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**THE ASSOCIATION OF PSYCHOLOGICAL DISTRESS
AND SELF-CARE BEHAVIORS WITH SELF-RATED
HEALTH IN PATIENTS WITH HEART FAILURE**

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Introduction

This thesis examines the association of psychological distress and self-care behaviors with self-rated health in patients with heart failure. In order to give an introduction to the main research problem, the first chapter of the present work briefly provides the reader with a definition of heart failure and some considerations about the epidemiology, etiology, and prognosis of the disease. Subsequently, the association of depression, anxiety and self-care behaviors with subjective and objective health outcomes is reviewed. Finally, the construct of self-rated health is introduced, followed by the description of a theoretical framework that provides a conceptualization of relevant predictors of self-rated health belonging to different domains of individual functioning.

Before addressing the main research question of this thesis, the second chapter of the present work assesses the factorial structure of the 9-item Patient Health Questionnaire by comparing the fit of a two-factor model, consisting of a somatic and cognitive depression factor, against a one-factor model consisting of a general depression factor in patients with heart failure. It has been assumed that in patients with cardiac disease, and specifically with heart failure, depression is different from that in the general population, and results from a combination of two distinct symptomatic dimensions, a somatic and a cognitive subtype, each with specific etiology, symptom expression, and progression. A significant amount of research has also confirmed the differential impact of these symptomatic dimensions on health outcomes in patients with cardiovascular disease and heart failure. However, due to several methodological inconsistencies affecting the findings of this research, the question whether the somatic and cognitive factors actually reflect different symptom dimensions of depression and are differently predictive of clinical outcomes has not yet been definitively established.

Therefore, assessing whether the PHQ-9 can actually detect two distinct symptomatic dimensions of depression, and the fit of a PHQ-9 two-factor model compared to the fit of a competing one-factor model may provide researchers with relevant theoretical and methodological information to guide future studies on the impact of depressive symptoms on health outcomes in patients with heart failure. Further, findings providing evidence for confirming or confuting the potential existence of purely cognitive and somatic symptomatic dimensions of depression may help clinicians in implementing adequately tailored therapeutic interventions for depressed heart failure patients.

In the third chapter, an evaluation of the association of psychological distress (depression and anxiety) and self-care behaviors with self-rated health in patients with heart failure is provided. Self-rated health, a single item measuring the subjective perception of global health status, has been found to predict all-cause and cardiovascular mortality among individuals with and without cardiovascular disease. In patients suffering from heart failure, self-rated health has also shown its association with mortality and hospitalization rates. Given the recognized prognostic value of self-rated health on clinical outcomes, a deeper understanding of the associations of psychological distress and self-care behaviors with overall health perceptions may help clinicians to implement effective interventions to address potentially modifiable risk factors, when a higher risk of poor health outcomes is detected. Moreover, recognizing the relevance of patient-reported outcomes, such interventions would have a significant impact on perception of current well-being in patients with heart failure.

Chapter 1

Psychological Distress, Self-Care Behaviors, and Self-Rated Health in Patients with Heart Failure.

1.1 Heart Failure: Definition and Diagnosis.

Heart failure is a complex syndrome characterized by typical signs and symptoms due to a structural and/or functional cardiac impairment (McMurray et al., 2012; Ponikowski et al., 2016). As a consequence of the structural and/or functional abnormality, the heart fails to deliver oxygen at a rate that is adequate to the needs of the metabolizing tissues (Dickstein et al., 2008; Ponikowski et al., 2016).

The underlying cardiac cause is essential in order to establish a diagnosis of heart failure, and is usually represented by a myocardial impairment which, in turn, cause a systolic and/or diastolic ventricular dysfunction. On the other hand, the syndrome can also be caused by abnormalities of the valves, endocardium, pericardium, heart rhythm, or specific metabolic abnormalities. Understanding of the underlying cardiac dysfunction is also important for therapeutic reasons, since the pathophysiology of the disorder guides the treatment decisions (Ponikowski et al., 2016; Yancy et al., 2013). Given the complex nature of the disease, it is not surprising that a single diagnostic test for heart failure is lacking, and that an accurate history and physical examination are required (Yancy et al., 2013). Generally, in addition to clinical evidence of cardiac impairment at rest (e.g. abnormal echocardiogram, and elevated plasma concentration of natriuretic peptides), typical symptoms such as breathlessness, ankle swelling and fatigue, may be accompanied by common signs such as high jugular venous pressure, and peripheral oedema (Ponikowski et al., 2016).

According to the European Society of Cardiology (ESC) guidelines (McMurray et al., 2012; Ponikowski et al., 2016), the current definition of heart failure refers to stages of the disease in which typical clinical signs and symptoms are evident. Before symptoms become clinically evident, asymptomatic structural or functional cardiac abnormalities can be detected which are precursors of heart failure. More specifically, patients are defined to be affected by asymptomatic left ventricular systolic dysfunction if they present with a reduced left ventricular ejection fraction without clinical signs or symptoms of the disease. Patients who have reported heart failure symptoms for some time are described as having chronic heart failure, and, if symptoms remain stable for at least one month, heart failure is said to be stable. On the other hand, patients who show a worsening in their clinical condition, often leading to hospital admission, are defined as decompensated. Finally, the term congestive heart failure is often used to denote acute or chronic heart failure with evidence of volume overload (Ponikowski et al., 2016).

1.2 Clinical Descriptive Terms in Heart Failure

Historically, heart failure has been described in terms of left ventricular ejection fraction (LVEF). Even if heart failure is recognized as a complex and multi-determined syndrome, patients can be classified as belonging to three different types of heart failure on the basis of the measurement of LVEF (Ponikowski et al., 2016). Specifically, heart failure with preserved ejection fraction comprises patients with normal LVEF (≥ 50), while patients with reduced LVEF (usually ≤ 40) are considered to be affected by heart failure with reduced ejection fraction. Finally, patients showing a LVEF in the range of 40-49% belong to the class of heart failure with mid-range ejection fraction. The classification of patients based on LVEF is clinically relevant due to the well-

established differences in etiologies, comorbidities, and response to medical therapies (e.g. Brouwers et al., 2013; Ho et al., 2013).

Additionally, the stages of heart failure proposed by the American College of Cardiology Foundation/American Heart Association (ACCF/AHA) (Hunt et al., 2009) and the New York Heart Association (NYHA) functional classification (Criteria Committee New York Heart Association, 1994) provide useful guidelines to assess the presence and severity of heart failure. The ACCF/AHA classification describes the progression of heart failure on the basis of the observed modifications in the cardiac structure. The NYHA functional classification assesses the severity of heart failure on the basis of patients' exercise tolerance and impairment in physical activity (Yancy et al., 2013). Further, as pointed out by the ESC guidelines (McMurray et al., 2012; Ponikowski et al., 2016), the Killip classification (Killip & Kimball, 1967) is generally used to describe the severity of acute patients' condition after myocardial infarction.

1.3 Heart Failure: Epidemiology, etiology, and prognosis.

Heart failure has been estimated to affect 1-2% of the adult population of developed countries, and more than 10% of individuals aged 70 and over (Bleumink et al., 2004; Ceia et al., 2002; Mosterd & Hoes, 2007). The prevalence of the syndrome seems to have been increasing over the past decades; this trend may reflect a combination of several potential explanations, such as an aging population, higher incidence of heart failure, improvements in the diagnosis of heart failure or in the treatment of cardiovascular disease (Bui, Horwich, & Fonarow, 2011). A recent review (van Riet et al., 2016) has shown that the median prevalence of heart failure was 11,8% among adults aged 60 or older, with stable rates in the last decade and with heart failure with preserved ejection fraction being more common than heart failure with reduced ejection

fraction. Moreover, the prevalence of diastolic dysfunction was found to be increasing and higher than the prevalence of systolic dysfunction. The ESC guidelines have also highlighted that the incidence of heart failure seems to be decreasing, specifically more for heart failure with reduced ejection fraction than for heart failure with preserved ejection fraction (Ponikowski et al., 2016).

With regard to heart failure etiology, coronary artery disease is the most common cause of systolic heart failure, even if hypertension and diabetes generally contribute to the onset and progression of the syndrome in most of the patients. Conversely, patients with heart failure with preserved ejection fraction are more likely to have hypertension and atrial fibrillation and, to a lesser degree, coronary artery disease. Further different causes of heart failure can include viral infections, alcohol abuse, chemotherapy and idiopathic dilated cardiomyopathy (McMurray et al., 2012). Recent progress in treatment and management of the syndrome have led to increased survival rates and lower hospital admissions among patients with heart failure with reduced ejection fraction, even if health outcomes are still poor (Ponikowski et al., 2016). Specifically, in European countries, all-cause 1-year mortality rate was found to be approximately 17% and 7% in acute and chronic heart failure respectively. One-year hospitalization rates were 44% and 32% among acute and chronic patients respectively (Maggioni et al., 2013). Cardiovascular mortality is usually due to sudden death or complications related to a worsening of the clinical condition, especially in patients with reduced ejection fraction. Hospital readmissions are generally caused by non cardiovascular complications, particularly among patients with preserved ejection fraction (Ponikowski et al., 2016).

1.4 Symptoms of Depression and Anxiety in Patients with Heart Failure

1.4.1 The association of depression with cardiovascular disease and heart failure

Depression, defined as either significant depressive symptoms on a well-validated depression questionnaire or a formal diagnosis of major depressive disorder, is common and persistent among individuals with cardiovascular disease, and often underrecognized and undertreated. Moreover, depression is more frequent in cardiovascular patients than in the general population, and the percentage of cardiac depressed patients is similar to those reported for patients affected by different chronic or disabling diseases, such as cancer or chronic liver disorders (Huffman, Celano, Beach, Motiwala, & Januzzi, 2013).

With regard to patients suffering from heart failure, the prevalence of clinically relevant depressive symptoms reported in different studies ranges from 9-10% to 60% (Rutledge, Reis, Linke, Greenberg, & Mills, 2006; Yohannes, Willgoss, Baldwin, & Connolly, 2010). The extremely wide range of prevalence is likely due to differences in the definition of depression and in the selection of the instruments to assess depressive symptoms in research studies (Moudgil & Haddad, 2013). Rutledge et al (2006) found the aggregate prevalence of major depressive disorder to be higher in women than in men, and an increased vulnerability to depression among younger patients (aged less than 60 years). Moreover, higher depression prevalence rates were found to be associated with higher NYHA functional class. While the prevalence rates within classes I or II and classes III or IV are comparable, the prevalence of depression among patients with class III or IV was considerably higher than that of patients with class I or II. The meta-analysis also showed that the prevalence of clinically relevant depressive symptoms was similar in inpatients and outpatients.

Given the high prevalence of depressive symptomatology among patients with heart disease, it could be argued that cardiovascular disease increases the risk of developing depressive disorders or, on the other hand, that depression may be one of the causes of cardiovascular disease. Moreover, both the etiologic mechanisms may account for the relationship between depression and cardiac disease (Hare, Toukhsati, Johansson, & Jaarsma, 2013). The available literature (de Jonge & Roest, 2012) suggests that both the unidirectional causal hypotheses or the simple overlap between the two hypothesized mechanisms are not sufficient to explain the complexity of the empirical findings. Conversely, the relationship between depression and cardiovascular disease may be best described as the outcome of two strictly intertwined and mutually reinforcing disorders, whose interaction presumably begins in youth.

On the one hand, the study by Åberg et al., 2012, among healthy individuals without known or subthreshold cardiovascular disorders, showed that indices of cardiovascular fitness, measured at 18 years old, were predictive of the onset of severe depression in adulthood, even after controlling for shared relevant risk factors (e.g. obesity, and familiar educational level). Such a finding provides evidence to the theoretical model assuming a cardiovascular contribution to the etiology of depressive disorders. On the other hand, findings of empirical research also suggest at least two mechanism by which depression may account for an increased cardiovascular risk. First, depression contributes to the incidence of cardiovascular disease; second, depressive disorders worsen the health outcomes in patients with established cardiovascular disease (Bradley & Rumsfeld, 2015).

Depression and depressive symptoms have shown to be independent risk factors for the onset of cardiovascular disease in the general population and among healthy individuals (Gan et al., 2014; Van der Kooy et al., 2007). However, a previous

meta-analysis (Nicholson, Kuper, & Hemingway, 2006), focusing on depression as an etiologic and prognostic factor in coronary heart disease, highlighted that depression cannot be formally considered as an independent risk factor for the onset of coronary heart disease since in most of the reported studies adjustment for commonly recognized cardiovascular risk factors is incomplete. Additionally, depressive symptoms and clinical depression were found to be independent predictors of mortality and both fatal and non-fatal cardiovascular events in patients with coronary heart disease and myocardial infarction, although the strength of the association resulted to be decreased after adjusting for conventional risk factors (Barth, Schumacher, & Herrmann-Lingen, 2004; Meijer et al., 2013). A recent meta-analysis by Doyle et al (2015) has also shown that depression is more prevalent in women than in men, although the association between depression and worse prognosis is stronger for men. Among men, the risk for all-cause mortality is partly accounted for by left ventricular ejection fraction, suggesting that depression after myocardial infarction may also reflect the cardiac disease severity among male patients. Moreover, a previous statement by the American Heart Association (AHA) (Lichtman et al., 2014) had already recommended to consider depression as a formal risk factor for adverse medical outcomes in patients with acute coronary syndrome. In fact, depression showed to be prospectively associated with an higher risk of all-cause and cardiac mortality and morbidity despite of the heterogeneity found in the published findings. With specific regard to heart failure patients, depression was found to be associated with an increased risk for all-cause and cardiovascular mortality, although the strength of the association is higher among patients with severe depression than those with moderate depression (Fan et al., 2014; Freedland, Carney, & Rich, 2011). Further, depression seems to independently predict

non-fatal cardiovascular events, even after adjusting for conventional cardiac risk factors (Newhouse & Jiang, 2014).

Several pathophysiological mechanisms seem to represent the most probable pathways linking depression to cardiovascular risk, defined as an increased incidence of cardiovascular disease, and worsening outcomes in individuals with established cardiovascular disease. Specifically, a hypothesized pathway implies the hyperactivity of the hypothalamic–pituitary–adrenal (HPA) axis and an impaired serotonin signaling caused by dysfunction of the amygdala (Bradley & Rumsfeld, 2015). Such abnormalities lead to a) autonomic dysfunction, in the form of increased sympathetic and/or diminished parasympathetic modulation, b) hypercortisolemia, due to an inactive inhibitory feedback loop on corticotropin-releasing hormone, c) elevated concentrations of catecholamines and inflammatory markers, especially C-reactive protein and cytokines (tumor necrosis factor- α and interleukins), d) platelet activation, e) endothelial dysfunction (Bradley & Rumsfeld, 2015; Cohen, Edmondson, & Kronish, 2015). Elevated blood pressure, lower heart rate variability, ventricular arrhythmias, increased atherosclerosis progression may result from the cited pathophysiological mechanisms, and are associated with an increased risk for cardiovascular events and outcomes among depressed individuals (Bradley & Rumsfeld, 2015).

In addition to these physiologic pathways, several behavioral mechanism are thought to be involved in the relationship between depression and cardiovascular disease risk and outcomes. More specifically, depression has been widely associated with behavioral risk factors such as lack of adequate physical activity, poor or unhealthy diet, smoking cessation, poor adherence to medical treatment and recommendations (Cohen et al., 2015; Dickens, 2015). On the basis of these results, some literature has argued that depression can be better described as a risk marker for behavioral pathways

causing higher cardiovascular risk and worse outcomes, and not a risk factor causing per se higher cardiovascular risk. However, regardless of the answers to this issue, the clinical management of both depression and health and treatment adherence behaviors is required to achieve optimal health (Cohen et al., 2015). Finally, reciprocal influences and feedback loops connecting physiological and behavioral mechanisms can be assumed. For example, it can be hypothesized that poor adherence to medical regimen may cause increased systemic inflammation which, in turn, lead to a poorer behavioral performance due to worsening depression (Cohen et al., 2015; de Jonge & Roest, 2012).

With regard to the impact of depression on patient-reported outcomes, it was found to exert a negative influence on health-related quality of life in individuals with coronary heart disease, especially affecting patients' perceptions of the disease severity, physical limitations and overall health status (Dickens, Cherrington, & McGowan, 2012). In patients with heart failure, depression was associated with poor quality of life, as measured by both disease-specific and generic instruments (Bekelman et al., 2007; Faller et al., 2010).

1.4.1.1 Symptom patterns of depression among patients with cardiovascular disease

Research has investigated specific characteristics of depression that showed to be predictive of worsening outcomes among people with known coronary heart disease. Characteristics such as the severity of depression, the timing of onset, the treatment responsiveness, and the symptom profiles have received most of the interest, and have shown to be associated with health outcomes among coronary heart disease patients (Dickens, 2015).

Specifically, since depression is a syndrome characterized by high heterogeneity, research has attempted to distinguish depression subtypes based on

differences in symptom pattern and etiology in cardiologic patients (Ormel & de Jonge, 2011). Previous research, focusing in identifying structural commonalities among depressive symptoms in individuals affected by depression, has generally suggested three-dimensional structures which include both a ‘cognition/mood’ and an ‘arousal/somatic’ dimension (e.g. Lux & Kendler, 2010; Wardenaar et al., 2010). Consistently, in cardiac patients, two symptom dimensions of depression, labeled as somatic/affective versus cognitive/affective, each with specific prototypical symptoms, have shown different association with cardiac prognosis (Hoen et al., 2010; E. J. Martens, Hoen, Mittelhaeuser, de Jonge, & Denollet, 2010; Stewart, Janicki, Muldoon, Sutton-Tyrrell, & Kamarck, 2007).

Based on these previous findings, an integrative model of the relationship between depression and cardiovascular disease has been proposed suggesting that depression in cardiovascular patients is not the same as in the general population, and results from a combination of two different dimensions, a somatic/affective and a cognitive/affective subtype, each with specific etiology, symptom expression, and progression (Ormel & de Jonge, 2011). According to the theoretical model, the depression subtypes have different etiology and course, and may be present in various combinations. The model also postulates different effects of depression on cardiovascular prognosis depending on type and duration of depressive symptoms. Specifically, persistent cognitive/affective depression show a significant association with cardiac outcomes mainly due to negative effects on health behavior; on the other hand, the somatic/affective depression is assumed to affect more strongly the prognosis due to the overlapping with indexes of the cardiac disease severity (e.g. inflammation and hypothalamus–pituitary–adrenal axis dysfunction) together with the negative influences on health behaviors. As a consequence of both the previous assumptions, the

third hypothesis of the model assumes that the main pathways mediating the effect of persistent or recurrent depression on cardiac prognosis is indirect by making depressed cardiovascular patients more susceptible to other risk factors such as non-adherence to treatment, and unhealthy lifestyle among others.

Recent findings show that cognitive and somatic depressive symptoms are related in different ways to cardiovascular outcomes. Specifically, a recent meta-analysis (de Miranda Azevedo, Roest, Hoen, & de Jonge, 2014) found that somatic depressive symptoms are more strongly associated with nonfatal cardiovascular events and/or increased mortality compared with cognitive/affective symptoms. These findings can be explained in light of several pathophysiological mechanisms linking somatic/affective depression to health outcomes in patients with heart diseases, such as inflammation and lower heart rate variability among others. However, the authors highlighted that, in spite of their robust findings, the association between somatic depressive symptoms and cardiovascular prognosis can be partly accounted by residual confounding due to cardiac disease severity (De Miranda Azevedo Roest, Hoen, & de Jonge, 2014). Consistent with these previous findings, a more recent prospective study (Roest et al., 2016) found empirically-based differences in severity and course of cognitive- and somatic-affective depressive symptoms in patients with myocardial infarction. Specifically, the study identified patients with persistent somatic depressive symptoms at higher risk for increased mortality than those with consistently low somatic and cognitive symptoms and with both somatic and cognitive symptoms higher and increasing. The authors, finally, argue that these findings are suggestive of different and specific physiological origins of somatic-affective depressive symptoms in cardiac patients that may explain their differential association with cardiovascular prognosis. With specific regard to patients with heart failure, only somatic depressive symptoms

were found to be predictive of all-cause mortality, even if both somatic and cognitive symptoms prospectively predicted health-related quality of life (Schiffer et al., 2009). Interestingly, with regard to the pathophysiological pathways linking depression to medical outcomes, cognitive depressive symptoms and change in somatic depressive symptoms were prospectively associated with inflammation factors, independent from clinical and demographic covariates (Kupper, Widdershoven, & Pedersen, 2012).

On the other hand, van Loo et al (2012) conducted a systematic review of studies reporting findings on data-driven subtypes of major depressive disorder among adults without comorbid somatic diseases. According to the authors, the published studies using latent factor analysis most consistently identified a factor explaining the variance of a mixture of cognitive and somatic symptoms of depression, thus failing to confirm the existence of a purely cognitive or somatic symptom dimension. With specific regard to patients with heart disease, Carney & Freedland (2012) argued that, in spite of several studies reporting a stronger association between somatic depressive symptoms and adverse cardiac outcomes than cognitive symptoms, these findings are typically affected by methodological inconsistencies, especially in factor analytic techniques, covariate adjustments, and response bias (assuming that patients tend to report somatic/affective symptoms with a greater extent than cognitive symptoms due to social acceptability). The authors thus conclude that symptom dimensions of depression are indicators of a general depression factor, and do not reflect distinct constructs. Consistently, a recent study by De Miranda et al. (2016) used a bifactor model of the Beck Depression Inventory (BDI) to generate a model consisting of a general depression factor and two depression-free factors, namely a somatic/affective and a cognitive/affective. The bifactor model fitted the data better than both a unidimensional model and a bidimensional model, consisting of a somatic and a cognitive factor. The

general depression factor was associated with adverse medical prognosis independent of somatic/affective symptoms that may be attributable to somatic illness.

Finally, some investigators have focused on the impact of specific depressive symptoms on medical prognosis as an alternative way to elucidate the relationships between depression and health outcomes in cardiovascular patients. Specifically, hopelessness and anhedonia were found to be predictive of fatal and non-fatal cardiac events in patients with myocardial infarction younger than 70 (Denollet, Freedland, Carney, de Jonge, & Roest, 2013). Moreover, a recent research showed that, while the specific impact of different depressive symptoms highly depended on the considered outcomes, loss of energy was able to predict an impairment in all the quality of life and functional status measures considered by the investigators (Kohlmann et al., 2016).

1.4.2 The association of anxiety with cardiovascular disease and heart failure

According to the extant literature, anxiety symptoms and disorders are common in patients with cardiovascular disease (Pająk et al., 2013; Todaro, Shen, Raffa, Tilkemeier, & Niaura, 2007; Tully & Cosh, 2013), and higher than in same-aged healthy individuals (Moser et al., 2010). Specifically, in patients with heart failure, the reported prevalence rates range from 11 to 44% across different studies (Moser et al., 2010; Yohannes et al., 2010).

A relatively recent meta-analysis by Roest et al (2010) showed that anxiety, measured as a set of several anxiety constructs (including anxiety, panic, phobia, post-traumatic stress, and worry), was associated to an increased risk for incident coronary heart disease and death due to cardiac events in initially healthy individuals, after controlling for the influence of demographic characteristics, biological recognized risk

factors, and health behaviors. However, the provided estimate for the association between anxiety and incidence of new coronary heart disease was not adjusted for depression, which is generally highly comorbid with anxiety (Cohen et al., 2015). The results from this study are similar to those reported by a prospective study among a large cohort of young male (Janszky, Ahnve, Lundberg, & Hemmingsson, 2010), in which any anxiety disorder strongly influenced coronary heart disease onset and acute myocardial infarction over a 37 years of follow-up. Surprisingly, the authors reported no evidence for such an effect concerning early-onset depression. On the contrary, a more recent prospective study (Seldenrijk et al., 2015) showed that having comorbid depressive and anxiety disorders or depression alone at baseline was significantly associated with increased incidence of cardiovascular disease, whereas anxiety alone or both the remitted disorders were not associated, after adjustment for sociodemographic characteristics, health and lifestyle factors. Similarly, another study (Nabi et al., 2010) reported that after adjustment for common confounders and concurrent depression, the association between anxiety and incidence of coronary heart disease completely attenuated while the only signal of an association of anxiety with fatal and nonfatal coronary heart disease was in women. Moreover, anxiety was found to further strengthen the association between depression and incidence of cardiovascular disease when it was considered as a specifier of depression severity (Almas, Forsell, Iqbal, Janszky, & Moller, 2015).

With regard to the association of anxiety with health outcomes in patients with recognized cardiac disease, the findings reported by the studies are similarly inconsistent (Cohen et al., 2015). Some studies have reported anxiety disorders to be associated with increased risk for cardiovascular events and all-cause mortality (Martens et al., 2010; Roest, Zuidersma, & de Jonge, 2012). On the other hand, other

studies have found no association between anxiety disorders and outcomes (Versteeg et al., 2013), or even evidence for a protective role played by generalized anxiety disorder, while accounting for measures of depression and other relevant covariates (Parker, Hyett, Hadzi-Pavlovic, Brotchie, & Walsh, 2011).

To summarize, literature on the association between anxiety and incidence or prognosis of heart disease seems to show inconsistent findings. Such inconsistencies may be, at least partly, attributable to the lack of adjustment for typically high comorbid depression among most of the existing studies (Cohen et al., 2015). More significantly, an amount of research has also failed to take into consideration possible measurement and construct overlaps between anxiety and depression, rather exclusively assessing the independent contribution of psychological symptoms and/or diseases that are actually highly correlated (Suls & Bunde, 2005).

The literature has confirmed the high prevalence of comorbid anxiety and depression in patients with cardiovascular disease (Watkins et al., 2013), and specifically in patients with heart failure (Dekker et al., 2014; Yohannes et al., 2010). In individuals suffering from heart failure, anxiety alone was found to be associated with a higher rate of heart failure-related hospital readmissions (Tsuchihashi-Makaya, Kato, Chishaki, Takeshita, & Tsutsui, 2009), and with all-cause mortality and rehospitalization due to cardiac causes when comorbid depression was also taken into account (Alhurani et al., 2015; Suzuki et al., 2014). Additional studies (Moser et al., 2013; Shen et al., 2011) showed that symptoms of anxiety were predictors of worse functional status, and perceived quality of life in patients with heart failure.

1.5 Self-care Behaviors in Heart Failure and their Association with Health Outcomes

According to the definition provided by the World Health Organization (1983), self-care in health comprises a series of activities undertaken by individuals, families, and communities, in order to enhance or restore health, prevent the onset or manage the effects of illness. Self-care is important throughout the lifespan, but performing adequate self-care behaviors can be as relevant as challenging with aging, especially in the presence of chronic conditions and multiple comorbidities.

With specific regard to patients with heart failure, Moser and Watkins (2008) originally described self-care as the process by which patients are actively involved in the management of their disease, in agreement with physicians' advices and often with the help offered by family members or caregivers. On the one hand, self-care includes maintenance behaviors which imply healthy lifestyle choices, such as physical exercising and smoking cessation, and treatment adherence, consisting of taking prescribed medications, symptoms monitoring, and following fluid and salt restrictions. On the other hand, self-care behaviors also comprise management activities defined as a series of cognitive processes and actions pertaining to the recognition of signs of heart failure worsening, strategies to restore a healthier functioning, and the evaluation of the adequacy of performed corrective actions. Similarly, other theoreticians (Jaarsma, Abu-Saad, Dracup, & Halfens, 2000) defined heart failure-related self-care as behaviors that patients undertake to maintain and restore health and well-being. The proposed definition includes behaviors such as adherence to medication, diet recommendations (including fluid, sodium and alcohol restrictions), and exercise. Moreover, the authors stressed the importance of patients' disposition to consulting behaviors, described as the

attitude to seek for medical assistance once a worsening in heart failure symptoms is detected.

Overall, self-care activities are assumed to exert a positive influence on health outcomes in patients with heart failure with regard to health-related quality of life, mortality rate and frequency of hospitalization. Indeed, better self-care abilities were found to be consistently associated with reduced rehospitalization rates and mortality, with better patient-reported quality of life, functional status, lower symptom burden, and with a decline in levels of biomarkers of stress and inflammation. (Moser et al., 2012; Riegel, Lee, & Dickson, 2011). Despite the well established advantages of self-care on health status, patients often fail to achieve optimal levels of self-care (Riegel, Lee, & Dickson, 2011).

Factors assumed to affect self-care performance in patients with heart failure are related to individual and environmental characteristics (i.e. socio-demographics, support systems, availability of resources, and health values), the aging status including cognitive and physical factors (i.e. cognitive and sensory impairment, decline in functional status, symptoms burden and comorbidities), the psychological functioning (e.g. depression and anxiety), and the previous experience with the health care system (Moser & Watkins, 2008; Sidani, 2003). The literature has broadly confirmed the predictive role of the socio-demographic, psychosocial and health-related determinants of heart failure self-care, such as age, gender, time since the diagnosis of heart failure, comorbidities, severity of heart failure symptoms and related level of physical functioning, social support, and psychological distress (Graven et al., 2014; Moser, & Watkins, 2008; Oosterom-Calo et al., 2012; Riegel, Lee, & Dickson, 2011).

With specific regard to the impact of health-related factors, several studies reported that a higher impairment in physical functioning due to heart failure symptoms was associated with better self-care performance (Lee et al., 2009; Riegel, Lee et al., 2011; Rockwell & Riegel, 2001; Suwanno, Petpichetchian, Riegel, & Issaramalai, 2009). Overall, these results seem to confirm that patients who do not experience burdensome limitations in their physical functioning may be not adequately motivated to effectively engage in self-care or even to learn the necessary self-care behaviors (Riegel, Lee, & Dickson, 2011). Consistently, two studies also found an association between the increasing number of diseases in comorbidity with heart failure and better self-care behaviors measured both cross-sectionally (Gallagher, 2010) and prospectively (Trojahn et al., 2013). On the other hand, a more recent prospective investigation of the effect of disabling heart failure symptoms on self-care abilities (Kessing, Denollet, Widdershoven, & Kupper, 2016) found that both the generalized sense of exhaustion (general fatigue) and the exertion fatigue directly related to physical activity were negatively associated with self-care at 12- and 18-month follow up, even after controlling for mood disorders and other relevant clinical covariates.

With regard to the potential effect of psychosocial factors, research has generally shown the influence of depression and anxiety on self-care performance (Riegel et al., 2009; Riegel, Lee, & Dickson, 2011). Specifically, Holzapfel et al (2009) found that depressive symptoms significantly predicted an overall worsening in self-care behaviors together with being older, unmarried, and showing greater disease severity as measured by multimorbidity and ejection fraction. Increasing depressive symptoms were also found to be significantly associated with worse patients' ability to recognize occurring changes in heart failure symptoms and implement adequate behavioural and pharmacological remedies (Cameron, Worrall-Carter, Riegel, Lo, &

Stewart, 2009). Moreover, depression and anxiety symptoms were found to be independent predictors of poor dietary adherence, when accounting for relevant socio-demographic and health-related variables (Luyster, Hughes, & Gunstad, 2009), while a comprehensive measure of psychological status, also including items assessing depression and anxiety, showed to predict self-care behaviors more broadly related to the therapeutic regimen, such as weighing daily, taking medications as prescribed, and exercising regularly (Schnell-Hoehn, Naimark, & Tate, 2009). On the other hand, a previous study failed to detect an association between depression and a wide range of heart failure self-care behaviors, while anxiety was found to be positively associated only with smoking and alcohol consumption (Schweitzer, Head, & Dwyer, 2007). Additionally, a relatively recent review (Graven, & Grant, 2014) has shown the positive influence of social support, especially provided by family members, on patients' self-care performance, by assisting with adherence to treatment regimen and by actively participating in symptoms self-management and seeking for specialized help.

1.6 Self-Rated Health: Definition and Association with Health Outcomes

One of the most commonly used subjective measures of health status is self-rated health, alternatively defined as self-assessed health, self-perceived health, or overall perceived health. The measure consists of a single question that asks respondents to rate their overall current health on a four- or five-point Likert scale along a continuum from excellent (very good) to poor (very bad), or to compare their health status with that of same-aged individuals (Jylhä, 2009; Krause & Jay, 1994). The exact wordings of both the question and the response options may vary slightly among different studies (Jylhä, 2009). Notably, the different measurements of self-rated health seem to represent parallel assessments of the same latent construct, even if the health levels derived from

such measurements were found to be not directly comparable (Jürges, Avendano, & Mackenbach, 2008).

Specifically, self-rated health is conceptualized as an individual's integrated perception and evaluation of health, and is assumed to reflect at the same time biological, psychological, and social dimensions (Idler & Benyamini, 1997; Miilunpalo, Vuori, Oja, Pasanen, & Urponen, 1997). Using different words, self-rated health can be conceptually described as a subjective and synthetic self-assessment in which a number of objective somatic and mental conditions are cognitively processed, taking also into account elements from the contextual framework such as present and past health experiences, reference groups, and cultural patterns of experiencing and reporting physical and mental symptoms (Jylhä, 2009).

The use of a single item question, providing a measure of the overall perceived health, has become increasingly common due to its reported association with mortality (Idler & Benyamini, 1997; Jylhä, 2009). Specifically, global self-rated health has shown to be an independent predictor of mortality in the general population, with the association remaining strong even after adjustment for relevant covariates such as socio-demographics, clinical measures, functional status, and psychological functioning (DeSalvo, Bloser, Reynolds, He, & Muntner, 2006; Idler & Benyamini, 1997). Additionally, a population-based study (Bopp, Braun, Gutzwiller, Faeh, & Group, 2012) reported that self-rated health was an independent predictor of all-cause mortality at a 30-year follow-up, even when socio-demographics, behavioral and clinical risk factors were taken into account. A previous study had already shown that the association between self-rated health and mortality rates is even stronger for death due to chronic conditions, such as diabetes or coronary heart disease (Benjamins, Hummer, Eberstein, & Nam, 2004).

With specific regard to cardiovascular disease, a meta-analysis by Mavaddat et al (2014) has demonstrated that reporting a poor relative to excellent self-rated health is associated with cardiovascular mortality and a combined outcome of fatal and non-fatal cardiovascular events in individuals with pre-existing cardiovascular disease or ischemic heart disease symptoms. Poor self-rated health was also found to be predictive of poorer health outcomes in previously healthy individuals, when adjustment for commonly recognized cardiovascular disease risk factors was taken into account. A recent study (Stenholm et al., 2016) confirmed these results, showing that increased rates of poor self-rated health were evident in individuals 13–15 years prior to death from ischemic and other cardiovascular disease when compared to surviving controls, adjusting for socio-demographics and lifestyle factors. The study also reported that, prior to death due to cardiovascular disease, poor self-rated health was more prevalent among healthy individuals, thus suggesting that the decline in self-rated health started before diagnosis of the disease leading to death were made.

Finally, self-rated health has also shown its role in predicting mortality and hospitalization in patients suffering from heart failure, after controlling for socio-demographic characteristics, functional limitation, disease severity, and comorbidities (Chamberlain et al., 2014; Inkrot et al., 2015; Lainscak et al., 2013; Masterson Creber, Allison, & Riegel, 2013). However, Masterson Creber et al (2013) found that the ability of the single item assessing self-rated health to predict all-cause mortality decreased within a month period until it became null by 60 days.

Several explanations have been offered as answers to the question why a single item measuring overall perceived health is a strong predictor of mortality and hospital readmission rates (Benyamini, 2011). First of all, self-rated health may represent a continuously evolving assessment of personal body and health status, thus summarizing

an amount of information, not directly available to clinicians and researchers, which account for the future trajectory of individual health. Self-rated health is also supposed to reflect the availability of external resources, such as education, income, and social support, and internal resources, such as optimism, and perceived control. Third, self-rated health is assumed to exert an influence on health behaviors and several behavioral risk factors. However, it has been highlighted that the inclusive and integrative nature of this single item is the most reasonable explanation for the predictive role of self-rated health on health outcomes. Self-rated health would summarize health information relevant to survival and overall health which are not covered by other measures due to the practical limitations of empirical studies and the expected inadequacy of current knowledge of other important health characteristics influencing individual health (Benyamini, 2011; Jylhä, 2009).

1.7 The Wilson and Cleary's Model of Health-Related Quality of Life

According to the model proposed by Wilson and Cleary (1995), health-related quality of life is defined as an individual sense of well-being resulting from feelings of happiness and satisfaction with life as a whole. Quality of life results from an evaluation of several aspects of individual health, i.e. biological functioning, physical and psychological symptoms, functional status, and general health perceptions, on a continuum of increasing integration and complexity. More specifically, the model offers a categorization of patient outcomes, related to different levels of individual functioning, based on the underlying health concepts. Moreover, the model postulates specific causal relationships between the different health concepts which are assumed to exert an influence on health-related quality of life. Within the model, global health perceptions are thought to be predictors of health-related quality of life, and are in turn defined as

individual evaluations of health status summarizing all the previous components in the model and their subjective importance (biological functioning, physical symptoms, psychological symptoms, functional status). The proposed model also takes into account the influence of individual and environmental characteristics, also including socio-demographic characteristics and perceived available social support respectively, on each level of individual functioning, except for the biological domain. In an attempt to revise the original model, Ferrans et al (2005) provided an extension to the causal pathways linking the different domains of individual functioning predicting overall quality of life, specifying that the individual and environmental characteristics also exert their effect on the first domain of individual functioning, the one pertaining to the biological function.

Additionally, a conceptual model has been developed in order to provide a specific theoretical and empirical framework to define and assess health-related quality of life in individuals suffering from heart failure (Rector, 2005). The model does not take into consideration the potential role of self-assessed health in predicting patients' quality of life. On the other hand, it highlights, among others, the fundamental contribution of clinical characteristics of the disease (i.e. symptoms, and impairments in functional status) and symptoms of psychological distress (negative psychological reactions mainly attributable to illness) on patients' assessment of their overall quality of life.

Chapter 2

The Factorial Structure of the 9-item Patient Health Questionnaire in Patients with Heart Failure

Introduction

Depression and depressive symptoms are common and persistent among patients with cardiac disease (Huffman et al., 2013), and heart failure (Rutledge et al., 2006; Yohannes et al., 2010). Moreover, depression seem to independently predict all-cause mortality and fatal and non-fatal cardiovascular events in individuals with heart failure (Fan et al., 2014; Freedland et al., 2011). To date, research has investigated the effects of specific characteristics of depression on health outcomes among people with established coronary heart disease. Several studies have focused on the role of characteristics such as the severity of depression, the timing of onset, the treatment responsiveness, and the symptom patterns in predicting worsening outcomes among coronary heart disease patients (Dickens, 2015).

More specifically, in patients with cardiac disease, two symptom dimensions of depression, labeled as somatic/affective versus cognitive/affective, have shown different association with cardiac prognosis (Hoen et al., 2010; Martens et al., 2010; Stewart et al., 2007). Based on these previous empirical findings, Ormel and de Jonge (2011) have hypothesized that depression in cardiovascular patients is not the same as in the general population, and comprise a combination of two different dimensions, a somatic and a cognitive subtype, each showing specific etiology, symptom expression, and progression. The model also provides a list of empirically-derived prototypical symptoms constituting the two subtypes of depression; while the cognitive subtype comprises symptoms such as depressed mood, lack of interest, and negative

feelings/cognitions about self, the somatic subtype includes symptoms such as fatigue, psychomotor agitation/retardation, and sleep problems. A subsequent meta-analysis (de Miranda Azevedo et al., 2014) has provided evidence for the differential association of cognitive and somatic dimensions of depression with cardiovascular outcomes among patients with heart disease (including the diagnosis of heart failure), with somatic depressive symptoms more strongly associated with cardiovascular events and increased mortality than cognitive symptoms. Additionally, in a recent study (Roest et al., 2016), patients with persistent somatic depressive symptoms after myocardial infarction were found to be at higher risk for mortality than those with low somatic and cognitive symptoms and with both somatic and cognitive symptoms higher and increasing. Overall, these empirical findings suggest that several pathophysiological mechanisms (e.g. inflammation and lower heart rate variability) may drive the exclusive association between somatic depression and health outcomes in patients with heart diseases, or that specific physiological origins of somatic depressive symptoms could explain their differential association with cardiovascular prognosis (de Miranda Azevedo et al., 2014; Roest, Wardenaar, & de Jonge, 2016).

On the other hand, Carney and Freedland (2012) have noted that the issue whether the empirically-derived somatic and cognitive factors actually reflect different symptom dimensions of depression and are differently predictive of clinical outcomes is far from being settled. In fact, the authors highlighted that most of the studies assessing the differential association of somatic and cognitive depressive symptoms with cardiac outcomes were affected by a number of relevant methodological inconsistencies. Among others, symptoms of depression, commonly evaluated using the Beck Depression Inventory (BDI), have been differently labeled as somatic or cognitive on the basis of factor analyses results or items face validity. Moreover, the studies have

used different factor analytic approaches (i.e. exploratory vs. confirmatory), producing different and hardly comparable factor structures, thus making it difficult to draw meaningful theoretical conclusions about the existence of two distinct subtypes of depression with potentially different etiology and differential impact on medical outcomes. Notably, when discussing the results of their meta-analysis, De Miranda et al (2014) also noted inconsistencies across the studies concerning the loadings of depressive symptoms on somatic and cognitive dimensions. Despite these inconsistencies, the authors considered the symptoms dimensions sufficiently similar to be pooled. Consistently with Carney and Freedland's argumentations, a recent study by De Miranda et al. (2016) found a general depression factor to be associated with adverse medical prognosis in patients with myocardial infarction. More specifically, the study used a bifactor model of the BDI to evaluate the fit of a model, consisting of a general depression factor and two general depression-free factors, namely a somatic and a cognitive factor, assumed to reflect symptoms or consequences of heart disease and neuroticism traits similar to cognitive symptoms of depression respectively. The bifactor model was found to fit the data better when compared to both a unidimensional and bidimensional model, consisting of a somatic and a cognitive depression factor. Finally, a systematic review by van Loo et al (2012) showed that studies reporting empirically-derived depressive symptom dimensions using latent factor analysis among adults without comorbid somatic diseases most consistently identified a common factor explaining the variance of a mixture of cognitive and somatic symptoms of depression, thus failing to confirm the existence of purely cognitive and somatic symptomatic dimensions.

While most of the existing research among patients with cardiovascular disease has measured symptoms of depression using the BDI (de Miranda Azevedo et al.,

2014), to the best of our knowledge, only three studies assessed the association of somatic and cognitive depression with medical outcomes using the 9-item Patient Health Questionnaire (PHQ-9; Kroenke, Spitzer, & Williams, 2001). The PHQ-9 is a self-report questionnaire designed to assess the severity of depressive symptoms, and consists of nine items based on the DSM-IV symptom criteria for major depressive disorder. The questionnaire was found to be a reliable and valid measure of depressive symptoms in heart failure (Hammash et al., 2013). In an attempt to evaluate the differential association of somatic and cognitive dimensions of depression with health outcomes, a study in patients with myocardial infarction (Smolderen et al., 2009) derived sum scores of cognitive and somatic symptoms dimensions according to the items face validity. Differently, other two studies reported the results of confirmatory factor analysis. Pressler et al., 2011 assessed the construct validity of the PHQ-8 in patients with heart failure, a briefer version of the PHQ-9 lacking of 9th item pertaining to suicidal or self-injury thoughts, using confirmatory factor analysis. The authors evaluated the fit of an a priori two-factor model with items constituting the somatic and cognitive factors specified on the basis of the items face validity. Due to a failed exact-fit test, the item related to trouble concentrating was allowed to load onto both the somatic and cognitive factors, thus improving the model goodness-of-fit. Moreover, the reported correlation between emotional and somatic latent variables was relatively high in size (0.71), thus potentially indicating a relatively poor factors distinctiveness. Differently, a previous work by de Jonge et al (2007) on patients with stable coronary artery disease provided support for a two-factor structure of the PHQ-9 consisting of somatic and cognitive dimensions that included items based on items face validity. The error-free latent factors were found to be correlated 0.60. Interestingly, these two studies investigated only one depression model, and no competing models were evaluated.

However, as stressed by Kline (2011), even when the theoretical background is accurate in defining the number of factors, the fit of a more parsimonious one-factor model should be estimated and compared. Assessing whether the PHQ-9 can actually detect two sufficiently distinct symptomatic dimensions of depression, and the fit of a PHQ-9 two-factor model compared to the fit of a competing one-factor model may first provide researchers with relevant theoretical and methodological information to guide future studies on the impact of depressive symptoms on health outcomes in patients with heart failure. Further, findings providing evidence for confirming or confuting the potential existence of purely cognitive and somatic symptomatic dimensions of depression may help clinicians in implementing adequately tailored therapeutic interventions for depressed heart failure patients.

Therefore, the aim of this study was to evaluate the factorial structure of the PHQ-9 in patients with heart failure by comparing two models using CFA to assess which model provide the best fit to the data. Specifically, the study sought to evaluate the fit of a two-factor model of the PHQ-9 consisting of a somatic and cognitive factor against a one-factor model consisting of a general depression factor. On the basis of the previously cited works by Carney and Freedland (2012) and van Loo et al (2012), and the relatively high correlation between somatic and cognitive factors previously reported in patients with heart failure (Pressler et al., 2011), it was hypothesized that a one-factor model would show the best fit to the data, thus supporting the assumption that a general depression factor would provide a better representation of the underlying structure of the PHQ-9.

Method

Design and sample

The study was cross-sectional, and data were collected through self-report questionnaires and electronic medical records. Eligible patients were contacted during consecutive outpatients visits at the Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT) in Palermo, Italy, between April 2014 and February 2015. Inclusion criteria included a diagnosis of systolic heart failure, New York Heart Association (NYHA) functional class <IV, and the ability to speak and read Italian fluently. Two patients were excluded due to the inability to complete questionnaires, and the inability or unwillingness to give informed consent. Moreover, patients were not invited to participate if they were classified as NYHA functional class IV during the cardiologic visit prior to the questionnaires administration, since they were expected to be too frail to participate. A total of 150 patients were enrolled and informed consent was obtained. Each participant was asked to complete the self-report measures by a psychologist during individual sessions scheduled on the same day of his/her outpatient visit. Data from medical records integrated the questionnaires data. This study was approved by the Institutional Review Board of the ISMETT (Palermo, Italy).

Measure

Socio-demographic characteristics

A structured questionnaire was designed specifically for the study, and was used to collect socio-demographic characteristics such as age, gender, educational level, annual household income, employment status, marital status, and cohabitation.

Clinical status

Clinical data regarding heart failure etiology, ejection fraction (EF), and New York Heart Association (NYHA) functional classification were evaluated by cardiologists during the outpatient visits, and subsequently collected from the medical records. NYHA class was assessed by a cardiologist based on patients' limitation regarding physical activities due to heart failure symptoms, such as fatigue, dyspnea, angina pain, or palpitation, as reported by the patients. According to the NYHA classification system (Criteria Committee New York Heart Association, 1994; Mills & Haught, 1996), the following criteria were applied: class I, if no limitation to physical activity was detected; class II, slight limitation to physical activity; class III, if a marked limitation to physical activity was identified.

Symptoms of depression

Symptoms of depression were assessed using the 9-item Patient Health Questionnaire (PHQ-9; Kroenke & Spitzer, 2002; Kroenke et al., 2001). The nine items of the PHQ-9 are based on the criteria of the diagnosis of DSM-IV major depressive disorder. Each item is rated on a 4-point Likert scale (0 = "not at all", 1 = "several days", 2 = "more than half of the days", and 3 = "nearly every day"), indicating the frequency of each symptom over the past two weeks. As an assessment of severity of depression symptoms, a total score can be derived ranging from 0 to 27, with higher scores indicating more severe depressive symptoms. Construct and criterion validity have been established, and the instrument has shown excellent internal and test-retest reliability. Moreover, a PHQ-9 total score equal or higher to 10 had a sensitivity of 88% and a specificity of 88% for major depression; cut-off scores of 5, 10, 15, and 20 were found to represent mild, moderate, moderately severe, and severe depression, respectively (Kroenke et al., 2001). Reliability, and concurrent and construct validity of the PHQ-9

have also been established in patients with heart failure (Hammash et al., 2013). In the present study, a Cronbach's alpha coefficient of .80 was found.

Statistical analysis

Descriptive statistics (means, standard deviations, and ranges) were computed to summarize the characteristics of the participants using SPSS (20). Confirmatory factor analysis of the PHQ-9 was performed in LISREL 8.71 (Jöreskog, & Sörbom, 2004). Robust diagonally weighted least-squares (RDWLS) was employed due to the ordinal response format of the PHQ-9 and the skewed distribution of several items (Joreskog, Olsson, & Wallentin, 2016). RDWLS is based on the polychoric correlation matrix of the variables included in the analysis, and uses the diagonal elements of the inverse of the asymptotic covariance matrix of polychoric correlations to fit models for ordinal data (Jöreskog, 1990). DWLS estimation is a mathematically simpler form of WLS estimation that seems to perform well when the sample size is not very large (Kline, 2011). DWLS estimation was also found to give consistent parameter estimates and correct standard errors by robustification using an estimate of the asymptotic covariance matrix of the polychoric correlations (Yang-Wallentin, Jöreskog, & Luo, 2010). First, polychoric correlations among the observed variables and their asymptotic covariance matrix were estimated using the PRELIS program (Jöreskog, 2005). Then, the asymptotic covariance matrix was analyzed in LISREL with DWLS (Joreskog, Olsson, & Wallentin, 2016). To identify the factor structure of the PHQ-9 a CFA was conducted CFA in the sample, testing the fit of one-factor (Model I) and two-factor (Model II) models. The one-factor model was specified with all 9 items loading onto one latent factor (labeled as depression). Additionally, the two-factor model (with the factors labeled as somatic vs. cognitive depression) was specified following previous work

among patients with coronary heart disease (Ormel & de Jonge, 2011) and with heart failure (Pressler et al., 2011). Items reflecting the cognitive dimension and thus specified in the model as loading on this factor included (I) lack of interest, (II) depressed mood, (VI) negative feelings about self, (VII) concentration problems, and (IX) suicidal ideation; on the other hand, those pertaining to (III) sleeping difficulties, (IV) tiredness, (V) appetite problems, (VIII) psychomotor agitation/retardation were specified to load on the somatic factor. In both the specified models, all residual error covariances were fixed to zero. In order to scale the factors within each model, we fixed an unstandardized loading to 1.0 for each latent factor. The goodness of fit of the models were first evaluated through the Satorra-Bentler corrected chi-square (LISREL's default chi-square for DWLS estimation). The Satorra-Bentler corrected chi-square was found to perform reasonably well when using robust estimation method, such as the DWLS (Yang-Wallentin et al., 2010). A non-significant chi-square test would suggest that the specified and observed models do not differ significantly, thus supporting the theoretically grounded model fit to the data (Kline, 2011). Second, additional goodness-of-fit statistics were evaluated, including the comparative fit index (CFI), non normed fit index (NNFI), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR). Models fitting very well (or adequately) are indicated by CFI and NNFI ≥ 0.95 (0.90–0.94), RMSEA ≤ 06 (0.07–0.08), SRMR ≤ 0.08 (0.09–0.10) (Hu & Bentler, 1999). For each model, unstandardized and standardized factor scores were computed, and z scores were used to evaluate whether each factor score was significantly different from zero. Finally, LISREL derived modification indices were evaluated to determine if the addition of new paths would improve the overall fit. Modification indices of 3.84 or greater were considered to be indicative of potential model misspecification (Jöreskog, & Sörbom, 1996).

Results

First of all, we estimated descriptive statistics for the sample characteristics and the PHQ-9 total scores (Table 1). Overall, the sample was mainly composed by male participants (84%), age ranging from 24 to 76 ($M = 57.65$, $SD = 10.47$). With regard to clinical status, the mean EF was 30.50% ($SD = 9.69\%$), and the distribution across NYHA functional class was 21.3% of participants in NYHA class I, 60.7% in NYHA class II, and 18.0% in NYHA class III. The mean scores of the PHQ-9 was 8.15 ($SD=5.47$). As a consequence, the sample as a whole showed moderate symptoms of depression using the suggested cut-off score of 10 or higher (Kroenke et al., 2001). Additionally, 56 participants (37,3%) reported a score of 10 or higher. For full details of patient characteristics see Study 2.

Table 1

Characteristics of the Participants

Characteristic	Mean (SD), or n (Percentage)	Range
Socio-demographic Characteristics		
Age	57.65 (10.47)	24 – 76
Male	126 (84.0)	
Educational Level		
Less Than High School	79 (52.7)	
High School	59 (39.3)	
Master Degree	12 (8.0)	
Annual Household Income		
< 15.000 €	89 (59.3)	

15.000 €–29.999 €	51 (34.1)	
30.000 € - 44.999 €	5 (3.3)	
≥ 45.000 €	5 (3.3)	
Employment Status		
Employed	34 (22.7)	
Unemployed	19 (12.7)	
Retired ^a	97 (64.6)	
Marital Status		
Single	15 (10.0)	
Married or Having a Partner	123 (82.0)	
Separated or Divorced	5 (3.3)	
Widowed	7 (4.7)	
Cohabitation		
Yes	139 (92.7)	
Clinical Status		
Etiology		
Ischemic (vs. Non-Ischemic)	59 (39.3)	
EF	30.50 (9.69)	11.00 – 66.00
NYHA		
I	32 (21.3)	
II	91 (60.7)	
III	27 (18.0)	
Symptoms of Depression	8.15 (5.47)	0 – 25
PHQ-9 score ≥ 10	56 (37.3)	

Note. N = 150. EF = Ejection Fraction; NYHA = New York Heart Association Functional Class;

^aThe category of Retired includes participants on disability.

The one-factor model (Model 1) with all 9 items loading on a general depression latent factor showed a reasonably adequate fit to the data, with the exception of the significant Satorra-Bentler χ^2 (see Table 2). The χ^2 value was 40.64 with 27 degree of freedom ($p=0.045$), thereby suggesting that the fit of the hypothesized model to the data may be not entirely adequate (Kline, 2011). On the other hand, CFI=0.98, NNFI=0.97, RMSEA=0.058, SMSR=0.072, all indicated an excellent fit to the data.

Table 2

Summary of PHQ-9 factor models

Model	Factors	Model specification	No. free parameters	χ^2 (df)	CFI	NNFI	RMSEA	SMSR
1	1	All items on 1 depression factor	18	40.64 (27)	0.98	0.97	0.058	0.072
2	2	Cognitive: 1, 2, 6, 7, 9 Somatic: 3, 4, 5, 8	19	35.90 (26)	0.99	0.98	0.051	0.067

Note. N=150. χ^2 = chi-square; df=degrees of freedom; CFI = comparative fit index; NNFI = non-normed fit index; RMSEA = root mean square error of approximation; SMSR = standardized root mean square residuals.

The unstandardized and standardized factor loadings are presented in Table 3. All factor loadings were statistically significant, with z statistics ranging from 6.21 to 8.80, thus indicating that all the parameters were significantly different from zero. Each item from the PHQ-9 also showed to have a substantial standardized loading on the common factor ($> .50$) (Brown, 2006). Moreover, the squared multiple correlations for the 9 items ranged from 0.26 to 0.72. Most of the items showed a squared multiple correlation <0.50 , with the exceptions of items 2 and 9. Specifically, item 5, 7, and 8 showed squared multiple correlations < 0.30 , thus indicating potential poor reliability in measuring the latent construct (Byrne, 2013). No standardized residuals values were

found to be greater than 2.58, thus indicating no potential for further improvement in the model (Byrne, 2013).

Table 3

Unstandardized and standardized factor loadings for the one-factor model (Model 1)

Item	Unstandardized	Standardized
Scarso interesse o piacere nel fare le cose	1.00 (–)	0.64
Sentirsi giù, triste o disperato/a	1.34 (0.16)	0.85
Problemi ad addormentarsi o a dormire tutta la notte senza svegliarsi, o a dormire troppo	0.98 (0.13)	0.62
Sentirsi stanco/a o avere poca energia	0.95 (0.13)	0.61
Scarso appetito o mangiare troppo	0.84 (0.12)	0.54
Avere una scarsa opinione di sé, o sentirsi un/una fallito/a o aver deluso se stesso/a o i propri familiari	1.09 (0.12)	0.69
Difficoltà a concentrarsi su qualcosa, per esempio leggere il giornale o guardare la televisione	0.81 (0.13)	0.51
Muoversi o parlare così lentamente da poter essere notato/a da altre persone. O, al contrario, essere così irrequieto/a da muoversi molto più del solito	0.84 (0.12)	0.53
Pensare che sarebbe meglio morire o farsi del male in un modo o nell'altro	1.17 (0.15)	0.74

Note. N=150.

The two-factor model (Model 2), with different items loadings on the somatic and cognitive depression factors as previously indicated, showed an overall excellent fit to the data (see Table 2). The Satorra-Bentler χ^2 value was 35.90 with 26 degree of freedom ($p=0.093$), thus indicating that the specified and observed models do not differ significantly, and supporting the fit of the model to the data. Additionally, CFI=0.99, NNFI=0.98, RMSEA=0.051, SMSR=0.067 also indicated an excellent model-data fit.

The unstandardized and standardized factor loadings and the variance/covariance matrix are given in Table 4 and 5, respectively. All unstandardized factor loadings were

statistically significant, with z statistics ranging from 5.59 to 8.08, thus indicating that all the factor loadings were significantly different from zero. The factor covariance and factor variances all differ significantly from zero. Each item also showed to have a salient standardized loading on the factor it was specified to load onto ($>.50$). Moreover, the squared multiple correlations for the 5 items specified to load on the cognitive depression factor ranged from 0.27 to 0.75; the squared multiple correlations for the 4 items specified to load on the somatic depression factor ranged from 0.31 to 0.45.

As found for the Model 1, no standardized residuals values were greater than 2.58, thus indicating the absence of localized areas of strain in the solution. A correlation of .88 was found between the latent terms of somatic and cognitive depression. This result suggests that the two latent constructs of depression have poor discriminant validity (Brown, 2006). Finally, following the cutoff criteria of modification indices equal to or higher than 3.84 (Jöreskog, & Sörbom, 1996), modification indices (between parentheses) indicated three points of strain between the error terms of the item 2 and the item 9 (5.76), item 6 and item 9 (7.60), and item 7 and item 8 (4.57) in Model 1. Similarly, modification indices indicated three points of strain between the error terms of the item 1 and the item 4 (5.21), item 6 and item 9 (6.77), and item 7 and item 8 (6.01) in Model 2. Due to the relatively small sample size and the reasonably adequate fit of the specified models, no respecification of the models were considered in order to avoid the risk of capitalization on chance associations in the sample data (Brown, 2006).

Table 4*Unstandardized and standardized factor loadings for the two-factor model (Model 2)*

Item	Cognitive		Somatic	
	Unstandardized	Standardized	Unstandardized	Standardized
Scarso interesse o piacere nel fare le cose	1.00 (-)	0.64		
Sentirsi giù, triste o disperato/a	1.35 (0.17)	0.87		
Problemi ad addormentarsi o a dormire tutta la notte senza svegliarsi, o a dormire troppo			1.00 (-)	0.67
Sentirsi stanco/a o avere poca energia			0.96 (0.15)	0.64
Scarso appetito o mangiare troppo			0.85 (0.14)	0.57
Avere una scarsa opinione di sé, o sentirsi un/una fallito/a o aver deluso se stesso/a o i propri familiari	1.09 (0.14)	0.70		
Difficoltà a concentrarsi su qualcosa, per esempio leggere il giornale o guardare la televisione	0.80 (0.14)	0.52		
Muoversi o parlare così lentamente da poter essere notato/a da altre persone. O, al contrario, essere così irrequieto/a da muoversi molto più del solito			0.84 (0.15)	0.56
Pensare che sarebbe meglio morire o farsi del male in un modo o nell'altro	1.17 (0.17)	0.75		

Note. N=150.

Table 5
Factors Variance-Covariance Matrix

PHQ-9 Factors	PHQ-9 Factors	
	1.	2.
1. Somatic	0.45 (0.10)	
2. Cognitive	0.38 (0.06)	0.41 (0.10)

Note. N=150. PHQ-9 = 9-item Patient health Questionnaire

Discussion

Overall, the findings of the current study confirmed the original hypothesis that a one-factor PHQ-9 model would provide a better fit to the data. Even if the two-factor PHQ-9 model, consisting of somatic and cognitive latent factors, was found to provide the best fit to the data as suggested by the not significant chi-square statistic, the current study found a very high correlation between the error-free latent factors ($r=.88$), thus providing evidence that the two latent dimensions of depression have poor discriminant validity (Brown, 2006). As suggested by (Brown, 2006), when factors in a satisfactory solution have a high degree of overlap, they may be combined into a single factor, and the fit of the new model should show an overall acceptable fit except for the high correlation between the two factors. In the current study, the one-factor PHQ-9 model showed a reasonably good fit to the model, thus further confirming that somatic and cognitive symptoms of depression, as evaluated by the PHQ-9 items, should be considered as indicators of a common general depression factor, and not indicators of two distinct latent constructs. In other words, the result showed that a common depression factor provided a better representation of the underlying structure of the PHQ-9.

Similar to the current findings, when evaluating the factorial structure of the PHQ-8 among patients with heart failure, Pressler et al., 2011 found a relatively high correlation (.71) between the somatic and cognitive depression factors, with the item concerning “trouble concentrating” loading on both factors. Even if the high correlation among the somatic and cognitive factors suggest that the two factors may not represent sufficiently differentiated constructs, the study did not focus on issues concerning discriminant validity between the constructs underlying the two factors, and the fit of a one-factor competing model was not assessed. It should be also considered that, when highly correlated predictors potentially measuring the same or overlapping construct are included in the same model, multicollinearity may be present producing results not interpretable (Carney & Freedland, 2012; Thombs, Grace, & Ziegelstein, 2006). As a consequence, the presence of multicollinearity may, at least partly, account for the inconsistencies reported in the literature on the differential association between somatic and cognitive dimensions of depression and medical outcomes in patients with cardiac disease (Carney & Freedland, 2012).

Differently from the findings of the present study, the study by de Jonge et al (2007) reported a lower correlation between the two symptomatic dimensions of depression in a large sample of patients with stable coronary heart disease, supporting the notion that depression may not be a homogeneous condition in cardiac patients. From a theoretical point of view, such a finding seems to provide some evidence to the assumption that somatic and cognitive symptoms dimensions may be attributable to different causes which in turn account for the differential association of these dimensions with cardiac outcomes (Ormel & de Jonge, 2011). According to the model by Ormel and de Jonge (2011), while both the symptomatic dimensions show an association with health outcomes due to their negative effects on health behaviors, the

effects on outcomes exerted by somatic depressive symptoms are due to the additional influences by severity of the cardiac disease and underlying pathophysiological mechanisms (e.g. atherosclerosis, and inflammatory processes). On the other hand, the study by de Jonge et al (2007) did not provide any further evaluation of competing models. In this regard, it should be noted that, applying a hierarchical factor analysis to data obtained using the BDI, the first order cognitive and somatic factors were found to reflect a single second-order depression factor in a previous study among primary care patients (Arnau, Meagher, Norris, & Bramson, 2001). As discussed by Carney and Freedland (2012), such a finding seems to confirm that, despite having multiple dimensions, the BDI comprises a set of items measuring depression, and that cognitive and somatic depression are not two distinct constructs but symptomatic dimensions of generic depression. Accordingly, using a bifactor factor analysis, De Miranda et al (2016) found that the explained common variance of a general depression factor was sufficiently large to suggest that the BDI can be considered as a valid measure of depression in patients with myocardial infarction, although the instrument is able to detect depression-free somatic and cognitive dimensions potentially reflecting the severity of cardiac disease or somatic comorbidities and specific personality traits respectively. Interestingly, in the cited study by de Jonge et al (2007), only the somatic dimension was found to be associated with lower heart rate variability in the unadjusted analysis although cognitive depressive symptoms were not, thus suggesting that specific symptoms of depression are predictive of lower heart rate variability. However, the reported association between somatic depression and heart rate variability disappeared when adjustment for comorbid conditions was introduced in the analysis (de Jonge et al., 2007). As also noted by the authors, such a result may suggest that the weak association found in this study is merely due to the

confounding effect of increasing comorbid conditions. The somatic depression as measured by the PHQ-9 may have detected, to some extent, features related to the severity of patients' physical condition, thus producing a spurious effect of somatic depression on the outcome and rather suggesting the lack of predictive value of overall depression. Finally, it should be considered that in the study by de Jonge et al (2007) distinct somatic and cognitive symptoms dimensions were found among a specific sample of patients with stable coronary artery disease comprising only a small number of participants with heart failure. As a consequence, the discrepancy between the results from the current study and those reported by de Jonge et al (2007) may be attributable to different characteristics of depression between the two populations of patients.

This study is affected by a number of limitations. The first limitation of this study concerns the relatively small sample size. In fact, a small sample size may affect the accuracy of standard errors and the reliability of parameter estimates (Kline, 2011). Even if the DWLS estimation used in the current study performs reasonably well with samples not very large in size (Kline, 2011), further studies with larger sample size are needed to confirm the present findings. An additional limitation of the present study is that all the recruited participants were classified as having NYHA functional class <IV, thus limiting the generalizability of the findings. Future studies should strictly address this issue in order to obtain results more generalizable to the target population.

The finding of the present study has relevant implications for both research and the development of clinical interventions designed to treat depressive disorders in patients with heart failure. With regard to implications for research, the current finding highlights the need for a more careful use of factor analytic techniques to derive scores of potential symptomatic dimensions of depression. As elsewhere

stressed (Carney & Freedland, 2012), researchers should strictly rely on theoretical considerations to decide whether to include traditionally defined somatic or cognitive symptoms in more than one factor, or to allow a cognitive or somatic symptom to load onto the opposite latent factor. Reliance on confirmatory factor analysis approach, instead of less generalizable results of exploratory factor analysis, may also help to reduce inconsistencies and facilitate comparisons among different studies. Moreover, a rigorous evaluation of the degree of overlap between potentially distinct symptomatic dimensions of depression may reduce the risk of not interpretable results due to multicollinearity. Finally, based on the findings by De Miranda et al (2016) using the BDI, future studies with larger samples of heart failure patients should assess the fit of a PHQ-9 bifactor model, compared to a two-factor (consisting of somatic and cognitive depression factors) and a one-factor competing models. In fact, the PHQ-9 could detect somatic and cognitive depression-free factors in addition to a general depression factor, as suggested by the results on the factorial structure of the BDI among patients with myocardial infarction.

The current findings also suggest that, since both somatic and cognitive depressive symptoms can be considered as phenomenological expressions of the same underlying depression factor, it may not be clinically significant to differentiate the treatment approach on the basis of a detected relevance of somatic or cognitive symptoms at the individual level. As already highlighted (Carney & Freedland, 2012), the aim of depression management should be to treat patients to complete remission, regardless of which symptoms appear to be the most relevant. With specific regard to the impact of depression on health outcomes, it has been argued that, given the assumed etiological specificity of somatic depressive symptoms, treatment efforts aiming at improving both depression and medical outcomes should focus on

promoting health behaviors and the general adherence to treatment, including cardiac rehabilitation and physical exercise, when patients present with mainly somatic depression (de Miranda Azevedo et al., 2014; Ormel & de Jonge, 2011). On the other hand, both biological and behavioral mechanisms have been hypothesized to mediate the relationships between symptoms of depression and cardiac events (Cohen et al., 2015). As a consequence, optimal patient care should simultaneously focus on complete depression remission and adequate adherence to medical regimen and lifestyle recommendations, regardless of which symptoms appear to be the most relevant.

Chapter 3

The Association of Psychological Distress and Self-Care Behaviors with Self-Rated Health in Patients with Heart Failure

Introduction

Self-rated health, a single item measuring the subjective perception of global health status, has shown to predict mortality risk in the general population (DeSalvo, Bloser, Reynolds, He, & Muntner, 2006; Idler & Benyamini, 1997) and cardiovascular mortality among individuals with and without prior cardiovascular disease (Mavaddat, Parker, Sanderson, Mant, & Kinmonth, 2014). Self-rated health has also shown its association with mortality and hospitalization in patients suffering from heart failure, even after controlling for socio-demographic characteristics, functional limitation, disease severity, and comorbidities (Inkrot et al., 2015; Lainscak et al., 2013; Masterson Creber et al., 2013). Despite the generally recognized prognostic value of self-rated health on clinical outcomes, few studies have focused on psychosocial determinants of subjective global evaluations of health status in heart failure patients. Since self-rated health cannot be directly improved, a deeper understanding of the associations between psychosocial determinants and overall health perceptions, adjusting for key clinical covariates, may help clinicians to develop effective intervention strategies to address potentially modifiable risk factors when a higher risk of poor health outcomes is detected. Moreover, recognizing the relevance of patient-reported outcomes (Deshpande, Rajan, Sudeepthi, & Abdul Nazir, 2011), such interventions would have a remarkable impact on patients' perception of well-being.

Self-rated health generally consists of a single item that measures respondents' overall perceived health along a continuum from excellent to poor (Jylhä, 2009; Krause

& Jay, 1994). It is defined as an individual's integrated evaluation of his/her own health, and has been assumed to reflect at the same time biological, psychological, and social dimensions (Idler & Benyamini, 1997; Miilunpalo et al., 1997). In other words, self-rated health can be conceptually described as a subjective and synthetic self-assessment in which a number of objective somatic and mental conditions are cognitively processed, taking also into account elements from the contextual framework such as present and past health experiences, reference groups, and cultural patterns of experiencing and reporting bodily and mental symptoms (Jylhä, 2009). It has been argued that the inclusive and integrative nature of this single item may account for its validity in predicting mortality risk (Benyamini, 2011; Jylhä, 2009).

With regard to predictors of self-rated health in the general population, increasing age, lower income and educational level, being unmarried, and lack of social support were consistently found to be related to worse ratings of global perceived health (Kelleher, Friel, Nic Gabhainn, & Tay, 2003; Molarius et al., 2007; Phillips, Hammock, & Blanton, 2005; Subramanian, Kim, & Kawachi, 2005). Not surprisingly, individuals reporting higher engagement in health behaviors such as not or quitting smoking, absence of or moderate alcohol assumption, following a healthy diet, and having regular physical activity, showed higher levels of overall perceived health (Conry et al., 2011; Phillips et al., 2005; Svedberg, Bardage, Sandin, & L.Pedersen, 2006). Moreover, among older individuals, the number of chronic diseases, functional ability, emotional well-being, and social support were found to be positively associated with self-rated health, in addition to socio-demographic determinants (Benyamini, Idler, Leventhal, & Leventhal, 2000; Cheng & Chan, 2006; French, Sargent-Cox, & Luszcz, 2012; Goldman, Gleib, & Chang, 2004). Similarly, disabilities and higher levels of psychological distress, together with smoking, drinking and lower physical activity,

were found to be related to worse overall perceived health among individuals with chronic disease and disability (Cott, Gignac, & Badley, 1999).

The model developed by Wilson and Cleary (1995; Ferrans, Zerwic, Wilbur, & Larson, 2005) offers a relevant theoretical and empirical framework in order to evaluate the contribution of factors pertaining to different conceptual levels to self-rated health. According to the model, health-related quality of life results from an evaluation of several aspects of individual health, i.e. biological functioning, physical and psychological symptoms, functional status, and general health perceptions, on a continuum of increasing integration and complexity. Specifically, global health perceptions are components of health-related quality of life, and are defined as subjective evaluations summarizing all the previous components in the model and their subjective importance. Notably, the proposed model takes into account the influence of individual and environmental characteristics such as socio-demographic characteristics and available social support on each level of individual functioning. Consistently, a conceptual model of health-related quality of life in patients with heart failure (Rector, 2005) has stressed the relevance of the contribution of clinical characteristics of the disease (i.e. pathophysiological variables and symptoms) and symptoms of psychological distress (negative psychological reactions mainly attributable to illness) on patients' assessment of their quality of life.

With specific regard to patients with heart failure, only few studies have evaluated the predictive value of variables pertaining to each of the above mentioned levels of individual functioning on self-rated health. Among socio-demographic characteristics, lower age and perceived sufficiency of income were found to be directly related to better self-rated health in fully adjusted analysis (i.e. accounting for several variables of each functional domain) (Beverly, Pozehl, Hertzog, Zimmerman, & Riegel,

2013; Clark, Tu, Weiner, & Murray, 2003). Moreover, lower comorbidity and symptoms burden, and higher levels of physical functioning showed to be associated with better overall perceived health (Beverly et al., 2013; Johansson et al., 2010; Rosen, Contrada, Gorkin, Kostis, 1997; Sullivan, Levy, Russo, Crane, & Spertus, 2007). Additionally, lower levels of emotional distress (including measurements of symptoms of anxiety and depression) (Rosen et al., 1997) and higher psychosocial functioning (a composite score accounting for depression, severity of physical symptoms, and sleep disturbances) were found to predict better global perceived health (Johansson et al., 2010). Another recent study (Böhme & Renneberg, 2015) found a composite measure of functional health, including symptoms of psychological distress (depression and anxiety) and the ability to perform daily activities, to be prospectively associated with self-rated health. On the other hand, other studies failed to find a significant association between depressive symptoms and self-rated health (Beverly et al., 2013; Sullivan et al., 2007). Similarly, results concerning the role of social support are inconsistent with a study showing a significant negative effect on perceived health (Rosen et al., 1997), and other studies failing to confirm such a finding (Clark et al., 2003; Sullivan et al., 2007).

Heart failure-related self-care behaviors are defined as actions that a patient undertakes to maintain and restore health and well-being, and include behaviors such as adherence to medication and to diet recommendations, exercise, and consulting behaviors described as the attitude to seek for medical assistance once a worsening in heart failure symptoms is detected (Jaarsma et al., 2000). Better self-care performance was found to be associated with reduced rehospitalization and mortality rates, with higher patient-reported quality of life, functional status, lower symptom burden, and with a decline in levels of biomarkers of stress and inflammation (Moser et al., 2012; Riegel, Lee, & Dickson, 2011). Despite the recognized relevant role of self-care

behaviors in predicting better health outcomes, to our best knowledge, only a study (Lee, Suwanno, & Riegel, 2009) sought to evaluate the contribution of self-care behaviors to global perceived health, showing a positive significant association after accounting for measures of severity of illness and comorbidities. Notably, the study did not account for measures of symptoms of psychological distress, factors known to negatively influence both self-care behaviors (Riegel, Lee, & Dickson, 2011) and evaluations of subjective health (e.g. Rosen et al., 1997). Another study (Britz & Dunn, 2010) only assessed the bivariate association between self-care behaviors and self-rated health, showing that patients with higher confidence in their self-care performance reported better evaluations of global health status.

Based on these previous findings among patients with heart failure, the present study aimed to evaluate 1) the unique predictive role of psychological distress (depression and anxiety) on self-rated health, accounting for individual characteristics (age, gender, income, and education), environmental characteristics (perceived social support), and clinical status (number of comorbid conditions, concentrations of NT-proBNP; functional impairment); and 2) the additional contribution provided by self-care behaviors in predicting patients' self-rated health, accounting for variables pertaining to individual, environmental, clinical, and psychological domains in a sample of outpatients with heart failure. Specifically, we hypothesized that psychological distress would show an independent negative association with patients' ratings of global perceived health, even after adjusting for covariates related to individual and environmental characteristics and to clinical status. Additionally, we expected to see an independent positive contribution of heart failure self-care behaviors to patients' self-assessed global health status.

Method

Design and sample

The study was cross-sectional and data were collected through self-report questionnaires and electronic medical records. Eligible patients were contacted during consecutive outpatients visits at the Mediterranean Institute for Transplantation and Advanced Specialized Therapies (ISMETT) in Palermo, Italy, between April 2014 and February 2015. Inclusion criteria included a diagnosis of systolic HF, New York Heart Association (NYHA) functional class <IV, and the ability to speak and read Italian fluently. Patients were excluded due to the inability to complete questionnaires, and the inability or unwillingness to give informed consent. Moreover, patients were excluded if they were classified as NYHA functional class IV during the cardiologic visit prior to the questionnaires administration, since they were expected to be too frail to participate. A total of 150 patients were enrolled and informed consent was obtained. Each participant was asked to complete the self-report measures by a psychologist during individual sessions scheduled on the same day of his/her outpatient visit. Data from medical records integrated the questionnaires data. This study was approved by the Institutional Review Board of the ISMETT (Palermo, Italy).

Measures

Socio-demographic characteristics

A structured questionnaire was designed specifically for the study, and was used to collect socio-demographic characteristics such as age, gender, educational level, annual household income, employment status, marital status, cohabitation.

Clinical status

Clinical data regarding body mass index (BMI), HF etiology, ejection fraction (EF), New York Heart Association (NYHA) functional classification, comorbid conditions

(chronic obstructive pulmonary disease, diabetes, hypertension, renal failure), and amino-terminal pro-B-type natriuretic peptide (NT-proBNP) were evaluated by cardiologists during the outpatient visits, and subsequently collected from the medical records. NYHA class was assessed by a cardiologist based on patients' limitation regarding physical activities due to heart failure symptoms, such as fatigue, dyspnea, angina pain, or palpitation, as reported by the patients. According to the NYHA classification system (Criteria Committee New York Heart Association, 1994; Mills & Haught, 1996), the following criteria were applied: class I, if no limitation to physical activity was detected; class II, slight limitation to physical activity; class III, if a marked limitation to physical activity was identified. Natriuretics peptides are produced by cardiomyocytes and subsequently released into the circulation in response to increased myocardial stretch. Circulating concentrations of cardiac natriuretic peptides, including brain natriuretic peptide (BNP) and its N-terminal pro-hormone N-terminal pro-brain natriuretic peptide (NT-proBNP), showed to be increased in patients with both asymptomatic and symptomatic left ventricular dysfunction (Bay et al., 2003). The concentration of NT-proBNP is recognized as a useful diagnostic and prognostic marker of heart failure (Yancy et al., 2013). With specific regard to comorbid conditions, the study protocol did not include any additional quantification of the comorbidity burden by the use of specific comorbidity scores. Hence, the number of comorbidities was calculated as the sum of all conditions abstracted from the medical records for each patient.

Perceived social support

Perceived social support was assessed using the Multidimensional Scale of Perceived Social Support (MSPSS; Zimet, Dahlem, Zimet, & Farley, 1988). The scale consists of 12 items that are rated on an 7-point Likert scale ranging from “very strongly disagree”

to “very strongly agree”. In addition to a total score, scores can be derived to assess perceived support from different sources (family, friends, significant others). Higher scores reflect higher levels of perceived social support. The psychometric properties of the instrument have been established (Zimet et al., 1988; Zimet, Powell, Farley, Werkman, & Berkoff, 1990). Internal consistency and construct validity of the Italian of the instrument have also been established among university students (Di Fabio, & Busoni, 2008), and in the general population (Prezza, & Principato, 2002). For the purpose of this study, only the total scores were derived, providing a measure of global perceived social support. The coefficient alpha for the total scores in the present sample was .86.

Psychological distress

Symptoms of depression. Symptoms of depression were assessed using the 9-item Patient Health Questionnaire (PHQ-9; Kroenke & Spitzer, 2002; Kroenke et al., 2001). The nine items of the PHQ-9 are based on the criteria of the diagnosis of DSM-IV for major depressive disorder (MDD). Each item is rated on a 4-point Likert scale (0 = “not at all”, 1 = “several days”, 2 = “more than half of the days”, and 3 = “nearly every day”), indicating the frequency of each symptom over the past two weeks. As an assessment of severity of depression symptoms, a total score can be derived ranging from 0 to 27, with higher scores indicating more severe depressive symptoms. Construct and criterion validity have been established, and the instrument has shown excellent internal and test-retest reliability. A PHQ-9 total score equal or higher to 10 had a sensitivity of 88% and a specificity of 88% for major depression; moreover, cut-off scores of 5, 10, 15, and 20 were found to represent mild, moderate, moderately severe, and severe depression, respectively (Kroenke et al., 2001). Reliability, and concurrent and construct validity of the PHQ-9 have also been established in patients with heart

failure (Hammash et al., 2013). The coefficient alpha for the total scores in the present sample was .80. The Italian version of the instrument can be retrieved from the PHQ Screeners website.

Symptoms of anxiety. Symptoms of anxiety were evaluated using the 7-item Generalized Anxiety Disorder (GAD-7; Spitzer, Kroenke, Williams, & Löwe, 2006). The seven items of the GAD-7 are based on the criteria of the diagnosis of DSM-IV for generalized anxiety disorder (GAD). For each item, respondents are asked to assess how often they have been affected by the corresponding symptom of GAD, during the past two weeks. The items are evaluated on a 4-point Likert scale (0 = “not at all”, 1 = “several days”, 2 = “more than half of the days”, and 3 = “nearly every day”), indicating the frequency of each symptom over the past two weeks. As an assessment of severity of GAD symptoms, a total score is derived ranging from 0 to 21, with higher scores indicating more severe symptoms of anxiety. The instrument showed satisfying internal consistency, and test-retest reliability. Criterion, construct, and factorial validity have also been established. Moreover, a score of ten or greater was found to be a reasonable cut-off point (sensitivity and specificity exceed 0.80) for detecting cases of generalized anxiety disorder. Cut-off of 5, 10, and 15 are suggested to represent mild, moderate, and severe levels of anxiety, respectively (Löwe et al., 2008; Spitzer et al., 2006). The coefficient alpha for the total scores in the present sample was .88. As for the PHQ-9, the Italian version of the instrument can be retrieved from the PHQ Screeners website.

Heart-failure self-care behaviors

Heart failure self-care behaviors were evaluated through the use of the European Heart Failure Self-Care Behaviour Scale (Jaarsma, Strömberg, Mårtensson, & Dracup, 2003). The scale consists of 12 items evaluating behaviors that patients perform to maintain healthy functioning, and well-being. Each item is rated on a 5-point Likert scale

between 1 (I completely agree) and 5 (I completely disagree). Possible total scores range from 12 to 60, with a higher scores indicating worse self-care. Internal consistency, test–retest reliability, content and concurrent validity have been established (Jaarsma et al., 2003; Shuldham, Theaker, Jaarsma, & Cowie, 2007). Moreover, the Italian version of the instrument has shown to be a reliable and valid measure of heart failure self-care behaviors (Pulignano et al., 2010). The coefficient alpha for the total scores in the present sample was 0.67.

Self-rated health

Self-rated health was assessed using the first item from the Italian version of the 36-Item Short Form Survey (SF-36; Apolone, Mosconi, & Ware, 1997). The item asks “In general, would you say your health is...”, and respondents are required to rate their answer on a 5-point Likert scale (1 = Excellent, 2 = Very good, 3 = Good, 4 = Fair, 5 = Poor). Higher scores indicate poorer self-rated health. Test-retest reliability, convergent and discriminant validity have previously been established, supporting the use of this single-item as a reasonably reliable and valid proxy for longer questionnaires measuring global health status (Chandola & Jenkinson, 2000; DeSalvo et al., 2006; Lundberg & Manderbacka, 1996).

Statistical analysis

Missing data were detected and dealt with only in some of the clinical measures (body mass index, NT-proBNP, ejection fraction, renal failure). Percentages of missing data ranged from 0 to 9.2%, with the renal failure measurement showing the highest missing percentage; body mass index, NT-proBNP, and ejection fraction measures showed only one or two missing values. Mean or modal imputation was used to substitute missing items by the means of the not missing values across the subjects. Prior to statistical analysis, the distribution of the NT-proBNP was checked for normality, resulting in a

correction by logarithmic transformation due to the positive skewness as previously reported in the literature (e.g. Brouwers et al., 2012). Moreover, educational level and annual household income were converted into dichotomous variables because of the low percentage of participants reporting master degree education (8.0%), and reporting an annual income higher than 30.000€. Specifically, the “Master Degree” category was collapsed into the “High School or More” category; both the income category higher than 30.000€ were collapsed into the income category “Higher than 15.000€”. Finally, dummy variables for NYHA functional classes II and III were used as a predictor variables in the regression model (NYHA class I was used as the reference category).

Descriptive statistics expressed as percentages, means, standard deviations, and ranges, were used to describe the socio-demographic and clinical characteristics, perceived social support, symptoms of depression and anxiety, self-care behaviours, and self-rated health of the participants. Bivariate analyses were performed to assess the relationships between self-rated health and all predictor variables. Pearson bivariate correlations were calculated for the relationships between self-rated health and all continuous predictor variables. A series of one-way ANOVAs were performed to assess the association between self-rated health and categorical predictor variables. Finally, in order to achieve aim 1 and 2, a multiple hierarchical regression analysis using four steps was performed with all new variables at each step entered simultaneously as a block. Data were analyzed using SPSS 20.0 software. The significance level for all tests was set at $p = .05$. Finally, due to the high correlation found between anxiety and depression, total scores for psychological distress were obtained by summing depression and anxiety scores in order to avoid multicollinearity.

Results

Descriptive statistics are presented in Table 1. Overall, the sample was mainly composed by male participants (84%), age ranging from 24 to 76 ($M = 57.65$, $SD = 10.47$). Notably, most of the participants were married or partnered (82%), and almost all of them were not living alone (92.7). Moreover, the participants reported high levels of perceived social support as indicated by the mean MSPSS scores ($M=69.82$, $SD=11.86$) being near to the upper limit of the scale range (12-84). With regard to clinical status, more than half (60.7%) of the participants were classified as NYHA class II, and had a low number of comorbid conditions ($M=1.05$, $SD=.97$). SRH had a mean of 3.59 ($SD=0.93$), which is close to a report of fair. With regard to psychological distress, both the mean PHQ-9 scores ($M=8.15$, $SD=5.47$) and the mean GAD-7 scores ($M=7.19$, $SD=5.36$) were below the suggested cut-off point (≥ 10) for clinically relevant symptoms of depression (Kroenke et al., 2001) and anxiety (Spitzer et al., 2006). Moreover, 56 participants (37,3%) reported a score of 10 or higher in the PHQ-9, and 39 participants (26.0%) reported a score of 10 or higher in the GAD-7.

Table 1

Characteristics of the Participants (N = 150)

Characteristic	Mean (SD), or Percentage	Range
Socio-demographic Characteristics		
Age	57.65 (10.47)	24 – 76
Male	84.0	
Educational Level		
Less Than high School	52.7	
High School	39.3	

Master Degree	8.0	
Annual Household Income		
< 15.000 €	59.3	
15.000 €–29.999 €	34.0	
30.000 € - 44.999 €	3.3	
≥ 45.000 €	3.3	
Employment Status		
Employed	22.7	
Unemployed	15.7	
Retired ^a	64.7	
Marital Status		
Single	10.0	
Married or Having a Partner	82.0	
Separated or Divorced	3.3	
Widowed	4.7	
Cohabitation		
Yes	92.7	
Perceived Social Support	69.82 (11.86)	32 – 84
Clinical Characteristics		
BMI	27.06 (4.02)	16.96 – 41.04
Etiology		
Ischemic (vs. Non-Ischemic)	39.3	
EF	30.50 (9.69)	11.00 – 66.00

NYHA		
I	21.3	
II	60.7	
III	18.0	
Comorbid Conditions		
COPD	11.3	
Diabetes	28.0	
Hypertension	25.3	
Renal failure	40.0	
Number of Comorbid Conditions	1.05 (.97)	0 – 3
Log BNP	6.21 (1.37)	1.95 – 9.23
Symptoms of Depression	8.15 (5.47)	0 – 25
Symptoms of Anxiety	7.19 (5.36)	0 – 21
Self-care behaviours	27.91 (8.20)	12 – 51
SRH	3.59 (0.93)	1 – 5

Note. N = 150. BMI = Body Mass Index; EF = Ejection Fraction; NYHA = New York Heart Association Functional Class; COPD = Chronic Obstructive Pulmonary Disease; SRH = Self-Rated Health.

^aThe category of Retired includes participants on disability.

Results of the bivariate correlations between self-rated health and all continuous predictor variables are showed in Table 2. The strongest association was found between symptoms of depression and anxiety and self-rated health, so that increased reported symptoms of psychological distress were related to worse self-rate health. Increasing age and higher concentrations of NT-proBNP were also associated to lower overall perceived health. On the other hand, no association was found between self-care behaviours and self-rated health. Notably, a high correlation was found between

symptoms of depression and anxiety. Due to the high correlation, total scores for psychological distress were obtained by summing depression and anxiety scores, and entered in the regression analysis in order to avoid multicollinearity.

Table 2

Correlations between Self-Rated Health and Continuous Predictor Variables

Measures	1	2	3	4	5	6	7
1. Self-Rated Health ^a							
2. Age	.17*						
3. Perceived Social Support	-.12	-.04					
4. log NT-ProBNP	.18*	.31**	.11				
5. No. of comorbid conditions	.12	.34**	-.11	.11			
6. Symptoms of Depression	.51**	-.05	-.16*	.04	.05		
7. Symptoms of Anxiety	.46**	-.02	-.17*	-.06	.04	.74**	
8. Self-Care Behaviours ^b	.11	-.17**	-.15	-.18*	.05	.10	.07

Note. log NT-proBNP = logarithmic transformation of N- terminal pro-B-type natriuretic peptide.

^a Higher scores mean worse self-rated health

^b Higher scores mean worse self-care behaviors

Table 3 reports the results of ANOVAs evaluating the bivariate associations between self-rated health and categorical predictor variables. An association was found between NYHA functional class and self-rated health. A Tukey post hoc test revealed that self-rated health was significantly worse in participants with NYHA class II ($3.67 \pm .88$, $p = .001$) and III ($4.04 \pm .94$, $p < .001$) compared to participants with NYHA class I ($3.00 \pm .80$). There was no statistically significant difference between participants with NYHA class II and III ($p = .14$).

Table 3*One-Way ANOVA of Self-Rated Health by Categorical Predictor Variables*

Source	df	SS	MS	F	p
<i>Gender</i>					
Between Groups	1	1.65	1.65	1.90	.17
Within Groups	148	128.55	.87		
Total	149	130.19			
<i>Annual Household Income</i>					
Between Groups	3	6.76	2.25	2.66	.05
Within Groups	146	123.44	.85		
Total	149	130.19			
<i>Educational Level</i>					
Between Groups	2	1.34	.68	.78	.46
Within Groups	147	128.83	.88		
Total	149	130.19			
<i>NYHA Functional Class</i>					
Between Groups	2	17.12	8.56	11.13	<.001
Within Groups	147	113.07	.77		
Total	149	130.19			

Note. NYHA = New York Heart Association. df = degrees of freedom. SS = sums of squares. MS = mean square.

The results of the hierarchical regression analysis are summarized in Table 4. In step one, age, gender, educational level, annual household income, and perceived social support accounted for 5% of the variance in self-rated health scores after adjustment for the number of variables (Adjusted $R^2=.05$, $R^2=.08$, $F(5, 144) = 2.55$, $p<.05$). Only age was a significant predictor in this model, with being older predicting worse self-rated health ($\beta=.22$, $t(144)=2.54$, $p<.05$). In step two, introducing log NT-proBNP, NYHA functional class, and number of comorbidities accounted for an additional 11% of variance in self-rated health scores and this change in R^2 was significant ($F(4, 140)=4.55$, $p<.01$). In this model, NYHA class II and NYHA class III (compared with NYHA class I) were significant predictors of poorer self-rated health ($\beta=.32$, $t(140)=3.11$, $p<.01$, and $\beta=.39$, $t(140)=3.61$, $p<.001$), uniquely explaining 6% and 8% of the variation in self-rated health respectively. Adding the psychological distress in the third step accounted for an additional 19% of variance in self-rated health ($\Delta R^2=.19$, $F(1, 139)=42.58$, $p<.001$). The psychological distress was a significant predictor in this model ($\beta=.50$, $t(139)=6.53$, $p<.001$), uniquely accounting for 19% in self-rated health. When the self-care behaviors were entered in the final step, the model showed an additional small but significant increase of 2% in explained variance in self-rated health ($F(1, 138)= 4.26$, $p<.05$). The final model accounted for 35% of the variance in self-rated health scores after adjustment for the number of variables (Adjusted $R^2=.35$, $R^2=.40$, $F(11, 138) = 8.26$, $p<.001$). Five variables were significant predictors of self-rated health: age ($\beta=.20$, $t(138)=2.45$, $p<.05$), annual household income ($\beta=-.19$, $t(138)=-2.33$, $p<.05$), NYHA class II ($\beta=.24$, $t(138)=2.67$, $p<.01$), psychological distress ($\beta=.49$, $t(138)=6.45$, $p<.001$), and self-care behaviors ($\beta=.15$, $t(138)=2.06$, $p<.05$). Lower self-rated health was predicted by increasing age, lower income, reporting a mild functional limitation (compared with no functional limitation), higher psychological

distress, and worse self-care behaviors. The most important predictor of self-rated health was psychological distress, uniquely accounting for 18% of the variance in self-rated health. Self-care behaviors uniquely explained only a small amount of variance in self-rated health.

Table 4

Summary of Hierarchical Regression Analysis for Variables predicting Self-Rated Health^a

Predictor	Step							
	1		2		3		4	
	B	β	B	β	B	β	B	β
Age	.02	.22*	.01	.10	.01	.16*	.02	.20*
Gender	.23	.09	.31	.12	-.09	-.04	-.08	-.03
Annual Household Income	-.33	-.17	-.29	-.15	-.28	-.15	-.35	-.19*
Educational Level	-.05	-.03	-.02	-.01	.07	.04	.08	.04
Perceived Social Support	-.01	-.07	-.01	-.05	.01	.02	.01	.05
Number of Comorbid Conditions			.06	.06	.01	.01	-.01	-.01
log NT-proBNP			.01	.01	.05	.07	.06	.09
NYHA II (vs. I)			.62	.32**	.46	.24**	.46	.24**
NYHA III (vs. I)			.94	.39**	.46	.19	.43	.18
Psychological Distress					.05	.50***	.05	.49***
Self-care behaviors							.02	.15*
R ²		.08*		.19***		.38***		.40***
Adjusted R ²		.05*		.14***		.33***		.35***

ΔR^2	.11**	.19***	.02*
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Note. log NT-proBNP: logarithmic transformation of N- terminal pro-B-type natriuretic peptide; NYHA: New York Heart Association.

^aFor self-rated health, higher scores mean worse health

^bHigher scores mean worse self-care behaviors

Discussion

The results of the current study showed that higher symptoms of psychological distress and a worse performance in heart failure self-care behaviors were associated to poorer evaluations of perceived global health, independent of individual and environmental characteristics, and indices of disease severity. Overall, these findings provide evidence to support the hypothesis that individuals suffering from heart failure may feel less healthy due to the experienced symptoms of depression and anxiety when compared with their more emotionally stable counterparts. Moreover, despite the small effect found, the results seem to confirm the hypothesis that being engaged in adequate self-care behaviors provide a significant contribution in helping individuals with heart failure to maintain an optimal health status.

Taken together, the results from the present study provide further support to the findings of other studies assessing the predictors of self-rated health among individuals of roughly the same age as participants of this study (i.e. aged 60 and older) (e.g. French et al., 2012), and with or without chronic conditions and disability (Cott et al., 1999). Interestingly, each set of variables pertaining to individual and environmental characteristics, clinical status, and psychological symptoms uniquely accounted for a significant portion of the variance in self-rated health, over and above those previously entered in the model. As a consequence, the current results seem to provide general support to the theoretical models which assume the integrative nature of self-rated health (Benyamini, 2011; Jylhä, 2009), and to the view of global health evaluations as influenced by factors belonging to different and increasingly complex levels of individual functioning (Ferrans et al., 2005; Wilson & Cleary, 1995). More specifically, the associations found in this study between functional impairment, psychological distress and self-rated health confirm the role theoretically assigned to functional status

and symptoms of depression and anxiety secondary to the disease in predicting well-being in patients with heart failure (Rector, 2005).

With specific regard to socio-demographic determinants of self-rated health, the present study found that increasing age and lower income were related to poorer evaluations of subjective health. Such a finding concurs with those reported by other studies assessing predictors of self-rated health among adults in the general population (Kelleher et al., 2003; Molarius et al., 2007; Phillips et al., 2005; Subramanian et al., 2005) and among individuals with heart failure (Clark et al., 2003; Rosen et al., 1997). Additionally, in line with previous findings among heart failure patients (Clark et al., 2003; Sullivan et al., 2007), perceived social support did not significantly contribute to the subjective assessment of global health status. On the other hand, social support showed a significant negative association with symptoms of both depression and anxiety in the bivariate analysis, thus suggesting that social support provided by significant others may contribute indirectly to better health perceptions by reducing negative affects potentially related to the disease. However, it should also be noted that participants in the present study showed relatively high levels of perceived social support, with mean scores in the measure of social support considerably above the midpoint of the scale, and most of them being married. The high reported social support, especially from spouses, may account for the lack of association between social support and self-rated health found in this study.

Additionally, higher functional limitation, as measured by the NYHA functional class, resulted to be associated with poorer levels of self-rated health. Specifically, reporting a slight limitation in ordinary physical activity due to symptoms of heart failure (NYHA class II), when compared to not experiencing functional limitations (NYHA class I), was a significant predictor of worsening self-assessed

health. Notably, a trend towards significance ($p=.07$, result not shown) was also found for the association between reporting a marked limitation of physical activity (NYHA class III), when compared to experiencing a slight limitation (NYHA class II), and poorer self-rated health. Overall, this finding is not surprising, and parallels other studies in which different measures of symptoms burden and functional limitation were used as predictors of global evaluations of health among patients with heart failure (Johansson et al., 2010; Rosen, 1997; Sullivan et al., 2007).

One of the most relevant findings from this study is the role of psychological distress in predicting a worsening patients' subjective appraisal of their own health status. First of all, a strong correlation between symptoms of depression and anxiety was detected in the current study. This findings is not surprising and is in line with other studies showing a high correlation between measures of severity of symptoms of depression and anxiety and the co-occurrence of symptoms of anxiety and depression in patients with heart failure (Dekker et al., 2014; Watkins et al., 2013). Moreover, we found a relatively strong association between symptoms of emotional distress and subjective evaluations of self-rated health, after controlling for the effects of previously entered individual, environmental, and biophysiological factors. This finding is consistent with previous studies that have evaluated the relationship between increasing levels of emotional suffering, characterized by symptoms of depression and anxiety, and poorer global evaluations of individual health status among individuals with chronic disease and disability (Cott et al., 1999), and in patients suffering from heart failure (Johansson et al., 2010; Rosen et al., 1997). As argued elsewhere (Rosen et al., 1997), since symptoms of depression and anxiety are rather common in patients with cardiovascular disease and heart failure, it is not surprising that symptoms of emotional suffering were relevant in the participants of this study, and that they provided a

significant contribution to patients' perceived health status. Moreover, the contribution of psychological symptoms to self-rated health seems to be stronger as a consequence of aging (French et al., 2012). Given that the average age of the sample of this study was relatively high, the relevant association between psychological distress and poorer evaluations of perceived health can be easily understood. More interestingly, such a result seems to lend support to the theoretical assumption that individual self-rated health is a synthetic evaluation of health status comprising not only biological or functional elements, such as symptoms burden and functional impairment, but also aspects from psychological and social dimensions (Idler & Benyamini, 1997; Miilunpalo et al., 1997). Additionally, it has been proposed that symptoms of mental suffering are not merely components that individuals take into account when judging their overall health, given that psychological distress, primarily symptoms of depression, may also predispose individuals toward more negative self-evaluations of health (Jylhä, 2009). On the other hand, the finding of a relatively strong predictive value of emotional suffering on self-rated health contrast the results of other studies which reported no association between overall perceived health and depression (Beverly et al., 2013) and symptoms of both depression and anxiety (Sullivan et al., 2007). In both these studies the unadjusted significant association between symptoms of psychological distress disappeared when controlling for measures of heart failure symptoms severity and functional and role limitation. As a consequence, the finding from this study may be affected by the lack of more comprehensive and sensitive measures of symptoms severity and functional limitation. On the other hand, it should be noted that the current study was able to account for the confounding effect of functional limitation as measured by HYHA functional class. NYHA classification represents a health-care provider's evaluation of physical limitation due to the heart

failure symptoms experienced by the patient, and has already been used as an assessment of functional status (Heo, Moser, Riegel, Hall, & Christman, 2005).

Finally, as hypothesized, a better performance in self-care behaviors was found to be significantly associated to higher self-rated health. Similarly, a previous study (Lee, Suwanno, et al., 2009) found behaviors related to adherence to treatment regimen and symptoms management to be associated to better evaluations of general health, while accounting for the confounding effect of disease severity. In this regard, the finding provides further confirmation of the salience of self-care behaviors in allowing patients with heart failure to maintain health and well being, at the same time reducing the risk of re-hospitalization and death. Interestingly, in this study, neither depression nor anxiety were significantly correlated with self-care behaviors, thus contrasting the findings of other studies which reported a negative association between depression and overall self-care performance (Holzapfel et al., 2009), depression and anxiety and dietary adherence (Luyster et al., 2009), and a global measure of psychological distress and patients' adherence to therapeutic regimen (Schnell-Hoehn et al., 2009). As a consequence, the current result seems to be also in contrast with part of the literature showing that the effects of symptoms of depression and anxiety on health outcomes implies, at least in part, behavioral mediating pathways, over and above pathophysiological pathways, which make cardiovascular patients more susceptible to risk behaviors, such as non-adherence to treatment, and unhealthy lifestyle, including poor diet, and limited physical activity (Bradley & Rumsfeld, 2015; Cohen et al., 2015). Rather, the current findings showed that symptoms of depression and comorbid anxiety had a direct association with self-rated health, thus suggesting that pathways other than behavioral, specifically physiological (e.g. inflammation processes), may be more strongly implied in the relationships of psychological distress with health status in

patients with heart failure. In this regard, future studies should evaluate the potential mediating effects of factors related to pathophysiological pathways in the association between symptoms of psychological suffering and global subjective evaluations of health status.

There are several limitations that should be considered when interpreting the results of this study. First of all, the sample was composed only of participants with NYHA functional class lower than class IV. The exclusion of patients with NYHA class IV may reduce the extent to which the results of the current study can be generalized to the population of outpatients with heart failure as a whole. Moreover, only the NYHA functional classification was used to derive a measure of functional impairment in this study. This measure of functional limitation, although commonly used in similar studies, may have not fully reflected the underlying variable thus potentially affecting the accuracy of the results. Further studies should address these issues by enrolling patients with NYHA class IV, and relying on more comprehensive and accurate measures of symptoms severity and functional limitation when trying to replicate the current findings. Finally, the exclusive use of cross-sectional data precludes establishment of casual relationships between variables.

In summary, results from this study imply that both psychological distress and self-care performance should be actively monitored and managed in heart failure care in order to help patients achieve and maintain positive health perceptions, given the current relevance attributed to patient-reported outcomes (Deshpande et al., 2011). Moreover, a better performance in self-care behaviors was found to be predictor of reduced hospital readmission and mortality rates (Moser et al., 2012; Riegel, Lee, & Dickson, 2011). In patients with heart failure, depression was found to be associated with an increased risk of all-cause and cardiovascular mortality (Fan et al., 2014;

Freedland et al., 2011), and non-fatal cardiovascular events (Newhouse & Jiang, 2014). Anxiety was also found to predict adverse outcomes in heart failure patients (Tsuchihashi-Makaya et al., 2009), especially when comorbid depressive symptoms were taken into account (Alhurani et al., 2015; Suzuki et al., 2014). As a consequence, interventions aiming to improve self-care behaviors and reduce symptoms of psychological distress may significantly decrease the risk of poor clinical outcomes, while contributing to better perceptions of current health status.

Conclusions

In order to conclude, the findings from this thesis first provide evidence to confirm the assumption that somatic and cognitive symptoms of depression, as evaluated by the items of the PHQ-9, should be considered as indicators of a common general depression factor, and not indicators of two distinct latent constructs. This result may have useful implications for both research and the development of clinical interventions to treat depressive disorders in patients with heart failure. With regard to implication for research, the present finding highlights the need to strictly rely on theoretical assumptions in making decisions about which items should compose somatic and cognitive dimensions of depression. Additionally, the use of confirmatory factor analysis approach, instead of less generalizable exploratory factor analyses, may reduce inconsistencies and facilitate comparisons across studies. Future studies should also focus on issues concerning the discriminant validity of somatic and cognitive latent factors, and assess the relative fit of different competing models. With regard to clinical implications, the current finding suggests that the treatment of depressed patients with heart failure should not be differentiated on the basis of the relevance of somatic or cognitive symptoms at the individual level. Depression management efforts should aim at treating patients to complete remission, regardless of which symptoms are found to be the most relevant.

Second, symptoms of psychological distress and worse self-care behaviors were associated to poorer self-rated health in the present work, after controlling for individual and environmental characteristics, and indices of disease severity. These findings suggest that, in patients with heart failure, perceived health status may be affected by symptoms of depression and anxiety, and by levels of patients' engagement in self-care behaviors. Given the impact of psychological distress and self-care

behaviors on mortality and rehospitalization rates, interventions designed to strengthen self-care performance and treat symptoms of psychological distress may contribute to ameliorate current perceptions of patients' health status, and reduce the risk of adverse medical outcomes.

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