Quality of Life in Patients with Chronic Heart Failure

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5.1 Introduction

Despite advances in treatment leading to prolongation of survival, chronic heart failure (CHF) remains the primary cause of death among individuals with cardiovascular diseases (CVDs) [1]. Heart failure is associated with heavy symptom burden, frequent admission into hospital, and high mortality. The incidence of CHF increases with age, and the prognosis is similar to the prevalence of mortality seen in certain malignant neoplasms [2]. Data from the West Midlands Regional Cancer Registry in the UK found that the 1-year survival of CHF patients was worse than that of patients with cancers of the breast, prostate gland, or bladder [3].

Symptomatic heart failure negatively influences the quality of life (QoL) of subjects by restricting various spheres of activity and social role functioning. Individuals with heart failure usually experience high levels of physical, functional and emotional distress, and their health-related quality of life (HRQoL) cannot be normalized even with optimal treatment [4, 5]. The QoL of patients with heart failure and their partners is poor compared with: (i) their age-matched peers from the general population; (ii) patients suffering from other chronic diseases. Moreover, depression is a strong determinant of the QoL of CHF patients [6]. It has been demonstrated that male patients complain about significant fatigue, a lack of energy, and a resigned demeanor [7]. Conversely, women are characterized by increased perception of all the negative symptoms of CHF: they lose trust in themselves, worry, and feel a heightened sense of anxiety [8]. These attitudes add to an increased dependence on their surroundings and negatively affect family life [9]. The psychological state of subjects, independent of the symptoms of CHF, leads to more frequent and extended hospitalization.

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In recent years, interest has focused on the HRQoL of CHF patients, which has since become an important endpoint in assessing the effects of different treatment options. However, when using the concept of HRQoL, one should be mindful that it does not equate to "health status". Current health status is one of the determinants of HRQoL but, in actuality, it is a concept used to consider only a clinical understanding of health. A physician is interested initially in the changes to the biochemical and physiologic parameters under treatment. However, patients are more interested in alleviating symptoms, improving everyday functioning, and fulfilling their social roles. For patients, QoL (e.g., symptoms and the impact of their illness on social, emotional and occupational functioning) may be as important as longevity [10]. Because it offers information concerning the patient's experience of treatment, measuring HRQoL is a useful and significant expansion of traditional, clinical medicine, which measures health status based on the results of physical examination or laboratory results [11].

HRQoL is also a valuable prognostic indicator. For patients in the same CHF functional class (for example, a class set by the New York Heart Association (NYHA)), those with low HRQoL are characterized by a significantly greater risk of hospitalization related to their underlying disease, including a higher risk of mortality [12]. Rodriguez-Artalejo et al. [13] found that poor HRQoL in patients first hospitalized for heart failure measured using physical, psychological, and general health dimensions was associated with a 63–75% higher risk of rehospitalization and mortality within 6 months. Thus, treatment and care should focus not only on the physical symptoms of heart failure, but also on a multidisciplinary care approach involving optimizing medical therapy, symptom management, education, and the interventions known to improve QoL.

The main symptoms of CHF restricting everyday activity and leading to decreased HRQoL include dyspnea, fatigue, weakness, limited exercise tolerance, drowsiness, and peripheral edema. The HRQoL of CHF patients is significantly worse compared with that of healthy individuals or even those suffering from other chronic diseases (e.g., hypertension, diabetes mellitus (DM), atrial fibrillation, angina, post-myocardial infarction, or chronic obstructive pulmonary disease (COPD)) [4, 14]. CHF patients suffer from limited exercise tolerance, which inhibits an active lifestyle. However, it has long been observed that evaluation of traditional clinical endpoints (e.g., physician-rated exercise tolerance, left ventricular ejection fraction, concentration of N-terminal prohormone of brain natriuretic peptide (NT-proBNP) in blood) correlate poorly (if at all) with the degree of everyday activity and general well-being of CHF patients [6] who, in similar stages of clinical advancement, function and react differently in various, everyday life situations. HRQoL could be (and usually is) impaired in heart-failure patients with preserved and reduced left ventricular ejection fraction (LVEF) [15].

Personal relationships, nutrition, sexual activity, and the ability to work are re-

stricted in heart-failure patients and coalesce with an increasing dependency upon others. HRQoL is determined not by the fact that these problems and difficulties are present, but by the manner in which they are dealt with, experienced, and how the patient responds to these events. Differences in how patients interpret their situation during the course of illness may lead to reductions in everyday functioning and social relationships, resulting in constrained social support. Conversely, the inability of family and one's surroundings to accommodate the illness-related needs of a close individual (i.e., ineffective support) leads to restrictions placed on contact with the patient, further decreasing HRQoL. The partners of CHF patients have also been found to report decreased HRQoL [16]. A worsening health status reminds the patient of impending death, leading to worsened psychosocial health (i.e., depression, increased anxiety and sleep disturbances) [6]. HRQoL therefore remains a significant problem for CHF patients and their families. "Objective health status", in the traditional, medical sense of the term, constitutes only a part of this problem.

5.2 Measuring HRQoL in Subjects with CHF

Measuring QoL (including measurements in CHF patients) is usually realized by the use of two types of questionnaire: generic and specific. Their application is meant to illustrate and describe the consequences of illness from the patient's perspective. The generic instruments most often used in heart-failure patients are the Psychological General Wellbeing (PGWB) Index, the Life Satisfaction Questionnaire, the Nottingham Health Profile (NHP), the Sickness Impact Profile (SIP) and the Short Form Health Survey 36 (SF-36) (see Appendix). Several specific questionnaires can also be applied to CHF patients. These can be used to measure HRQoL or measure selected dimensions of QoL (Table 5.1).

Specific questionnaires are usually less broad than the generic questionnaires, and allow for better understanding of how treatment influences a specific problem, such as symptoms, physical activity, and sexual dysfunction. The specific questionnaires most often used in CHF patients are the Quality of Life in Severe Heart Failure Questionnaire (QLQ-SHF), the Chronic Heart Failure Questionnaire (CHFQ), the Kansas City Cardiomyopathy Questionnaire (KCCQ), the Left Ventricular Dysfunction Questionnaire (LVD-36), the Minnesota Living with Heart Failure Questionnaire (MLHF), and the European Heart Failure Self-Care Behavior Scale [17, 18]. These questionnaires have good psychometric properties (validity and sensitivity to change), though in patients suffering from CHF current evidence would primarily support the use of the MLHF, followed by the KCCQ and CHFQ.

The MLHF has been applied in research such as the Studies of Left Ventricular

Table 5.1 Questionnaires used to measure health-related quality of life in subjects with chronic heart failure (see Appendix)

Generic	Chronic heart failure-specific or targeted	Domain or factor-specific
Short Form Health Survey 36 (SF-36)	Minnesota Living with Heart Failure (MLHF)	Hospital Anxiety Depression Scale (HADS)
Sickness Impact Profile (SIP)	Chronic Heart Failure Questionnaire (CHFQ)	Duke Activity Status Index (DASI)
Dortmund COOP Scale (COOP)	QoL in Severe Heart Failure Questionnaire (QLQ-SHF)	Reitan Trail-making Test
EuroQoL 5D (EQ-5D)	Subjective Symptoms Assessment Profile (SSA-P)	Six-minute Walking Test (6MWT)
Nottingham Health Profile (NHP)	Heart Failure Functional Status Inventory (HFFSI)	Katz Index of Activities of Daily Living (KIAD)
Psychological General Wellbeing Index (PGWB)	MacNew Questionnaire (MacNew)	International Index of Erectile Dysfunction (IIEF-5)
Quality of Life Index (QLI)	European Heart Failure Self-Care Behaviour Scale	Profiles of Mood States (POMS)
The Self Assessment of Global Wellbeing (SAGWB)	QoL in Severe Heart Failure Questionnaire (QLQ-SHF)	
WHO Quality of Life Questionnaire (WHOQoL)	Kansas City Cardiomyopathy Questionnaire (KCCQ)	
Cantril Ladder of Life (CLL)	Left Ventricular Dysfunction Questionnaire (LVD-36)	

Dysfunction, Vasodilator-Heart Failure Trials (V-HeFT II and III), and to measure the results of using different beta-blockers in the treatment of heart failure. A randomized study comparing the influence of digoxin and placebo on HRQoL was done using the CHFQ. Also, the QLQ-SHF was used in various studies examining how the course of CHF is influenced by the use of angiotensin-converting enzyme inhibitors (ACEIs). Further discussion is required regarding the use of specific questionnaires applied in the measurement of HRQoL in patients with heart failure (see Appendix).

5.2.1 QLQ-SHF

QLQ-SHF comprises 26 Likert-type questions used to measure quantitatively physical activity as well as an analogous scale to measure life satisfaction and social/emotional factors. The higher the point score, the more negatively affected

is HRQoL. QLQ-SHF has been used in several clinical studies, and its validity has been determined in comparative studies with other questionnaires (e.g., SIP). The validity of the QLQ-SHF is sufficient for the dimensions of physical symptoms and life satisfaction. However, this validity is decreased for somatic complaints and physical activity.

Studies have shown that the QLQ-SHF is moderately sensitive to small changes in the QoL of CHF patients. However, further study is required because it is not known if this questionnaire can be used to differentiate between patients in terms of CHF severity (see Appendix).

5.2.2 CHFQ

CHFQ contains 20 questions which can be applied in an interview with trained personnel. It can be used to differentiate between three problem categories: dyspnea, fatigue, and emotional functioning. A higher score denotes higher HRQoL. CHFQ is highly sensitive to changes in the degree of severity of the main CHF symptoms (i.e., dyspnea and fatigue). Therefore, CHFQ is used in patients at varying levels of CHF advancement (see Appendix).

5.2.3 MLHF

MLHF was developed for CHF patients to measure how such patients interpret the influence of CHF on their exercise tolerance, socioeconomic functioning, and psychological status (see Appendix). Patients answer 21 questions using a six-level, Likert-type scale, earning 0–5 points for each answer. One can measure the dimensions of physical and emotional functioning separately. MLHF is short, easy to use, and understandable by patients. It can be administered as a survey and completely independently by patients in their homes or in the physician's office. MLHF has satisfactory validity compared with other scales measuring the influence of CHF on the HRQoL of patients [19].

It can be used to differentiate between subjects with and without symptomatic left ventricular dysfunction (LVD) (i.e., NYHA classes I and II) but it poorly differentiates between advanced stages of symptomatic CHF. Thers are reservations as to whether MLHF can also be used to differentiate between symptoms of heart failure from similar symptoms in other diseases [20]. MLHF is usually employed to measure heart-related QoL in CHF patients, but it is a specific questionnaire that is meant to be used in clinical studies to measure the influence of pharmacotherapy or other interventions on HRQoL. It does not ensure a full measure of HRQoL [20].

5.3 Clinical Factors and the HRQoL of CHF Patients

Burdensome symptoms reported by 20–75% of heart-failure patients include dyspnea, fatigue, pain, peripheral edema, and lack of appetite. Beyond these typical symptoms of failing health, ≤ 70% of CHF patients experience anxiety and 50% report depressive symptoms, excessive stress, and cognitive dysfunction (i.e., difficulty with concentration). Approximately 50% of patients also experience dry mouth, trouble with taste sensations, excessive sweating, palpitations, and constipation [21].

Dyspnea and fatigue are the basic symptoms reported by CHF patients. Patients also complain about sleep disturbances, described by them as "even worse and more burdensome" than dyspnea [21], leading to even greater fatigue and negative influences on HRQoL [22]. A significant percentage of CHF patients report aggravated sleep disturbances, especially insomnia. These disturbances are associated directly not only with fatigue, but also the frequent occurrence of depression and poor HRQoL [22]. It seems that CHF patients who report chronic fatigue along with tiredness during the day should also be evaluated carefully for sleep disturbances [23].

Worse HRQoL has been linked to a younger age of the CHF patient, greater severity of symptoms, and to a greater number of restrictions on physical activity resulting from CHF [21]. Decreasing the severity or eliminating the symptoms of CHF leads to an improved ability to engage in normal activity and may positively influence HRQoL. Most CHF patients know that their illness is related to reduced longevity, which leads to additional stress.

Female CHF patients are characterized by having lower HRQoL than men [24]. Their HRQoL is also lower than that of women who have experienced a myocardial infarction (MI) or in those with other chronic diseases, such as DM, Parkinson's disease, or COPD [25]. Compared with men, the HRQoL of female CHF patients is most affected in the dimensions of: sleep; symptoms; the energy that they have every day; physical and psychological functioning; and self-rated health. Improvement in HRQoL after hospitalization due to CHF is also lower in women than in men.

Not all studies confirm the decreased HRQoL of women with heart failure. Compared with women, some authors observe decreased HRQoL in male subjects with heart failure, especially in older age groups [4, 26]. However, these differences disappeared after adjusting for the NYHA classification system, ejection fraction, and age. When explaining differences in the HRQoL of male and female subjects with CHF, the different ways in which the sexes perceive the influence of their disease on everyday functioning must be stated. Men tend to focus most of their attention on the restrictions their disease places on physical functioning. Conversely, women tend to focus their attention on the negative affects of their disease on emotional, family and social functioning. Women with poor social support, who live alone, and who

have a pessimistic personality are characterized by especially lower HRQoL [27].

Congestive heart failure is one of the diseases that affects HRQoL most negatively, in which older (compared with younger) patients seem to report higher levels of QoL [22, 24, 26]. This difference is based primarily on the varied way in which health and illness is interpreted at different ages. Younger individuals are affected more greatly by the restrictions placed on them by their illness, even if this involves only their family and professional activities. Sexual dysfunction constitutes an often encountered problem in male CHF patients. This involves loss of libido and an increased incidence of erectile dysfunction [28].

Ejection fraction does not correlate significantly with HRQoL in CHF patients. Austin et al. reported that, at 8 years follow-up in patients living with heart failure, HRQoL scores were similar regardless of systolic function (i.e., the KCCQ scores were not different in the survivors with preserved and reduced ejection fraction) [29]. Recently, Hoekstra et al. confirmed that QoL measured with generic and diseases-specific questionnaires was impaired by similar amounts in CHF patients with preserved ejection fraction as in CHF patients with reduced ejection fraction [15].

5.4 Influence of Treatment for Heart Failure on HRQoL

Studies have shown that pharmacological and non-pharmacological (e.g., restricting intake of salt and fluids) treatment options may positively influence the HRQoL of CHF patients (though this effect is not appreciable). In patients with symptomatic left ventricular dysfunction, certain ACEIs, beta-blockers (especially carvedilol) [30], and diuretics yield only a modest advantage over placebo in terms of improving HRQoL. In this respect, differences exist within groups of particular drugs. For example, compared with placebo, one study did not find rampril to significantly improve the HRQoL of patients treated for moderately advanced CHF.

Certain angiotensin-II receptor antagonists called sartans are characterized by their positive influence on the HRQoL of subjects with heart failure as measured using the McMaster questionnaire. The recently published results of the Candesartan in Heart Failure (CHARM) study [31] reported that, after 26 months, the addition of candesartan to current CHF treatment led to significant improvement in HRQoL. Moreover, the Valsartan Heart Failure Trial (Val-HeFT) found that adding valsartan to an ACEI regimen that did not include beta-blockers led to improvement in HRQoL if measured using MLHF [32]. Both studies suggested that, from the viewpoint of patient QoL, sartans may be used in CHF patients already being treated with ACEIs, or even before beginning treatment with beta-blockers.

However, not all studies have confirmed the additional benefits of sartan use on the HRQoL of heart-failure patients. The Losartan Heart Failure Survival Study

(ELITE II) measured HRQoL in CHF patients treated with losartan. It found that losartan did not have an advantage over captopril in terms of influencing the QoL of patients in NYHA classes II–IV and decreased left ventricular ejection fraction. The Replacement of Angiotensin Converting Enzyme Inhibition (REPLACE) study also did not find changes to the HRQoL of patients with heart failure treated with telmisartan compared with those treated with enalapril if measured using MLHF [33].

The dimensions most sensitive to pharmacological therapy include the symptoms of CHF and exercise tolerance. Changes to HRQoL influenced by pharmacological treatment are minimal or absent after the administration of drugs that are similar in their clinical effects and side effects. For example, of 10 studies examining the influence of beta-blockers on the HRQoL of patients with heart failure, only 3 reported improvement [34]. A study by Baxter et al. [35] found only modest improvement in general QoL and decreased severity of depression and anxiety if bisoprolol was used in CHF patients aged ≥ 70 years. Also, as part of a prospective study, a direct comparison of carvedilol and metoprolol found that they influenced the HRQoL of CHF patients in a similar way, despite certain hemodynamic differences favoring carvedilol [36]. Even with the use of new-generation beta-blockers (e.g., carvedilol, nebivolol), heart failure inevitably decreases the longevity and wellbeing of patients [37, 38].

Several drugs used to treat subjects with heart failure can reduce heart rate (HR), but their effects on symptoms are diverse and can be undesirable. Results from the Systolic Heart Failure Treatment with the If Inhibitor Ivabradine Trial (SHIFT) showed that HR reduction with ivabradine in CHF patients reduced cardiovascular mortality or hospital admissions for worsening heart failure. In addition, there was an improvement in NYHA class and in patient-reported QoL measured using the KCCQ [39]. HRQoL at follow-up was better preserved in the ivabradine group compared with placebo (ivabradine reduced HR by 10 bpm versus placebo). This study suggested that the ivabradine-associated reduction in CHF severity (as reflected by a reduced number of hospital admissions and improved NYHA functional class) also translated into a favorable impact on HRQoL. In contrast, treatment with beta-blockers (which were associated with similar HR reduction and reduction in CHF mortality) did not result in improved HRQoL, as reported in a meta-analysis by Dobre et al. [40].

Volterrani et al. found in the Effect of Carvedilol, Ivabradine or their Combination on Exercise Capacity in Patients with Heart Failure (CARVIVA HF) Trial that patients with heart failure treated with a maximal dose of ACEI who then received ivabradine or ivabradine plus carvedilol had better QoL than patients treated only with carvedilol. HR in this relatively small study (n = 121) was reduced in all three groups, but to a graeter extent by the combination [41]. The studies described above suggest that ivabradine alone or in combination with some beta-blockers may be effective in improving exercise tolerance and QoL in CHF patients.

How non-pharmacologic interventions influence HRQoL is even less conclusive. The results of recently published studies concerning different treatment options, beginning from basic nursing and ending with nasal continuous positive airway pressure (NCPAP), noted only a small positive influence of these interventions on the HRQoL of CHF patients. Patient education and regular support from nursing personnel seems to improve the HRQoL of patients at various stages of advanced heart failure [42].

Another problem in CHF patients is anemia, which is caused mainly by iron deficiency. Anemia is a strong risk factor for increased mortality in patients with CVDs (including CHF) and may be considered to be the biological background for one frequently reported complaint: chronic fatigue. Conversely, some CHF patients have iron deficiency without anemia. Beyond erythropoesis, iron is involved in many biological processes crucial for the maintenance of homeostasis. Its deficiency may impair the aerobic and oxidative metabolism of cells, leading to limitation in exercise capacity, decreased wellbeing and a poor prognosis in CHF patients [43]. The Ferinject Assessment in Patients with Iron Deficiency and Chronic Heart Failure (FAIR-HF) Trial [44] demonstrated that intravenous administration of ferric carboxymaltose in patients with CHF and iron deficiency with and without anemia could improve exercise performance and QoL in ≈50% of these patients as compared with 28% patients receiving placebo.

5.5 Influence of Physical Exercise on the HRQoL of CHF Patients

There is a direct relationship between CHF and worsened exercise tolerance resulting from a lack of physical training. Exercise improves the HRQoL of patients through benefits to their general physical condition and the possibility of independent functioning. The first randomized clinical study measuring the influence of physical training on patients with chronic CHF found that subjects, in general, felt better, more self-reliant, and had better control over their lives through participation in everyday activities with greater independence and less awareness of their illness [45].

Physical training in patients with heart failure usually involves the use of large muscle groups as well as strength exercises in small (i.e., peripheral) muscle groups. Training of large muscle groups consists of walking, step training, and ergometer cycling. Strength training in small muscle groups comprises exercises using arms or legs while sitting or lying down. It was recently observed that concentrated leg exercises (i.e., physical training of knee muscles), carried out over 8 weeks, led, in general, to improved exercise tolerance and improved HRQoL. This improvement was greater in the group training both legs as opposed to the group training only one leg. Therefore, the HRQoL of patients may (at least in part) be dependent

upon the type of exercises done. Tyni-Lenne, et al. [46] conducted a study directly comparing changes in HRQoL resulting from the strength training of small muscle groups and ergometer cycling for large muscle groups. Improvement in HRQoL was noted only in patients who underwent small-muscle training of the lower limbs. This finding suggested that such training may be beneficial for subjects with more advanced CHF who are not very physically active, and that training small-muscle groups may correct the negative changes which occur in the peripheral muscles of CHF patients.

Studies examining the HRQoL of CHF patients subjected to physical training usually involve small patient groups who are typically middle-aged and therefore not representative of all patients with heart failure. Nevertheless, the vast majority of studies reported significant recovery in different dimensions of HRQoL in male and female subjects with CHF. Improving the HRQoL of heart-failure patients undergoing physical training is one of the most elusive elements of clinical improvement. Progress is associated with enhanced exercise tolerance, decreased fatigue and dyspnea, and an expansion in the everyday activity of patients (including an emotional dimension) [47]. Gradually increasing the resistance of weekly ergometer cycling is safe for CHF patients, and significantly develops their HRQoL as well as oxygen consumption, more so than training at a constant level of resistance [48]. Another study confirmed that gradually increasing the intensity of physical training improved HRQoL more so than less intensive training [49]. However, the long-term effects of such training on HRQoL remain to be determined; one study found a return to pre-training HRQoL levels 6 months after halting the exercise regimen [47].

Based on the studies mentioned above, supervised physical training of varied intensity may be advantageous for individuals with stable CHF in whom significant improvement in HRQoL occurs regardless of NYHA class or LVEF [45]. Physical training in older patients with exacerbated CHF symptoms leads to less improvement in HRQoL than in younger patients [50].

5.6 Conclusions

In CHF patients, HRQoL is worse than in patients suffering from other chronic diseases. Heart failure is associated with a heavy symptom burden, frequent hospitalization and high mortality. Many CHF patients are conscious of the fact that their illness is related to decreased longevity, which leads to added stress. They also suffer from chronic fatigue, depression, anxiety and sleep disturbances. QoL measured using appropriate questionnaires is also impaired in CHF patients with preserved ejection fraction as it is in those with reduced ejection fraction. However, contemporary pharmacotherapy, based mainly on ACEIs, sartans and beta-blockers, has a small (but beneficial) influence on symptoms and HRQoL. Moreover,

patient education, support from nursing personnel, and regular physical training seem to improve the HRQoL of patients at various stages of heart failure.

References

1. Dickstein K, Cohen-Solal A, Filipatos G et al (2008) ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. Eur Heart J 29:2388-2442
2. Stewart S, MacIntyre K, Hole DA et al (2000) More malignant than cancer? Five year survival following a first admission for heart failure in Scotland. Eur J Heart Fail 102:1126-1131
3. Cowie M, Kirby M (2001) Heart failure: an overview. Managing heart failure in primary care: a practical guide. Oxfordshire, UK, Bladon Medical Publishing, pp 1-5
4. Hobbs FDR, Kenkre JE, Roalfe AK et al (2002) Impact of heart failure and left ventricular systolic dysfunction on quality of life. Eur Heart J 23:1867-1876
5. Bekelman DB, Havranek EP, Becker DM et al (2007) Symptoms, depression, and quality of life in patients with heart failure. J Card Fail 13:643-648
6. Müller-Tasch T, Peters-Klimm F, Schellberg D et al (2007) Depression is a major determinant of quality of life in patients with chronic systolic heart failure in general practice. J Card Fail 13:818-824
7. Martensson J, Karlsson J-E, Friedlund B (1997) Male patients with congestive heart failure and their conception of life situation. J Adv Nures 25:579-586
8. Martensson J, Karlsson J-E, Friedlund B (1998) Female patients with congestive heart failure: how they conceive their life situation. J Adv Nures 28:1216-1224
9. Jaarsma T, Johansson P, Agren S et al (2010) Quality of life and symptoms of depression in advanced heart failure patients and their partners. Curr Opin Support Palliat Care 4:233-237
10. Stanek EJ, Oates MB, McGhanWF et al (2000) Preferences for treatment outcomes in patients with heart failure: symptoms vs. survival. J Card Fail 6:225-232
11. Johansson P, Agnebrink M, Dahlstrom U et al (2004) Measurement of health-related quality of life in chronic heart failure from a nursing perspective - a review of the literature. Eur J Cardiovasc Nurs 3:7-20
12. Alla F, Briancon S, Guillemin F et al (2002) Self-rating of quality of life provides additional prognostic information in heart failure. Insight into the EPICAL study. Eur J Heart Fail 4:337-343
13. Rodriguez-Artalejo F, Guallar-Castillon P, Pascual CR et al (2005) Health-related quality of life as a predictor of hospital readmission and death among patients with heart failure. Arch Intern Med 165:1274-1279
14. Juenger J, Schellberg D, Kraemer SH et al (2002) Health-related quality of life in patients with congestive heart failure: compared with other chronic diseases and relation to functional variables. Heart 87:235-241
15. Hoekstra T, Lesman-Leegte I, van Veldhuisen DJ et al (2011) Quality of life is impaired similarly in heart failure patients with preserved and reduced ejection fraction. Eur J Heart Fail 13:1013-1018
16. Luttik ML, Jaarsma T, Veeger NJ et al (2005) For better and for worse: Quality of life impaired in HF patients as well as in their partners. Eur J Cardiovasc Nurs 4:11-14
17. Jaarsma T, Stromberg A, Martensson J et al (2003) Development and testing of the European Heart Failure Self-Care Behaviour Scale. Eur J Heart Fail 5:363-370
18. Garin O, Ferrer M, Pont A et al (2009) Disease-specific health-related quality of life questionnaires for heart failure: a systematic review with meta-analyses. Qual Life Res 18:71-85
19. Hak T, Willems D, van der Wal G et al (2004) A qualitative validation of the Minnesota Living with Heart Failure Questionnaire. Qual Life Res 13:417-426
20. Sneed N, Paul S, Michel Y et al (2001) Evaluation of 3 quality of life measurement tools in patients with chronic heart failure. Heart Lung 30:332-340

21. Zambroski CH, Moser DK, Bhat G et al (2005) Impact of symptom prevalence and symptom burden on quality of life in patients with heart failure. Eur J Cardiovasc Nurs 4:198-206
22. Brostrom A, Stromberg A, Dahstrom U et al (2004) Sleep difficulties, daytime sleepness and health-related quality of life in patients with chronic heart failure. J Cardiovasc Nurs 4:234-242
23. Johansson P, Dahlstrom U, Brostrom A (2006) Factors and interventions influencing health-related quality of life in patients with heart failure: a review of the literature. Eur J Cardivasc Nurs 5:5-15
24. Steptoe A, Mohabir A, Mahon NG et al (2000) Health-related quality of life and psychological well-being in patients with dilated cardiomyopathy. Heart 83:645-650
25. Riedinger MS, Dracup KA, Brecht ML (2002) Studies of left ventricular dysfunction. Quality of life in women with heart failure, normative groups, and patients with other chronic conditions. Am J Critical Care 11:211-219
26. Ekman I, Fagerberg B, Lundman B (2002) Health-related quality of life and sense of coherence among elderly patients with severe chronic heart failure in comparison with healthy control. Heart Lung 31:94-101
27. Luttik ML, Jaarsma T, Veeger N et al (2006) Marital status, quality of life, and clinical outcome in patients with heart failure. Heart Lung 35:3-8
28. Jaarsma T (2002) Sexual problems in heart failure patients. Eur J Cardiovasc Nurs 1:61-67
29. Austin BA, Wang Y, Smith GL et al (2008) Systolic function as a predictor of mortality and quality of life in long-term survivors with heart failure. Clin Cardiol 31:119-124
30. Rickli H, Steiner S, Muller K et al (2004) Beta-blockers in heart failure: Carvedilol Safety Assessment (CASA 2-trial). Eur J Heart Fail 6:761-768
31. O'Meara E, Lewis E, Granger C et al (2005) Patient perception of the effect of treatment with candesartan in heart failure. Results of the Candesartan in Heart failure: Assessment of Reduction in Mortality and morbidity (CHARM) programme. Eur J Heart Fail 7:650-656
32. Krum H, Carson P, Farsang C et al (2004) Effect of valsartan added to background ACE inhibitor therapy in patients with heart failure: results from Val-HeFT. Eur J Heart Fail 6:937-945
33. Dunselman PH (2001) Effects of the replacement of the angiotensin converting enzyme inhibitor enalapril by the angiotensin II receptor blocker telmisartan in patients with congestive heart failure. The replacement of angiotensin converting enzyme inhibition (REPLACE) investigators. Intern J Cardiol 77:131-138
34. Reddy P, Dunn AB (2000) The effect of beta-blockers on health-related quality of life in patients with heart failure. Pharmacotherapy 20:679-689
35. Baxter AJ, Spensley A, Hildreth A et al (2002) Beta blockers in older persons with heart failure: tolerability and impact on quality of life. Heart 88:611-614
36. Metra M, Giubbini R, Nodari S et al (2000) Differential effects of beta-blockers in patients with heart failure: A prospective, randomized, double-blind comparison of the long-term effects of metoprolol versus carvedilol. Circulation 102:546-551
37. Cleland JG, Charlesworth A, Lubsen J et al (2006) A comparison of the effects of carvedilol and metoprolol on well-being, morbidity, and mortality (the "patient journey") in patients with heart failure: a report from the Carvedilol Or Metoprolol European Trial (COMET). J Am Coll Cardiol 47:1603-1611
38. Conraads VM, Metra M, Kamp O et al (2012) Effects of the long-term administration of nebivolol on the clinical symptoms, exercise capacity, and left ventricular function of patients with diastolic dysfunction: results of the ELANDD study. Eur J Heart Fail 14:219-225
39. Ekman I, Chassany O, Komajda M et al (2011) Heart rate reduction with ivabradine and health related quality of life in patients with chronic heart failure: results from the SHIFT study. Eur Heart J 32:2395–2404
40. Dobre D, van Jaarsveld CH, deJongste MJ et al (2007) The effect of beta-blocker therapy on quality of life in heart failure patients: a systematic review and meta-analysis. Pharmacoepidemiol Drug Saf 16:152-159

41. Volterrani M, Cice G, Caminiti G et al (2011) Effect of carvedilol, ivabradine or their combination on exercise capacity in patients with heart failure (the CARVIVA HF trial). Int J Cardiol 151:218-224
42. Kasper EK, Gerstenblith G, Hefter G et al (2002) A randomized trial of the efficacy of multidisciplinary care in heart failure outpatients at high risk of hospital readmission. J Am Coll Cardiol 39:471-480
43. Jankowska EA, Rozentryt P, Witkowska A et al (2010) Iron deficiency: an ominous sign in patients with systolic chronic heart failure. Eur Heart J 31:1872-1880
44. Anker SD, Comin Colet J, Filippatos G et al (2009) Ferric carboxymaltose in patients with heart failure and iron deficiency. N Engl J Med 361:2436-2448
45. Belardinelli R, Georgiou D, Cianci G et al (1999) Randomized, controlled trial of long-term moderate exercise training in chronic heart failure. Effects on functional capacity, quality of life and clinical outcome. Circulation 99:1173-1182
46. Tyni-Lenne R, Gordon A, Jensen-Urstad M et al (1999) Aerobic training involving a minor muscle mass shows greater efficacy than training involving a major muscle mass in chronic heart failure patients. J Cardiac Fail 5:300-307
47. Willenheimer R, Erhardt L, Cline C et al (1998) Exercise training in heart failure improves quality of life and exercise capacity. Eur Heart J 19:774-781
48. Klocek M, Kubinyi A, Bacior B et al (2005) Effect of physical training on quality of life and oxygen consumption in patients with congestive heart failure. Intern J Cardiol 103:323-329
49. Sledge SB, Ragsdale K, Tabb J et al (2000) Comparison of intensive outpatient cardiac rehabilitation to standard outpatient care in veterans: effects on quality of life. J Cardiopulmon Rehabil 20:383-388
50. Owen A, Croucher L (2000) Effect of an exercise programme for elderly patients with heart failure. Eur J Heart Fail 2:65-70