptoms. In the study of Holzapfel and associates affective depressive symptoms (e.g., depressed mood and empty/ shamefaced) were more frequently reported by depressed cases with HF than those without HF, while the frequency of physical depressive symptom experience didn't differ. In a study in which depressive symptoms were measured with the Beck Depression Inventory (BDI)- II, physical depressive symptom scores weren't different between cases with post-acute myocardial infarction and psychiatric rehabilitants matched on age, gender, and cognitive/ affective depressive symptom scores. Simon and Von Korff demonstrated that the overall pattern of physical symptoms, similar as weight and appetite changes, fatigue, and sleep disturbances, was analogous to depressed cases with and without habitual illness. The junking of lapping physical symptoms from tone- report depressive symptom instruments doesn't ameliorate the discriminating capability for the presence of depression using individual interview grounded on the DSM- IV criteria for major depressive occasion in cases with habitual pain.

In the study of Azevedo and associates in which the association between depressive symptoms, which were measured with the BDI, and HF stages, which were defined by the American College of Cardiology and American Heart Association, cases with a advanced stage (more advanced HF) had advanced situations of depressive symptoms. This relationship between HF stages and depressive symptom situations remained significant after deleting physical symptom particulars (i.e., fatigue, sleep disturbance, and changes in appetite) from the BDI.

We set up that the unique donation of the physical depressive symptoms to pitfalls for a cardiac event faded with the addition of health status (comorbidities and NYHA functional class) in retrogression models. This might indicate the significant association between health status and physical depressive symptoms. There are several studies in which the relationship between health

status and physical depressive symptoms was demonstrated. In a former study in which the BDI was used to measure depressive symptoms in cases with HF scores of the BDI physical/ affective depressive symptom dimension (e.g., perversity, crying, fatigue, and sleep disturbances), but not scores of the BDI cognitive/ affective symptom dimension (e.g., sense of failure, tone-blameworthiness, and suicidal ideas), were different by NYHA classes. Significant differences in depressive symptom situations between cases with and without HF were observed only when using a depressive symptom measure incorporating physical symptoms (the Centers for the Epidemiological Studies of Depression Questionnaire), but not measures free of physical symptoms (Profile of Mood States- Short form dejection- depression and the Sanitarium Anxiety and Depression Scale-depression).

Also, the BDI physical/ affective symptoms, but not the BDI cognitive/ affective symptoms, were significantly related to the Charlson Comorbidity Index in cases with myocardial infarction. Watkins and associates also showed a stronger relationship of comorbidities, which were measured by the Charlson Comorbidity Index, with the BDI physical depressive symptoms ($r = 0.24$) than the BDI cognitive symptoms ($r = 0.06$) in cases after acute myocardial infarction.

Barefoot and associates demonstrated the important part of affective depressive symptoms in prognosticating cardiac death among cases with coronary roadway complaint. Hazard rates of four depressive symptom confines, which were measured with the Zung tone- standing Depression Scale (SDS), were compared between unacclimated models and an acclimated model in which all depressive symptom confines were entered contemporaneously. The hazard rate of the SDS affective symptoms (e.g., sadness, perversity, restlessness, and suicidal ideas) remained also while the hazard rates of the others including physical (e.g., frazzle and sleep difficulties) and well- being (e.g., satisfaction and sanguinity) confines mainly reduced. also, affective depressive symptoms were associated with cardiac mortality in cases after coronary roadway bypass surgery while physical depressive symptoms were not. This result suggests that the relationship between depressive symptom situations and cardiac mortality isn't altered by physical symptoms due to complaint conditions. Clashing findings that physical depressive symptoms, not affective depressive symptoms, prognosticate cardiac issues (e.g., mortality or hospitalizations) are observed in former studies in cases with coronary heart conditions, similar as acute myocardial infarction. The significant relationship between physical depressive symptoms and each- beget mortality was also reported in the HF

population. Schiffer and associates reported that the BDI physical/ affective symptom dimension (e.g., perversity, crying, fatigue, and sleep disturbances) was an independent predictor of all- cause mortality while the BDI cognitive/ affective symptom dimension (e.g., sense of failure, tone-blameworthiness, and suicidal ideas) wasn't in cases with HF. This disagreeing finding with the current study may be related to different outgrowth variables. The outgrowth of their study was each-beget mortality while ours was the concerted end point of mortality, hospitalization, and ED visit related to cardiac reasons. The maturity of cardiac events in this study were hospitalizations. It's possible that factors related to death are different from factors related to hospitalizations. For case, left ventricular ejection bit or NYHA functional class was an independent predictor of mortality, but not hospitalization.

The use of different measures to assess depressive symptoms may contribute to the inconsistent findings. The particulars in the BDI and the PHQ- 9 are different although there are some particulars that are lapped between the two measures including anhedonia, suicidal creativity, psychomotor agitation/ deceleration, and fatigue. Physical and affective depressive symptom confines were defined with different particulars between the study of Schiffer etal. and ours. An item indicating psychomotor agitation/ deceleration was distributed as the BDI physical/ affective symptom dimension in the study of Schiffer etal. while the item was distributed as the PHQ- 9 affective depressive symptoms in our study.

One intriguing finding in this study is the association between being specified anti-depressants and advanced threat for cardiac events. The tradition of anti-depressants was a significant predictor of a cardiac event in the multivariable model which included the PHQ- 9 physical symptom dimension. still, this relationship wasn't significant in the acclimated models using total PHQ- 9 scores or PHQ- 9 affective symptom dimension scores. We decide that the impact of taking anti-depressants differs by confines of depressive symptoms. still, we cannot determine from out data whether cases specified anti-depressants actually took the drug or that the cure specified was acceptable to treat depressive symptoms. thus, our results should be interpreted as demonstrating that defining anti-depressants was associated with an increased threat for a cardiac event. Our results do, still, suggest that simply defining anti-depressants isn't sufficient and without proper follow- up to assure acceptable treatment, it may increase the threat for a cardiac event.

It's important to admit the discrimination influence of physical and affective depressive

symptoms on cardiac event-free survival in cases with HF. The use of the measures including physical depressive symptoms doesn't inflate the association between depressive symptoms and cardiac event-free survival.

There are limitations that should be noted in this study. The sample may not be representative of the HF population because men and Caucasians predominated. Because this was an observation study, no definitive consequences can be drawn regarding unproductive connections. The number of covariates include in our multivariable models exceeded the recommended number of covariates per event. still, our model testing demonstrated that the full model handed as dependable vaticinator as models with smaller covariates without causing an overfitting issue. thus, the full model, which had empirical support, was the optimal model to include in the analyses.

Conclusion

The accurate assessment of depressive symptoms in cases with HF has been a critical issue because of their adverse goods on issues. still, participated physical symptoms between HF and depressive symptoms are walls to help assessing the inflexibility of depressive symptoms in HF. In this study we demonstrated a distinctive prognostic capability between physical and affective depressive symptoms to issues in cases with HF. Affective depressive symptoms were associated with cardiac event-free survival independent of health status, but not physical depressive symptoms. The use of depressive symptom measures including physical symptoms doesn't inflate the relationship of depressive symptoms to cardiac event-free survival. therefore, clinicians can use instruments that contain physical depressive symptoms to assess depressive symptoms in their cases with HF without concern that the instruments overrate the relationship between depressive symptoms and issues.

Reference:

1. Hobbs FD, Kenkre JE, Roalfe AK, Davis RC, Hare R, Davies MK. Impact of heart failure and left ventricular systolic dysfunction on quality of life: a cross-sectional study comparing common chronic cardiac and medical disorders and a representative adult population. Eur Heart J 2002;23:1867-76.
2. Ekman I, Cleland JG, Swedberg K, Charlesworth A, Metra M, Poole-Wilson PA. Symptoms in patients with heart failure are prognostic predictors: insights from COMET. J Card Fail 2005;11:288-92.
3. Bruera E, Kuehn N, Miller MJ, Selmser P, Macmillan K. The Edmonton Symptom Assessment System (ESAS): a simple method for the assessment of palliative care patients. J Palliat Care

1991;7:6-9.

4. Albert N, Trochelman K, Li JB, Lin SH. Signs and Symptoms of Heart Failure: Are You Asking the Right Questions? Am J Crit Care 2010;19:443-52.
5. Friedman MM. Older adults' symptoms and their duration before hospitalization for heart failure. Heart Lung 1997;26:169-76.
6. Carlson B, Riegel B, Moser DK. Self-care abilities of patients with heart failure. Heart Lung 2001;30:351-9.
7. Riegel B, Dickson VV. A situation-specific theory of heart failure self-care. The Journal of cardiovascular nursing 2008;23:190-6.
8. Riegel B, Dickson VV. A situation-specific theory of heart failure self-care. J Cardiovasc Nurs 2008;23:190-6.
9. Kirkova J, Davis MP, Walsh D, et al. Cancer symptom assessment instruments: a systematic review. J Clin Oncol 2006;24:1459-73.
10. Lindenfeld J, Albert NM, Boehmer JP, et al. HFSA 2010 Comprehensive Heart Failure Practice Guideline. Journal of cardiac failure 2010;16:e1-194.
11. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics--2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Circulation 2009;119:480-6.
12. Teunissen SC, de Graeff A, de Haes HC, Voest EE. Prognostic significance of symptoms of hospitalised advanced cancer patients. Eur J Cancer 2006;42:2510-6.
13. Ekman I, Ehrenberg A. Fatigue in chronic heart failure--does gender make a difference? Eur J Cardiovasc Nurs 2002;1:77-82.
14. De Jong M, Moser DK, Chung ML. Predictors of health status for heart failure patients. Prog Cardiovasc Nurs 2005;20:155-62.
15. Jiang W, Kuchibhatla M, Clary GL, et al. Relationship between depressive symptoms and long-term mortality in patients with heart failure. Am Heart J 2007;154:102-8.
16. Rockwell JM, Riegel B. Predictors of self-care in persons with heart failure. Heart Lung 2001;30:18-25.
17. Woo MA, Kumar R, Macey PM, Fonarow GC, Harper RM. Brain injury in autonomic, emotional, and cognitive regulatory areas in patients with heart failure. J Card Fail 2009;15:214-23.
18. Chin MH, Goldman L. Gender differences in 1-year survival and quality of life among patients admitted with congestive heart failure. Med Care 1998;36:1033-46.
19. Holzapfel N, Muller-Tasch T, Wild B, et al. Depression profile in patients with and without chronic heart failure. J Affect Disord 2008;105:53-62.
20. Faris R, Purcell H, Henein MY, Coats AJ. Clinical depression is common and significantly associated with reduced survival in patients with non-ischaemic heart failure. Eur J Heart Fail 2002;4:541-51.

21. Jencks SF, Williams MV, Coleman EA. Rehospitalizations among patients in the Medicare fee-for-service program. N Engl J Med 2009;360:1418-28.

22. Ni H, Nauman D, Burgess D, Wise K, Crispell K, Hershberger RE. Factors influencing knowledge of and adherence to self-care among patients with heart failure. Arch Intern Med 1999;159:1613-9.

23. Moser DK, Doering LV, Chung ML. Vulnerabilities of patients recovering from an exacerbation of chronic heart failure. Am Heart J 2005;150:984.

24. Riegel B, Lee CS, Dickson VV. Self care in patients with chronic heart failure. Nat Rev Cardiol 2011;8:644-54.