Prevalence and associated factors for decreased appetite among patients with stable heart failure

Christina Andreae, Anna Strömberg and Kristofer Årestedt

Journal Article

Original Publication:

Christina Andreae, Anna Strömberg and Kristofer Årestedt, Prevalence and associated factors for decreased appetite among patients with stable heart failure, Journal of Clinical Nursing, 2016. 25(11-12), pp.1703-1712.
http://dx.doi.org/10.1111/jocn.13220

Abstract

Aims and objectives. To explore the prevalence of decreased appetite and factors associated with appetite among patients with stable heart failure.

Background. Decreased appetite is an important factor for the development of undernutrition among patients with heart failure, but there are knowledge gaps about prevalence and the factors related to appetite in this patient group.

Design. Observational, cross-sectional study.

Methods. A total of 186 patients with mild to severe heart failure were consecutively recruited from three heart failure outpatient clinics. Data were obtained from medical records (heart failure diagnosis, comorbidity and medical treatment), and self-rated questionnaires (demographics, appetite, self-perceived health, symptoms of depression, and sleep). Blood samples were taken to determine myocardial stress and nutrition status. Heart failure symptoms and cognitive function were assessed by clinical examinations. The Council on Nutrition Appetite Questionnaire was used to assess self-reported appetite. Bivariate correlations and multivariate linear regression analyses were conducted to explore factors associated with appetite.

Results. Seventy-one patients (38%) experienced a loss of appetite with a significant risk of developing weight loss. The final multiple regression model showed that age, symptoms of depression, insomnia, cognitive function, and pharmacological treatment were associated with appetite, explaining 27% of the total variance.

Conclusion. In this cross-sectional study, a large share of patients with heart failure was affected by decreased appetite, associated with demographic, psychosocial and medical factors.

Relevance to clinical practice. Loss of appetite is a prevalent problem among patients with heart failure that may lead to undernutrition. Health care professionals should routinely assess appetite

and discuss patients' experiences of appetite, nutrition intake and body weight and give appropriate nutritional advice with respect to individual needs.

Keywords: age, appetite, cognitive function, depression, heart failure, insomnia, outpatient, pharmacological treatment

What does this paper contribute to the wider global clinical community?

- Decreased appetite is a prevalent problem in patients with stable heart failure.
- Health care professionals should routinely assess appetite in patients with heart failure, particularly those of older age, with depressive symptoms, insomnia, decreased cognitive function and in patients with suboptimal pharmacological treatment.

Introduction

Heart failure (HF) is a progressive and symptomatic syndrome, characterized by lifelong medical treatment and great health care needs. HF affects around 2% of the population in developed countries, and the prevalence is particularly high in older people. At age >65, the estimated prevalence is about 10% (McMurray *et al.* 2012, Go *et al.* 2014). In recent decades, the treatment of HF has undergone major improvements. However, the syndrome is still associated with poor prognosis, especially in patients with undernutrition (Bonilla-Palomas *et al.* 2011). Decreased appetite may play a role in the development of undernutrition. However, the underlying causes for decreased appetite in HF have mainly been studied from a pathophysiological perspective and are not fully clear (Fudim *et al.* 2011). Decreased appetite among patients with HF is a problematic and unrecognized issue, and a better understanding of its manifestations will provide valuable support in efforts to prevent or delay undernutrition among patients with HF.

Background

Appetite is a complex phenomenon that contributes to an individual's body weight. Loss of appetite, defined as the reduced desire to eat, may vary due to psychobiological changes and environmental factors (Muscaritoli *et al.* 2010). The phenomenon becomes more complicated in cases of chronic illness, and it can be hypothesized that appetite may interplay with a series of components. Older age can possibly contribute to decreased appetite. In chronic conditions, studies have shown that patients >60 years report worsened appetite compared to younger patients (Cheung *et al.* 2011). Among the elderly, the aeging process may cause poor appetite due to a disturbance of appetite hormones (Malafarina *et al.* 2013). Impaired health status may also cause decreased appetite; a study among older people living in nursing homes showed that patients with dementia,

depression, and gastrointestinal problems ran twice the risk of having poor appetite compared to those not affected by these barriers (Landi *et al.* 2013). However, appetite in the context of older people and in chronic conditions needs to be further explored.

Currently, there are no available standard treatments to improve poor appetite in HF or any other chronic disease (von Haehling & Anker 2014). One possible reason is that appetite is a complex phenomenon and that it is difficult to measure due to a lack of validated self-reported instruments. Furthermore, a small study (n=135) has showed that appetite may be worse in patients with HF compared to healthy older people (Lennie *et al.* 2006). In addition, it seems like depression negatively affects appetite. A study among 572 hospitalized older patients with HF showed that decreased appetite is more prominent among those with depressive symptoms (Lesman-Leegte *et al.* 2006). The role of cognitive function and insomnia for appetite is not clear, despite other studies having shown that cognitive function (Orsitto *et al.* 2009, Farid *et al.* 2013) and insomnia (Westergren *et al.* 2013) are associated with undernutrition. With regard to this, poor appetite may possibly contribute to undernutrition as well. Since the cardinal symptoms of HF include breathlessness and fatigue, it is possible that these symptoms, as well as side effects of medical treatment and gastrointestinal oedema, also play a role in reduced appetite.

Based on few available studies, we hypothesised that the influence on appetite is multifactorial, and that demographic, psychosocial and medical factors may interplay. Accordingly, an expanded knowledge on the scope of decreased appetite and possible contributing factors in HF may guide health care professionals to prevent and treat undernutrition. Thus, the aim of this study was to explore the prevalence of decreased appetite and the factors associated with appetite among patients with stable HF.

Methods

Design and sample

This Swedish multicenter cross-sectional study was carried out between 2009 and 2012. In accordance with the Declaration of Helsinki, the patients received oral and written study information and provided informed consent. Approval was obtained by the Regional Ethical Review Board in Linköping (study code: M222-08/T81-09).

Patients with stable HF were consecutively recruited from three outpatient HF clinics at one university hospital and two county hospitals. The inclusion criteria were ≥18 years old, having mild to severe left ventricle systolic dysfunction and presence of HF symptoms. Patients on dialysis due to renal failure, and/or short life expectancy due to other diseases than HF, were excluded. The recruitment was performed during a regular HF outpatient visit. A total of 316 patients were invited to participate in the study, of whom 186 accepted (59%) (Table 1). This sample size was justified by a priori power analysis, conducted to determine the minimum sample size that would be acceptable for a multiple linear regression model. The calculation was based on a regression model including 13 independent variables, medium effect size (f^2=0.15), a significance level of 0.05 and a power of 0.90. To detect a R^2 deviation from 0, the minimum sample size was estimated to 162 individuals. The non-participants were significantly older than the participants ($t(313)=3.64$, $p<0.001$), but there was no significant difference regarding sex ($\chi^2(1)=0.10$, $p=0.701$).

Procedure and data collection

The study was conducted during two visits, first at the hospitals and then in the patients' homes. During the first visit, data collection included a review of the patients' medical records (diagnosis,

comorbidity, and medical treatment). A physical examination (six minutes' walk test) was also performed to assess HF symptoms according to New York Heart Association (NYHA) functional classification (McMurray *et al.* 2012). The patients were instructed to walk 30 m back and forth for six minutes. After that, the walking distance in meters was calculated. Longer distance implies better functional capacity (Rostagno & Gensini 2008). In addition, assessment of anthropometrics (Body Mass Index (BMI), waist-to-hip ratio) and blood samples (albumin) was performed using principles of nutritional assessment (Gibson 2005) and European guidelines for diagnosis and treatment of HF (McMurray *et al.* 2012). A BMI of >20kg/m^2 (Kondrup *et al.* 2003) and albumin ≥30g/l (McMurray *et al.* 2012) were considered to be indicators of normal nutrition status. Myocardial stress was determined by blood sample B-type natriuretic peptide (BNP) (McMurray *et al.* 2012). Comorbidity was assessed with the Charlson Comorbidity Index (CCI). In the CCI, nineteen diseases are divided into four weighted classification groups (1, 2, 3, and 6). Based on these classifications, comorbidities are summed to an index. Higher scores indicate more problems with comorbidity (Charlson *et al.* 1987). A questionnaire was also handed out for patients to complete at home. This included demographic questions and validated self-rating scales to assess appetite, symptoms of depression, self-perceived health, daytime sleepiness, and insomnia.

The purpose of the home visit was to collect the questionnaires and assess global cognitive function using the Mini Mental State Examination (MMSE). This screening tool was developed to assess cognitive function and contains questions about orientation with regard to time and place, memory by repeating words, attention by counting or spelling backwards, ability to recall previously mentioned words, and language tests (Folstein *et al.* 1975). The maximum score is 30, where a score of 24-30 indicates no cognitive impairment and a lower score, usually with a cut-off level of

≤23, is considered as mild to severe cognitive impairment (Tombaugh & McIntyre 1992). In this study, MMSE was used as a continuous varable.

The questionnaires

Appetite was assessed by The Council on Nutrition Appetite Questionnaire (CNAQ) (Wilson *et al.* 2005). The instrument which has been validated in HF populations (Andreae *et al.* 2015) includes a scale with eight items, each rated on a five-point scale. The total score ranges from 8-40, with lower scores indicating poorer appetite, and a CNAQ score ≤28 indicating a risk of significant weight loss over a six-month time period. In this study, internal consistency reliability was satisfactorily high; Cronbach´s α was 0.74.

The Patient Health Questionnaire (PHQ-9) was used to measure symptoms of depression.
The items grade patients' experiences of bothersome symptoms of depression in the last two weeks. A total of 9 items are rated on a four-point Likert-type scale, ranging from the lowest score "not at all" (0) to the worst "nearly every day" (3). The total score ranges from 0-27; (0-4) none to minimal, (5-9) mild, (10-14) moderate, (15-19) moderately severe and (20-27) severe depression (Kroenke *et al.* 2001). In this study, Cronbach´s α was 0.81.

The EuroQol EQ-5D was used to measure self-perceived health. The patients were asked to rate five dimensions including mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each dimension consists of three levels: (level 1) no problem, (level 2) some problems and (level 3) extreme problems. In this study, all five dimensions were converted to the EQ-5D three-level index (EQ-5D-3L index), with higher scores indicating better self-perceived health. EQ VAS was used to measure the current state of health on a 0-100 thermometer scale,

where zero indicates the worst imaginable state of health and 100 the best imaginable state of health (Brooks 1996).

The Epworth Sleepiness Scale (ESS) was developed to measure daytime sleepiness. The initial item deals with the likeliness of dozing off or falling asleep in different situations, e.g., when reading or watching TV. The eight items in the ESS are answered on a four-point Likert-type scale with a possible score between 0-24, where a higher score indicates more problems with daytime sleepiness (Johns 1991). Cronbach´s α in this study was 0.75.

The Minimal Insomnia Symptom Scale (MISS) was developed to assess sleeping difficulties. Three items covering difficulties falling asleep, night awakening and not being rested by sleep are answered on a five-point Likert-type scale. The total score ranges from 0, indicating no problem at all, to a high of 12, indicating major problems. A total score of ≥6 indicates increased risk of insomnia (Broman *et al.* 2008). Cronbach´s α in this study was 0.80.

Analysis

Descriptive statistics were used to describe sample characteristics and study variables. According to the level and distribution of the data, continuous variables are presented with median and quartiles and categorical variables with frequencies and percentages. Mean and standard deviation was used when appropriate. Chi-square statistics, Mann-Whitney *U* test and independent sample *t*-tests were performed to compare different sample characteristics for patients at risk of and at no risk of weight loss according to CNAQ, i.e., scores ≤28 or >28.

Spearman´s rank correlation coefficient (rho) was used to explore bivariate associations between appetite and the predictor variables, i.e., sex, age, cohabitation, functional capacity (NYHA-class), comorbidity (CCI), myocardial stress (BNP), symptoms of depression (PHQ-9), self-perceived health (EQ-5D and EQ VAS), daytime sleepiness (ESS), insomnia (MISS), cognitive function (MMSE) and medical treatment (beta-blocker, angiotensin-covering-enzyme-inhibitor and angiotensin-receptor-blocker).

To further explore the association between appetite and the predictor variables, all variables in the correlation analysis with a probability value <0.05 were included in the multiple linear regression analysis, which was performed in a stepwise procedure (backward selection). The CNAQ was used as the outcome variable and nine variables in the correlation analysis were included as predictor variables: age, cohabitation, functional capacity (NYHA), symptoms of depression (PHQ-9), self-perceived health (EQ-5D and EQ VAS), insomnia (MISS), cognitive function (MMSE) and medical treatment. Functional capacity was dummy coded and NYHA class II was selected as reference category. No problems with multicollinearity were detected according to the variance inflation factor (range 1.00-1.69). According to the D'Agostino test ($\chi2(2)=24.23$, $p<0.001$) and Breusch-Pagan/Cook-Weisberg test ($\chi2(5)=51.96$, $p<0.001$) respectively, the assumption of normality and homoscedasticity was violated. Thus, a robust regression analysis was finally applied (Huber/White sandwich estimators of variance) to validate the ordinary regression model.

The level of statistical significance was set to $p<0.05$. The statistical analyses were carried out using IBM SPSS statistics version 20.0 (SPSS Inc., Chicago, IL, USA) and STATA version 13.1 (StataCorp, College Station, TX, USA).

Results

Patient characteristics

A description of the sample characteristics is presented in Table 2. A total of 186 patients, 130 men and 56 women, completed the study. Median age was 72 years (IQR=65-78), and the majority had HF symptoms corresponding to NYHA class II (61%). Most of the patients were treated with conventional HF medications, i.e., beta-blockers (94%), ACE-inhibitors (60%) and angiotensin-receptor-blockers (41%). The majority had a normal nutrition status with BMI >20kg/m^2 (*n*=182) and albumin ≥30g/l (*n*=180). Most patients had normal cognitive function, although symptoms of depression (42%) and insomnia (39%) were highly prevalent.

Appetite

The results of this study show that 71 (38%) of the patients had poor appetite, i.e., CNAQ scores ≤28, with a risk of developing future weight loss. The CNAQ scores ranged between 17-37 with a median value of 30 (IQR=27-31) (Table 2).

Bivariate associations

Nine variables correlated significantly with appetite (Table 3). Older age, living alone, decreased functional capacity (i.e., higher NYHA class), worse self-perceived health (both EQ-5D index and EQ VAS), higher level of symptoms of depression, insomnia, decreased cognitive function and insufficient medical treatment were associated with lower levels of appetite. Depressive symptoms was the factor that correlated the strongest with appetite (rho=-0.422, p<0.001). Neither sex, comorbidity, myocardial stress (BNP) nor daytime sleepiness correlated significantly with appetite.

Multivariate associations

Overall, the stepwise multiple regression analyses showed that age, symptoms of depression, insomnia, cognitive function and medical treatment were significantly associated with appetite (Table 4). Older age, higher level of depressive symptoms, insomnia, decreased cognitive function and insufficient medical treatment were associated with poor appetite. Living with someone, functional capacity (NYHA class III-IV) and self-perceived health were not significantly associated with appetite in the multiple regression analysis. The final model explained 27% of the total variance in appetite. The robust regression model reproduced the findings from the original regression model.

Discussion

This study aimed to explore decreased appetite prevalence and factors among patients with stable HF. The findings showed that decreased appetite is a major problem among patients with HF. Furthermore, appetite was associated with age, symptoms of depression, insomnia, cognitive function and pharmacological treatment.

More than one third of the patients (38%) reported appetite levels that put them at risk of weight loss. The prevalence of decreased appetite in this study was, however, lower than has been observed in other chronic conditions, for example kidney disease (50%) (Gama-Axelsson *et al.* 2013) and cancer (88%) (Liu *et al.* 2013). A previous study by Song *et al.* (2010) reported that approximately 60% of patients with HF had poor appetite. The prevalence discrepancy between Song *et al.* and the present study may be due to appetite being assessed with different instruments. Another explanation may be that participants in the present study had stable HF and were recruited from

outpatient clinics. This can be compared with Song *et al.* (2010) who recruited patients hospitalised with decompensated HF, which may be associated with even more impaired appetite. As decreased appetite is associated with undernutrition and worsened prognosis (Landi *et al.* 2013, Malafarina *et al.* 2013), these findings need to be addressed in the care of patients with HF. In particular, efforts should be made to identify patients at risk of decreased appetite, for example by structured appetite assessments. Standard treatment to improve appetite is still lacking (von Haehling & Anker 2014). Therefore, health care professionals should offer individualised dietary advice to help patients with poor appetite maintain weight and prevent undernutrition, for example by using energy and protein rich food and nutritional supplements to reach their daily energy intake. Patients can also be recommended to divide their daily food intake into smaller and more frequent meals. For this, a nutritional care plan for setting nutritional goals may be helpful. Despite the large share of patients with poor appetite in this study, the majority were well nourished. One explanation may be that the participants had less HF symptoms and that most of them were treated with conventional HF medications, which have been shown to protect against undernutrition (Anker *et al.* 2003).

Several factors in the present study were found to be associated with appetite: age, symptoms of depression, insomnia, cognitive function and pharmacological treatment. Older age was found to be associated with lower levels of appetite. This corresponds with a study by Cheung *et al.* (2011), which showed that decreased appetite was more common among the older compared to younger people. Furthermore, the aeging process may contribute to poor appetite due to hormonal changes (Landi *et al.* 2013). It has been shown that the appetite hormone ghrelin was reduced in older people, which may have negative effects on gastric emptying and gut motility (Malafarina *et al.* 2013).

Related to older age, lower levels of cognitive function were associated with decreased appetite. To our knowledge, no previous study has explored the association between cognitive function and appetite. A study among 623 older hospitalised patients with mild cognitive impairment showed that 58% were at risk of becoming undernourished (Orsitto *et al.* 2009). Nutrition status in that study was measured by the Mini Nutritional Assessment (MNA), a screening tool for determining the risk of undernutrition in hospital care, not appetite. Similar associations between impaired cognitive function and body weight have been observed in patients with cardiovascular disease as well (Farid *et al.* 2013).

Neither age nor cognitive function are clear targets for interventions. In order to prevent undernutrition, particularly in these groups, health care professionals should routinely assess and discuss appetite in HF care. As the CNAQ has been shown to have acceptable measurement properties in patients with HF (Andreae *et al.* 2015), structured assessments with this tool can be useful for identifying patients at risk of weight loss. Discussions about appetite and dietary habits with patients and family members may serve for individualised nutrition advice and interventions. Patients with decreased appetite in combination with signs of undernutrition, for example weight loss, should preferably be referred to a dietician for expert advice and treatment.

In contrast to age and cognitive function, symptoms of depression, insomnia and pharmacological treatment are factors more suitable for interventions. Findings from this study showed that higher levels of symptoms of depression are associated with poor appetite. These findings corresponds with other studies that have demonstrated that symptoms of depression constitute a barrier for nutrition intake (Lennie *et al.* 2006, Lesman-Leegte *et al.* 2006). A study by Lesman-Leegte *et al.* (2006) showed that poor appetite was more common among depressive patients than in

nondepressive patients with HF, 68% vs. 49% respectively. The prevalence of poor appetite in this study was nearly half of that. A possible explanation for this might be that the majority of the participants had less HF symptoms and less comorbidity. Another explanation is that appetite in this study was assessed by the CNAQ, which is in contrast to Lesman-Leegte *et al.* (2006), who determined appetite through interviews. Another study on 114 older nursing home residents also showed a significant association between symptoms of depression and appetite, but to a lesser extent (Smoliner *et al.* 2009). As depression can be a barrier for performing adequate nutritional self-care activities, health care professionals should routinely screen for and treat symptoms of depression (Lainscak *et al.* 2011).

A large share of the patients in this study reported problems with insomnia, which was associated with decreased appetite. Sleep disturbance might negatively affect daily life with both psychological and physical consequences, such as daytime tiredness (Redeker *et al.* 2010). The consequences of tiredness might lead to disrupted food routines and a potential risk of meals being postponed until a later time, or in the worst case being skipped altogether. That can in turn lead to decreased food intake and development of undernutrition. To our knowledge, there are no previous studies that have specifically investigated insomnia and appetite in patients with HF. Further studies are needed for a better understanding of this association.

In this study, BMI was assessed in order to describe nutrition status. Studies have shown an association between low BMI, decreased appetite and unintentional weight loss (Westergren *et al.* 2009). Therefore, assessing BMI and self-perceived appetite may be of value for determining the risk of undernutrition. However, in cases of acute deterioration of HF, BMI can be misleading as

decompensated HF often leads to fluid retention and weight gain (Gibson 2005). In this study, the patients were stable at inclusion, but they might have had oedema.

Limitations

This study has some limitations that need to be considered. Most importantly, the study had a cross-sectional design, which limits the possibilities to draw any causal conclusions regarding the relationship between the identified factors and appetite level. This addresses the need for further prospective studies, for example trajectories of appetite over time and associated factors. In accordance with other HF studies (Näsström *et al.* 2014), there was a large number of nonparticipants. This can be explained by the fact that many patients with HF suffer a high symptom burden, often combined with old age, which makes it difficult to participate in research studies. Another limitation is that the sample had a history of predominantly mild to moderate HF, which makes it difficult to generalise the findings to the most symptomatic patients in NYHA class IV.

There are different methods to assess appetite and previous studies have mainly used single items or scales, such as the appetite item in Mini Nutritional Assessment (MNA), visual analogue scale (VAS), numerical rating scale (NRS) or verbal rating scale (VRS). However, appetite is a complex construct that not easily can be measured with a single item. Of this reason appetite was measured with the CNAQ in this study, which have shown good measurement properties among patients with HF (Andreae *et al.* 2015). This resulted in difficulties comparing the finding with other studies. Appetite is not a variable likely to generate more socially desirable responding. However, response bias related to the home visit cannot be excluded. Participants completed the questionnaire at home; they were instructed to do it on their own and to follow the provided instructions. However, we

could not control for if someone else was consulted when they completing the survey. Another limitation was the small number of assessments to determine nutritional status. However, both BMI (Kondrup *et al.* 2003) and albumin (McMurray *et al.* 2012) have been described as potential assessment tools in order to detect risk of undernutrition. The mean age in this study was some years lower than the general HF population according to the Swedish HF registry (Lund *et al.* 2014). Due to the gender distribution also not being equal, this may limit the generalisability of the findings to the oldest and women.

Conclusion

This study adds new insights into appetite prevalence in patients with stable HF. Decreased appetite is a significant problem, associated with demographic, psychosocial and medical factors. These findings need to be confirmed by further studies, preferably with prospective designs.

Relevance to clinical practice

Decreased appetite plays an important role in the development of undernutrition and is therefore a significant clinical problem. Early management of decreased appetite may prevent or delay undernutrition. This study underlines that appetite should be given special attention in older patients with HF, especially those with decreased cognitive function, symptoms of depression, sleeping difficulties and suboptimal HF treatment. In clinical practice, health care professionals should routinely assess appetite and especially focus on the older frail patients with HF and multimorbidity. All patients with decreased appetite should be offered nutritional advice and support to improve nutritional self-care in order to maintain their weight and prevent undernutrition. As appetite is a complex phenomenon, assessments can be facilitated by using a

short, validated self-rating scale such as the CNAQ. Besides patients themselves and health care professionals, it is important that also family members and significant others pay attention to signs of decreased appetite and undernutrition and actively participate in interventions to improve nutrition. The family plays a very important role in nutritional and eating habits of the patient and should therefore routinely be involved in the HF care.

Acknowledgements

We would kindly like to thank all study participants, HF nurses and administration staff for their assistance in completing this study. We also thank Mats Fredriksson at the Linköping Academic Research Centre for statistical advice.

Disclosure

All authors confirm that the criteria for authorship have been met according to the International Committee of Medical Journal Editors (ICMJE) with regard to (1) substantial contributions to conception and design of, or acquisition of data or analysis, and interpretation of data; (2) drafting the article or revising it for important intellectual content; and (3) final approval of the manuscript to be published.

Funding

This study was funded by the Centre for Clinical Research Sörmland, Uppsala University, Eskilstuna, Sweden, the Swedish Heart and Lung Foundation, King Gustaf V and Queen Victoria´s Freemason Foundation, and the Medical Research Council of Southeast Sweden.

Conflict of interest

None.

References

Andreae C, Strömberg A, Sawatzky R & Årestedt K (2015) Psychometric Evaluation of Two Appetite Questionnaires in Patients With Heart Failure. *Journal of Cardiac Failure* **21**, 954-958.

Anker SD, Negassa A, Coats AJ, Afzal R, Poole-Wilson PA, Cohn JN & Yusuf S (2003) Prognostic importance of weight loss in chronic heart failure and the effect of treatment with angiotensin-converting-enzyme inhibitors: an observational study. *Lancet* **361**, 1077-1083.

Bonilla-Palomas JL, Gamez-Lopez AL, Anguita-Sanchez MP, Castillo-Dominguez JC, Garcia-Fuertes D, Crespin-Crespin M, Lopez-Granados A & Suarez de Lezo J (2011) Impact of malnutrition on long-term mortality in hospitalized patients with heart failure. *Revista Espanola Cardiologia* **64**, 752-758.

Broman JE, Smedje H, Mallon L & Hetta J (2008) The Minimal Insomnia Symptom Scale (MISS): a brief measure of sleeping difficulties. *Upsala Journal of Medical Sciences* **113**, 131-142.

Brooks R (1996) EuroQol: the current state of play. *Health Policy* **37**, 53-72.

Charlson ME, Pompei P, Ales KL & MacKenzie CR (1987) A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *Journal of Chronic Diseases* **40**, 373-383.

Cheung WY, Le LW, Gagliese L & Zimmermann C (2011) Age and gender differences in symptom intensity and symptom clusters among patients with metastatic cancer. *Support Care Cancer* **19**, 417-423.

Farid K, Zhang Y, Bachelier D, Gilson P, Teixeira A, Safar ME & Blacher J (2013) Cognitive impairment and malnutrition, predictors of all-cause mortality in hospitalized elderly subjects with cardiovascular disease. *Archives of Cardiovascular Diseases* **106**, 188-195.

Folstein MF, Folstein SE & McHugh PR (1975) "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research* **12**, 189-198.

Fudim M, Wagman G, Altschul R, Yucel E, Bloom M & Vittorio TJ (2011) Pathophysiology and treatment options for cardiac anorexia. *Current Heart Failure Reports* **8**, 147-153.

Gama-Axelsson T, Lindholm B, Bárány P, Heimbürger O, Stenvinkel P & Qureshi AR (2013) Self-Rated Appetite as a Predictor of Mortality in Patients With Stage 5 Chronic Kidney Disease. *Journal of Renal Nutrition* **23**, 106-113.

Gibson RS (2005) *Principles of nutritional assessment*. Oxford University Press, New York.

Go AS, Mozaffarian D, Roger VL, Benjamin EJ, Berry JD, Blaha MJ, Dai S, Ford ES, Fox CS, Franco S, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Huffman MD, Judd SE, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Mackey RH, Magid DJ, Marcus GM, Marelli A, Matchar DB, McGuire DK, Mohler ER, 3rd, Moy CS, Mussolino ME, Neumar RW, Nichol G, Pandey DK, Paynter NP, Reeves MJ, Sorlie PD, Stein J, Towfighi A, Turan TN, Virani SS, Wong ND, Woo D, Turner MB, American Heart Association Statistics C & Stroke Statistics S (2014) Heart disease and stroke statistics--2014 update: a report from the American Heart Association. *Circulation* **129**, e28-e292.

von Haehling S & Anker SD (2014) Treatment of cachexia: an overview of recent developments. *Journal of the American Medical Directors Association* **15**, 866-872.

Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. *Sleep* **14**, 540-545.

Kondrup J, Allison SP, Elia M, Vellas B, Plauth M, Educational, Clinical Practice Committee ESoP & Enteral N (2003) ESPEN guidelines for nutrition screening 2002. *Clinical Nutrition* **22**, 415-421.

Kroenke K, Spitzer RL & Williams JB (2001) The PHQ-9: validity of a brief depression severity measure. *Journal of General Internal Medicine* **16**, 606-613.

Lainscak M, Blue L, Clark AL, Dahlstrom U, Dickstein K, Ekman I, McDonagh T, McMurray JJ, Ryder M, Stewart S, Stromberg A & Jaarsma T (2011) Self-care management of heart failure: practical recommendations from the Patient Care Committee of the Heart Failure Association of the European Society of Cardiology. *European Journal of Heart Failure* **13**, 115-126.

Landi F, Lattanzio F, Dell'Aquila G, Eusebi P, Gasperini B, Liperoti R, Belluigi A, Bernabei R & Cherubini A (2013) Prevalence and potentially reversible factors associated with anorexia among older nursing home residents: results from the ULISSE project. *Journal of the American Medical Directors Association* **14**, 119-124.

Lennie TA, Moser DK, Heo S, Chung ML & Zambroski CH (2006) Factors influencing food intake in patients with heart failure: a comparison with healthy elders. *Journal of Cardiovascular Nursing* **21**, 123-129.

Lesman-Leegte I, Jaarsma T, Sanderman R, Linssen G & van Veldhuisen DJ (2006) Depressive symptoms are prominent among elderly hospitalised heart failure patients. *European Journal of Heart Failure* **8**, 634-640.

Liu Y, Zhang PY, Na J, Ma C, Huo WL, Han L, Yu Y & Xi QS (2013) Prevalence, intensity, and prognostic significance of common symptoms in terminally ill cancer patients. *Journal of Palliative Medicine* **16**, 752-757.

Lund LH, Benson L, Dahlstrom U, Edner M & Friberg L (2014) Association between use of beta-blockers and outcomes in patients with heart failure and preserved ejection fraction. *The Journal of the American Medical Association* **312**, 2008-2018.

Malafarina V, Uriz-Otano F, Gil-Guerrero L & Iniesta R (2013) The anorexia of ageing: physiopathology, prevalence, associated comorbidity and mortality. A systematic review. *Maturitas* **74**, 293-302.

McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Bohm M, Dickstein K, Falk V, Filippatos G, Fonseca C, Gomez-Sanchez MA, Jaarsma T, Kober L, Lip GY, Maggioni AP, Parkhomenko A, Pieske BM, Popescu BA, Ronnevik PK, Rutten FH, Schwitter J, Seferovic P, Stepinska J, Trindade PT, Voors AA, Zannad F, Zeiher A, Bax JJ, Baumgartner H, Ceconi C, Dean V, Deaton C, Fagard R, Funck-Brentano C, Hasdai D, Hoes A, Kirchhof P, Knuuti J, Kolh P, McDonagh T, Moulin C, Reiner Z, Sechtem U, Sirnes PA, Tendera M, Torbicki A, Vahanian A, Windecker S, Bonet LA, Avraamides P, Ben Lamin HA, Brignole M, Coca A, Cowburn P, Dargie H, Elliott P, Flachskampf FA, Guida GF, Hardman S, Iung B, Merkely B, Mueller C, Nanas JN, Nielsen OW, Orn S, Parissis JT & Ponikowski P (2012) ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *European Journal of Heart Failure* **14**, 803-869.

Muscaritoli M, Aversa Z, Laviano A, Fanelli FR, Anker SD, Argilés J, Bauer JM, Sieber CC, Biolo G, Boirie Y, Bosaeus I, Cederholm T, Costelli P, Fearon KC, Maggio M, Schneider SM &

Schols A (2010) Consensus definition of sarcopenia, cachexia and pre-cachexia: Joint document elaborated by Special Interest Groups (SIG) " cachexia-anorexia in chronic wasting diseases" and " nutrition in geriatrics". *Clinical Nutrition* **29**, 154-159.

Näsström L, Jaarsma T, Idvall E, Årestedt K & Strömberg A (2014) Patient participation in patients with heart failure receiving structured home care--a prospective longitudinal study. *BMC Health Services Research* **14**, 633.

Orsitto G, Fulvio F, Tria D, Turi V, Venezia A & Manca C (2009) Nutritional status in hospitalized elderly patients with mild cognitive impairment. *Clinical Nutrition* **28**, 100-102.

Redeker NS, Jeon S, Muench U, Campbell D, Walsleben J & Rapoport DM (2010) Insomnia symptoms and daytime function in stable heart failure. *Sleep* **33**, 1210-1216.

Rostagno C & Gensini GF (2008) Six minute walk test: a simple and useful test to evaluate functional capacity in patients with heart failure. *Internal and Emergency Medicine* **3**, 205-212.

Smoliner C, Norman K, Wagner KH, Hartig W, Lochs H & Pirlich M (2009) Malnutrition and depression in the institutionalised elderly. *British Journal of Nutrition* **102**, 1663-1667.

Song EK, Moser DK, Rayens MK & Lennie TA (2010) Symptom clusters predict event-free survival in patients with heart failure. *Journal of Cardiovascular Nursing* **25**, 284-291.

Tombaugh TN & McIntyre NJ (1992) The mini-mental state examination: a comprehensive review. *Journal of the American Geriatrics Society* **40**, 922-935.

Westergren A, Lindholm C, Mattsson A & Ulander K (2009) Minimal eating observation form: reliability and validity. *The Journal of Nutrition, Health & Aging* **13**, 6-12.

Westergren A, Edfors E, Hedin G & Hagell P (2013) Improving nursing students research knowledge through participation in a study about nutrition, its associated factors and assessment. *Journal of Nursing Education and Practice* **3**, 50-58.

Wilson MM, Thomas DR, Rubenstein LZ, Chibnall JT, Anderson S, Baxi A, Diebold MR & Morley JE (2005) Appetite assessment: simple appetite questionnaire predicts weight loss in community-dwelling adults and nursing home residents. *The American Journal of Clinical Nutrition* **82**, 1074-1081.

Table 1 Flow chart illustrating the recruitment process

Participants who fulfilled the study inclusion criteria, and those who declined to participate at each hospital.		
University hospital Fulfilled inclusion criteria *n*=124 Declined to participate *n*=50	County hospital Fulfilled inclusion criteria *n*=26 Declined to participate *n*=1	County hospital Fulfilled inclusion criteria *n*=166 Declined to participate *n*=79
The final number of participants in the study University hospital *n*=74 County hospital *n*=25 County hospital *n*=87 *Total n=186*		

Table 2 Characteristics of the study population (*n*=186)

		CNAQ		
	All (*n*=186)	>28 (*n*=115)	≤28 (*n*=71)	*p*-value
Demographics				
Age, md (IQR)	72 (65-78)	71 (63-78)	75 (66-82)	0.010[a]
Gender, *n* (%)				0.593[b]
Male	130 (70)	82 (71)	48 (68)	
Female	56 (30)	33 (29)	23 (32)	
Cohabitation, *n* (%)				0.019[b]
Living with someone	124 (67)	31 (27)	40 (56)	
Living alone	62 (33)	84 (73)	31 (44)	
Medical variables				
Duration of HF, *n* (%)				0.950[b]
0-5 years	45 (24)	28 (24)	17 (24)	
> 5 years	141 (76)	87 (76)	54 (76)	
NYHA class, *n* (%)				0.003[b]
II	114 (61)	81 (70)	33 (46)	
III	60 (32)	30 (26)	30 (42)	
IV	12 (6)	4 (4)	8 (11)	
BNP (qmol/l), md (IQR)	129 (58-250)	120 (50-230)	160 (62-280)	0.205[a]

Six minute walk test (meters), md (IQR)	375 (285-450)	390 (330-486)	302 (180-404)	<0.001[a]
Comorbidity (CCI), md (IQR)	1 (1-2)	2 (1-2)	1 (1-3)	0.542[a]
Pharmacological treatment, *n* (%)				
BB	174 (94)	109 (95)	65 (92)	0.684[b]
ACEI	111 (60)	77 (67)	34 (48)	0.036[b]
ARB	76 (41)	44 (38)	32 (45)	0.599[b]
Aldosteron antagonist	63 (34)	37 (32)	26 (37)	0.762[b]
Optimal pharmacological treatment, *n* (%)	134 (72)	88 (77)	46 (65)	0.223[b]
Nutritional variables				
Albumin (g/l), md (IQR)	40 (37-42)	40 (38-43)	39 (37-42)	0.446[a]
Waist-to-hip ratio, m (SD)	0.99 (0.10)	0.99 (0.10)	0.98 (0.10)	0.268[c]
BMI (kg/m^2), md (IQR) [range]	28 (25-32) [17-48]	28 (25-31) [17-42]	29 (24-33) [20-48]	0.524[a]
Self-reported variables				
CNAQ, md (IQR)	30 (27-31)	31 (30-32)	26 (24-28)	n/a
MMSE, md (IQR)	29 (27-29)	29 (28-30)	28 (27-29)	<0.001[a]
PHQ-9, md (IQR)	4 (1-7)	3 (1-6)	6 (3-10)	<0.001[a]
MISS, md (IQR)	5 (2-7)	3 (1-6)	6 (4-8)	<0.001[a]
ESS, md (IQR)	9 (6-12)	9 (6-11)	9 (6-12)	0.507[a]

EQ-5D index, md (IQR)	0.73 (0.66-0.81)		0.80 (0.69-1.00)		0.69 (0.62-0.73)		<0.001[a]
EQ VAS, md (IQR)	60 (50-70)		65 (50-80)		50 (45-70)		<0.001[a]

a=Mann-Whitney *U* test.

b=Chi- square test.

c=Independent sample *t*-test.

NYHA-class, New York Heart Association Classification; BNP, B-type natriuretic peptide; CCI, Charlson Comorbidity Index; BB, beta-blocker; ACEI, angiotensin-covering-enzyme-inhibator; ARB, angiotensin-receptor-blocker; BMI, Body Mass Index; CNAQ, Council on Nutrition Appetite Questionnaire; MMSE, Mini Mental State Examination; PHQ-9, Patient Health Questionnaire; MISS, Minimal Insomnia Symptom Scale; ESS, Epworth Sleepiness Scale.

Table 3 Bivariate correlations between appetite and hypothesised predictor variables

	CNAQ		
	Spearman's rho	*p*-value	*n*
Sex, male	0.072	.328	186
Age, years	-0.204	0.005	186
Cohabitation, living with someone	0.194	0.008	186
NYHA functional class	-0.237	0.001	186
Comorbidity, CCI	-0.017	0.822	186
BNP	-0.081	0.269	186
Symptoms of depression, PHQ-9	-0.422	<0.001	186
Self-perceived health, EQ-5D	0.389	<0.001	186
Self-perceived health, EQ VAS	0.320	<0.001	186
Daytime sleepiness, ESS	-0.126	0.086	186
Insomnia, MISS	-0.390	<0.001	186
Cognitive function, MMSE	0.251	0.001	182
Optimal pharmacological treatment [a]	0.158	0.032	184

NYHA, New York Heart Association Classification; CCI, Charlson Comorbidity Index; BNP, B-type natriuretic peptide; PHQ-9, Patient Health Questionnaire; ESS, Epworth Sleepiness Scale; MISS, Minimal Insomnia Scale; MMSE, Mini Mental State Examination

[a] Having optimal dose of one or both beta-blocker and angiotensin-covering-enzyme-inhibator/angiotensin-receptor-blocker

Table 4 Predictor variables for appetite (CNAQ) based on a stepwise multivariate regression analysis (*n*=181)

	Ordinary regression model			Robust regression model		
Independent variables	B	SE	*p*-value	B	SE	*p*-value
Age, years	-0.05	0.02	0.015	-0.05	0.02	0.009
Symptoms of depression, PHQ-9	-0.22	0.07	0.001	-0.22	0.09	0.020
Insomnia, MISS	-0.22	0.09	0.015	-0.22	0.09	0.021
Cognitive function, MMSE	0.25	0.09	0.007	0.25	0.12	0.036
Optimal pharmacological treatment [a]	1.18	0.50	0.021	1.18	0.50	0.019
Model statistics	$F(175, 5)=13.11$, $p<0.001$, $R^{2=}.27$			$F(175, 5)=10.63$, $p<0.001$, $R^{2=}.27$		

B is the unstandardized regression coefficient.

CNAQ, Council on Nutrition Appetite Questionnaire; PHQ-9, Patient Health Questionnaire; MISS, Minimal Insomnia Scale; MMSE, Mini Mental State Examination.

[a] Having optimal dose of one or both beta-blocker and angiotensin-covering-enzyme-inhibator/angiotensin-receptor-blocker.