

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: <http://www.elsevier.com/locate/crvasa>

Review article

Palliative care in cardiology

Martin Gřiva^{a,*}, Martin Loučka^b, Jiří Šťastný^a^a Department of Internal Medicine, Tomáš Baťa Regional Hospital, a.s., Zlín, Czech Republic^b Palliative Care Center, Prague, Czech Republic

ARTICLE INFO

Article history:

Received 16 November 2014

Received in revised form

29 November 2014

Accepted 2 December 2014

Available online 5 January 2015

Keywords:

Palliative care

Communication

Cardiology

Chronic heart failure

ABSTRACT

Palliative care is an approach aimed at improving the quality of life of patients (and their families) faced with a life-threatening condition. Chronic heart failure (CHF) is a progressive disease with increasing incidence and prevalence. Despite (or perhaps, because of) all the advances in medicine, CHF remains one of the leading causes of death. Even with the availability of numerous prognostic tools, an estimate of the course and outcome of a CHF patient continues to pose a challenge. As a result, palliative care should be initiated early and provided in parallel with curative treatment. The cornerstone of palliative care is communication based, mainly, on listening to the patient, telling the patient their unfavorable diagnosis, and therapeutic dialog. Drug therapy is provided in an effort to alleviate the symptoms. Non-pharmacological options of improving the quality of life of the patient include nutritional care, rehabilitation and, possibly, treatment of sleep apnea. Deactivation of the implantable cardioverter/defibrillator should also be considered as an option. Last but not least, the attending physician should focus on the psychological and spiritual needs of the patient. Palliative care in cardiology poses a major challenge to all members of teams caring for the CHF patient not only over the last weeks of their lives, but during their entire course of treatment.

© 2014 Published by Elsevier Urban & Partner Sp.z.o.o. on behalf of The Czech Society of Cardiology.

Contents

Introduction	e40
Prognostic stratification and optimal timing of palliative care initiation	e40
Communication	e40
Palliative care and medical therapy	e42
Non-pharmacological therapy	e42
Psychological and spiritual needs	e43
Conclusion	e43
Conflict of interest	e43
Funding body	e43
Ethical statement	e43
References	e43

* Corresponding author. Tel.: +420 739094518.

E-mail address: m.griva@seznam.cz (M. Gřiva).<http://dx.doi.org/10.1016/j.crvasa.2014.12.005>

0010-8650/© 2014 Published by Elsevier Urban & Partner Sp.z.o.o. on behalf of The Czech Society of Cardiology.

Introduction

Cardiac and cancer patients alike face numerous physical, psychological, and social problems. Due to the advances in modern medicine, the incidence of CHF is on the increase and its mortality continues to be high and comparable with those of the most common malignancies [1]. Symptoms deteriorating the quality of life occur in CHF patients at the same rate as in cancer patients [2]. Despite all the advances in CHF management, the final stage of the disease is associated with very poor quality of life [3]. Generally, the term palliative care refers to an approach designed to improve the quality of life of patients (and families thereof) faced with a life-threatening condition [4]. All these facts taken together, there is logically an effort to implement palliative approaches also in cardiology. However, the concept of palliative care in cardiology has not been clearly defined. To date, no methodology of palliative care has been developed, there are no large randomized trials providing the evidence base for current cardiology, many cardiologists actually do not think in the context of palliative care, there is a lack of experience and, occasionally, also willingness to communicate about end-of-life issues, patients' feelings and preferences. Some reports have documented an astonishingly low level of agreement between the views of the patient and his physician (cardiologist) regarding priorities for care toward the end of life [5,6].

When exploring the issue of palliative care in cardiology, it is worthwhile to highlight some aspects distinguishing palliative care in cardiology from that in oncology. It is a well-known fact that the end stage of the heart failure patient may be largely different [7]. In addition to the underlying disease, other factors significantly affecting the quality of life of the cardiac patient include their often older age, polypharmacy, and comorbidities. Likewise, in some patients, the side effects of commonly used drugs may pose a problem bigger than the disease *per se*. Multiple episodes of heart failure progression experienced by the patient and perceived by their family members with a gradually waning response to therapy are often in stark contrast with their expectations and absence of an explanation why this is so. In oncology, the limitations of therapeutic options are almost generally anticipated, and different rates of disease progression to death are accepted. Given the impressive strides in reducing morbidity and mortality rates, the situation is just the opposite in cardiology, a specialty associated – among lay people – with triumph of medical science over disease and patient recovery, all this despite the fact that cardiovascular disease remains the number one killer in Europe (42% of males, 52% of females) [8].

Prognostic stratification and optimal timing of palliative care initiation

Establishing the prognosis of an individual heart failure patient, that is, estimating the time until their death at various stages of the disease is indeed a major challenge. In this context, the question naturally arises as to the timing of palliative care initiation. To date, up to 300 potential prognostic markers have been investigated. A rough estimate

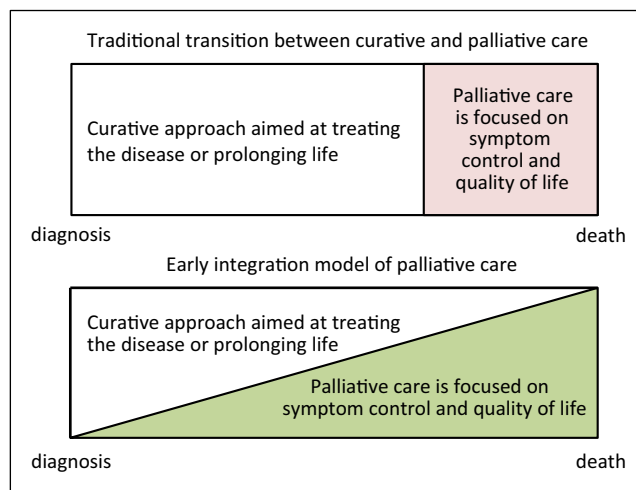


Fig. 1 – Mode of care integrating palliative and curative approaches.

Adapted from [45].

of prognosis can be based on the NYHA classification combined with some biochemical markers (B-type natriuretic peptide, natremia), and exercise capacity or cardiac output measurement. Several comprehensive tools and scoring systems have been developed and tested to estimate the prognosis of heart failure patients; these include the Seattle Heart Failure Score [9] available online at (<http://depts.washington.edu/shfm/>). Other scoring systems such as the CardioVascular Medicine Heart Failure (CVM-HF) index [10] or that employed in the EFFECT trial [11] have incorporated comorbidities into the prognostic scheme. Still, in most cases, the presence of progressive renal insufficiency, cachexia, and increased diuretic use serve as reliable markers of a dismal prognosis in elderly and polymorbid patients [12]. While an estimate of survival of an individual patient remains difficult despite the above options, the following situations may lead to the decision to initiate palliative care: repeated episodes of heart failure over the last 6 months despite optimal management, occurrence of malignant arrhythmias, frequent need for intravenous diuretics or their continuous administration, long-term poor quality of life, refractory NYHA IV class symptoms, and signs of cardiac cachexia [13]. Recently, there has been general consensus that palliative care should optimally be initiated in parallel with full curative therapy with a gradual increase in the proportion of palliative care and adequate decrease in curative therapy toward the end of life, that is, both approaches run in parallel. The previous strategy whereby curative therapy is replaced by palliative care several weeks before death is being discarded (Fig. 1). The current integrating strategy seems to be the most advantageous particularly because many heart failure patients do not show major deterioration of their quality of life in its final stages [14].

Communication

Communication is the cornerstone of palliative care. Unlike oncologists, cardiologists find themselves in a much more

difficult situation since, as postgraduate students, they receive virtually no training in communication skills allowing them to address issues related to the diagnosis of an incurable disease (which heart failure doubtless is), the process of dying, and the therapeutic options available in the individual stages of the disease. It is not usual to listen to a patient's preferences. At this point, it should be mentioned that communication with the patient is as important as communication with his family and/or the caregiver. All physicians and nurses alike taking care of heart failure patients should be prepared, if asked by the patient or his family, for discussion about the nature of the disease and the process of dying. Still, what is really needed is a more proactive approach by the attending physician toward either party involved as, though every effort is made to improve a patient's functional fitness and defer death, it is critical to talk to the patient and his family – once the diagnosis of heart failure has been established – about the progressive nature of the disease which will eventually impair the quality of life and survival. Such an approach, whilst helping to optimally fight the disease immediately after diagnosis, will also prevent experiencing distress later should symptoms recur and progress gradually [15].

Besides essential information about body weight self-monitoring and the possibility of adjusting diuretic doses, communication in palliative care plays other roles. First and foremost, it is what is referred to as “active listening”, which certainly does not mean only a properly taken patient's medical history. Of equal importance is knowledge of the patient's attitude toward his disease, understanding his fears and concerns, his list of life priorities, and what he is actually worried about. The aim of this process is to learn whether the patient and family understand the implications of the disease [16].

A most specific, dreadful task is to convey the unfavorable information about the presence of an incurable progressive disease to the patient (and subsequently, if agreed, to their

family and/or caregivers). Every clinician taking care of a heart failure patient should receive basic training in delivering the bad news to the patient, and discussing facts about the end of life along the same lines as in oncology. The key aspects of communication are summarized in Table 1.

A third major feature of mutual communication in palliative care is therapeutic dialog. Occasionally, the patient is not asked about the way he would like to be managed in the given stage of his disease at all, or his views are simply disregarded. During the course of treatment, the patient should be repeatedly updated about the reasons for, and potential implications of his current therapy and alternative options. At the same time, a patient with a reasonable level of information should be able to refuse any of the procedures, particularly at a later stage of the disease. Thus, due attention should be given to relevant issues such as, for example, a patient's decision not to have cardiac surgery, attempted resuscitation and stop or, possibly, refuse treatment with the implantable cardioverter/defibrillator [17].

Discussion about a patient's attitude to cardiopulmonary resuscitation (CPR) is just another uneasy task for the clinician and one associated with concern about upsetting the patient. However, as the SUPPORT trial clearly showed that the attitude of patients toward CPR is inconsistent, discussion about one's end of life should not only be initiated but, also, encouraged repeatedly to possibly allow for revision [6].

Optimization of contact with the family and care givers in palliative care is of utmost importance. It is just these individuals who will remember the quality of life of their loved one over the last months and weeks of life, and the way he or she was dying and, also, the way he or she was being treated in a most emotion-laden period of time. This is also a period of time when a well-trained nurse may prove simply invaluable to the physician as she is able to repeatedly educate the patient and family on the above topics and, possibly, obtaining answers to questions she is unable to handle. The

Table 1 – Elements of communication about a grim prognosis; adapted from [46].

Conversation with “bad news”	Proper timing of delivering sad and unexpected news; warn the patient we have bad news for him/her; and proceed as follows.
Ask-Tell-Ask	Ask the patient what he actually knows about his/her disease. Correct any misunderstanding. Tell the patient your information. Ask if there are any questions and provide clarification if needed.
Simple, honest language, simple statistics	Explain medical terms, use plain language and avoid euphemisms, statistical data and percentages (preferably “one in five patients...”).
Describe the multifaceted nature of reality Hope for the best, plan for the worst (“Not only ..., but also ...”)	Describe the chances of both death and cure as well as a chance to defer death. Ask the patient what he/she hopes for. Tell the patient what we can ideally both hope for in medical terms. Plan for death or another bad outcome “if things do not go they way we hope for”.
Normalize uncertainty Partner and plan	Acknowledge we cannot know for sure “...like many things in life...” Tell the patient you and (your team) will do our best to help the patient and his/her family to cope with difficult situations.
Set the length of life in a broad range Empathy	Set a broad range of “months to years” and allow for error at either end. Name your emotions (“I am sad”) and identify the emotions either explicitly expressed by the patient or such he/she can reasonably experience (“I know it comes as a surprise ...”, “it is normal to feel anger, fear ...”)
Follow-up	Summarize the plan and set an appointment to follow-up on plans and his/her status.

attitude toward communication is most cogently summarized in the American Heart Association scientific guidelines stating that “...difficult discussions now will simplify difficult decisions in the future” [18].

Palliative care and medical therapy

As large clinical trials searching for optimal algorithms in the treatment of heart failure have mostly excluded elderly and polymorbid patients or those in the end stage of a disease, no consistent data are available as to managing these cases. There is consensus that standard management of heart failure should be provided in cardiology almost until the last moment unless the patient, after being thoroughly informed, has refused to accept any of the options available. Medication should be revised on a regular basis. In cases showing clinically obvious signs of the end stage of the disease, it is appropriate to individualize management and possibly withdraw some of the drugs that could potentially deteriorate the quality of life at a time when no one can reasonably expect the prognosis will improve. Here again, the care giver should see the model shown in Fig. 1.

The most common symptoms in a large proportion of patients with advanced chronic heart failure include dyspnea, pain, cough, edema and fatigue as well as low exercise tolerance, anxiety, depression, sleeplessness, nausea, loss of appetite, weight loss, constipation, and other problems often refractory to standard therapy [19–21]. Regular thorough assessment of symptoms may not only help focus on procedures to alleviate these problems, but also to estimate the patient's prognosis.

The mainstay of dyspnea management throughout the course of the disease is standard therapy consistent with current guidelines [22,23]. Should dyspnea persist despite maximum tolerated medical therapy in the end-of-life stage, morphine administration should be considered. Morphine should hypothetically reduce respiratory work and prevent premature respiratory muscle weakness, and a decreased sense of difficulty breathing due to morphine action on opioid receptors in the brain and lungs; the anxiolytic-like effect of morphine should also not be disregarded [24–26]. Its side effects may include constipation. While there is no generally accepted morphine administration protocol based on data from clinical trials and divergent opinions persist, it is empirically assumed that therapy should be initiated in a manner similar to that in the management of otherwise uncontrollable cancer-related pain, with further dose titration guided individually by the clinical outcome. A meta-analysis of 18 trials demonstrated a significant beneficial effect of oral or parenteral opiates on dyspnea relief [27]; opiate administration over periods as long as several months seems to be both effective and safe [28].

Quite often, patients with chronic heart failure will complain of non-specific pain, not always clearly related to heart failure. As a result, targeted questions and effective pain control are just another option for improving the quality of life [29,30]. However, when selecting the active substance, it is imperative to avoid the use of non-steroidal anti-inflammatory drugs increasing sodium and water retention.

Non-pharmacological therapy

Together with symptoms and overall psychological ill-being, poor functional fitness levels and reduced mobility constitute the main factors significantly deteriorating the quality of life of heart failure patients [31]. The decrease in functional fitness is due partly to generalized muscular atrophy or directly to cardiac cachexia associated with loss of adipose tissue. These conditions are caused by neuroendocrine and immunological processes, not infrequently combined with loss of appetite and malabsorption in the presence of gastrointestinal tract congestion or as a result of side effects of the drugs used to treat comorbidities. Cardiac cachexia not only deteriorates the quality of life, it worsens the prognosis [32].

In patients with inadequate oral intake, enteral nutrition by means of oral nutritional supplements or tube feeding helps maintain or increase nutrient intake, and halt or reverse weight loss. It is not indicated in the prophylaxis of cardiac cachexia. Although no data from large clinical trials regarding the effect of enteral nutrition on cachexia in chronic heart failure are currently available, the physiological arguments lead to absolute consensus [33].

In the fight against catabolism, optimal nutrition cannot be separated from physical activity. According to some reports, rehabilitation is just another non-pharmacological modality to improve a patient's overall status, increase exercise tolerance and maximum oxygen uptake, improve NYHA functional class and, possibly decrease mortality. Rehabilitation including exercise testing should be initiated under professional supervision. The recommendation is to start with light continuous endurance training to be later combined with interval resistance training [34–36]. However, the well designed large HF-ACTION study documented only a mild reduction in mortality and re-hospitalization rates [37]. Still, consistent with the guidelines of the Czech and European Societies of Cardiology, a reasonable level of supervised physical activity in the earlier stages of the disease is only advisable if the patient enjoys a better quality of life.

Sleep-related difficulty breathing (central or obstructive sleep apnea) is a relatively frequent finding in chronic heart failure patients [38,39]. This comorbidity should also be considered as effective therapy that can again appreciably improve one's quality of life.

The issue of implantable cardioverter/defibrillator (ICD) deactivation continues to be the most difficult and controversial one. In patients receiving predominantly palliative care in end-stage heart failure, the ICD should be deactivated [40]. The patient and their family should be advised over time and gently that, under certain circumstances, anti-arrhythmic therapy may in fact only prolong the suffering associated with the dying process. At the same time, they should be assured that ICD deactivation will not result in sudden death. Nevertheless, the final decision must be made by the particular, well-informed, and competent patient. Several reports have suggested some patients may be reluctant to have the device deactivated or try to delegate decision-making to their physician [41]. These issues should be discussed relatively early, ideally at a time when the patient is not yet confronted with impending death. There is no doubt ICD

deactivation should be considered in cases where the patient is clearly dying, has signed informed consent for a do-not-resuscitate (DNR) order, or the quality of life is so poor that sudden cardiac death can in fact be perceived as some sort of liberation [13]. In patients receiving cardiac resynchronization therapy (CRT), it is preferred to let the device—given its significant beneficial symptomatic effect—work until the end of life.

Psychological and spiritual needs

The psychological burden building up as the patient sees their overall health steadily decline is one of the main causes of deteriorating quality of life [31]. Not infrequently, chronic heart failure patients develop a depressive illness with a prevalence of more than 20%, and the figure rises as NYHA class increases. Some authors have suggested it is yet another independent factor increasing mortality [42,43]. While hard data showing an association between antidepressant therapy and reduced mortality are unavailable, drug therapy and psychotherapy may improve the quality of life.

As spiritual satisfaction and acceptance of the life situation as it is are clearly associated with a lower incidence of depression and better quality of life [44], the physician should seek to learn more about the spiritual needs of the patient whatever their denomination, and support the patient in this area. In cases where the physician feels incompetent and finds it uneasy, this task should be undertaken by another member of the multidisciplinary team.

Conclusion

Palliative care is a critical component of care provided to patients with advanced chronic heart failure. These approaches are intended to improve the quality of life of patients and their families in cases of refractory symptoms through early identification and intervention in physical, psychological, social, as well as spiritual terms. Palliative care poses a major challenge for all members of teams providing comprehensive care to this patient population not only during the final weeks of their life.

Conflict of interest

None of the authors have any financial relationship with any commercial identity used in this paper

Funding

The article was written without financial support of any subject or object.

Ethical statement

Research was done according to ethical standards.

REFERENCES

- [1] S. Stewart, K. MacIntyre, D.J. Hole, et al., More 'malignant' than cancer? Five-year survival following a first admission for heart failure, *European Journal of Heart Failure* 3 (2001) 315–322.
- [2] J.P. Solano, B. Gomes, I.J. Higginson, A comparison of symptom prevalence in far advanced cancer. AIDS, heart disease, chronic obstructive pulmonary disease and renal disease, *Journal of Pain and Symptom Management* 31 (2006) 58–69.
- [3] C. Ward, The need for palliative care in the management of heart failure, *Heart* 87 (2002) 294–298.
- [4] <http://www.who.int/cancer/palliative/definition/en/>.
- [5] J.E. Heffner, C. Barbieri, End-of-life care preferences of patients enrolled in cardiovascular rehabilitation programs, *Ethics in Cardiopulmonary Medicine* 117 (2000) 1474–1481.
- [6] H.M. Krumholz, R.S. Phillips, M.B. Hamel, et al., Resuscitation preferences among patients with severe congestive heart failure: results from the SUPPORT project. Study to understand prognoses and preferences for outcomes and risk of treatments, *Circulation* 98 (1998) 648–655.
- [7] R.E. Kheirbek, F. Alemi, B.A. Citron, et al., Trajectory of illness for patients with congestive heart failure, *Journal of Palliative Medicine* 16 (5) (2013) 478–484.
- [8] M. Nichols, N. Townsend, P. Scarborough, M. Rayner, Cardiovascular disease in Europe: epidemiological update, *European Heart Journal* 34 (2013) 3028–3034.
- [9] W.C. Levy, D. Mozaffarian, D.T. Linker, et al., The Seattle Heart Failure Model: prediction of survival in heart failure, *Circulation* 113 (2006) 1424–1433.
- [10] M. Senni, G. Santilli, P. Parrella, et al., A novel prognostic index to determine the impact of cardiac conditions and co-morbidities on one-year outcome in patients with heart failure, *American Journal of Cardiology* 98 (2006) 1076–1082.
- [11] D.S. Lee, P.C. Austin, J.L. Rouleau, et al., Predicting mortality among patients hospitalized for heart failure. Derivation and validation of a clinical model, *Journal of the American Medical Association* 290 (2003) 2581–2587.
- [12] M. Metra, P. Ponikowski, K. Dickstein, et al., Advanced chronic heart failure: a position statement from the Study Group on Advanced Heart Failure Association of the European Society of Cardiology, *European Journal of Heart Failure* 9 (2007) 684–694.
- [13] T. Jaarsma, J.M. Beattie, M. Ryder, et al., Palliative care in heart failure: a position statement from the palliative care workshop of the Heart Failure Association of the European Society of Cardiology, *European Journal of Heart Failure* 11 (2009) 433–443.
- [14] J.W. Levenson, E.P. McCarthy, J. Lynn, et al., The last six months of life for patients with congestive heart failure, *Journal of the American Geriatrics Society* 48 (5 Suppl.) (2000) S101–S109.
- [15] S.J. Goodlin, T.E. Quill, R.M. Arnold, Communication and decision-making about prognosis in heart failure care, *Journal of Cardiac Failure* 14 (2008) 106.
- [16] C. Saunders, Terminal care, in: D.J. Weatherall, J.G.G. Ledingham, D.A. Warrell (Eds.), 2nd ed., *Oxford Textbook of Medicine*, vol. 28, Oxford Medical Publications, Oxford, 1987, p. 12.
- [17] K. Bramstedt, Ethical dilemmas in therapy withdrawal, in: J. Beattie, S. Goodlin (Eds.), *Supportive Care in Heart Failure*, Oxford University Press, Oxford, 2008, pp. 443–450.
- [18] L.A. Allen, L.W. Stevenson, K.L. Grady, et al., Decision making in advanced heart failure: a scientific statement from the American Heart Association, *Circulation* 125 (2012) 1928–1952.

- [19] T. Rustøen, A. Stubhaug, I. Eidsmo, et al., Pain and quality of life in hospitalized patients with heart failure, *Journal of Pain and Symptom Management* 36 (2008) 497–504.
- [20] I. Ekman, J.G. Cleland, B. Andersson, K. Swedberg, Exploring symptoms in chronic heart failure, *European Journal of Heart Failure* 7 (2005) 699–703.
- [21] D. Janssen, M. Spruit, E. Wouters, J. Schols, Daily symptom burden in end-stage chronic organ failure: a systematic review, *Palliative Medicine* 22 (2008) 1–11.
- [22] J. Špinar, J. Vítovec, J. Hradec, et al., Czech Society of Cardiology guidelines for the diagnosis and treatment of chronic heart failure, *Cor et Vasa* 54 (2012) e113–e134.
- [23] J.J.V. McMurray, S. Adamopoulos, S.D. Anker, et al., ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012, *European Heart Journal* 33 (2012) 1787–1847.
- [24] P.B. Bascom, Dyspnea Can Be, Should be effectively palliated with opioids, *Journal of Palliative Medicine* 16 (2013) 465.
- [25] M.J. Johnson, T.A. McDonagh, A. Harkness, et al., Morphine for the relief of breathlessness in patients with chronic heart failure – a pilot study, *European Journal of Heart Failure* 4 (2002) 753–756.
- [26] B. Stuart, Palliative care and hospice in advanced heart failure, *Journal of Palliative Medicine* 10 (2007) 210–228.
- [27] A.L. Jennings, A.N. Davies, J.P. Higgins, et al., A systematic review of the use of opioids in the management of dyspnoea, *Thorax* 57 (2002) 939–944.
- [28] S.G. Oxberry, J.M. Bland, A.L. Clark, et al., Repeat dose opioids may be effective for breathlessness in chronic heart failure if given for long enough, *Journal of Palliative Medicine* 16 (2013) 250–255.
- [29] S.J. Goodlin, S. Wingate, S.J. Pressler, et al., Investigating pain in heart failure patients: rationale and design of the Pain Assessment. Incidence & Nature in Heart Failure (PAIN-HF) study, *Journal of Cardiac Failure* 14 (2008) 276–282.
- [30] L.S. Evangelista, E. Sackett, K. Dracup, Pain and heart failure: unrecognized and untreated, *European Journal of Cardiovascular Nursing* 8 (2009) 169–173.
- [31] C.D. Blinderman, P. Homel, J.A. Billings, et al., Symptom distress and quality of life in patients with advanced congestive heart failure, *Journal of Pain and Symptom Management* 35 (2008) 594–603.
- [32] S.D. Anker, P. Ponikowski, S. Varney, et al., Wasting as independent risk factor of survival in chronic heart failure, *Lancet* 349 (1997) 1050–1053.
- [33] S.D. Anker, A. Laviano, G. Filippatos, et al., ESPEN guidelines on parenteral nutrition: on cardiology and pneumology, *Clinical Nutrition* 28 (2009) 455–460.
- [34] S. Schwarz, M. Halle, Exercise training in heart failure patients, *Deutsche Medizinische Wochenschrift* 139 (2014) 845–850.
- [35] A. Gasiorowski, J. Dutkiewicz, Comprehensive rehabilitation in chronic heart failure, *Annals of Agricultural and Environmental Medicine* 20 (2013) 606–612.
- [36] E.J. Davies, T. Moxham, K. Rees, et al., Exercise training for systolic heart failure: cochrane systematic review and meta-analysis, *European Journal of Heart Failure* 12 (2010) 706–715.
- [37] C.M. O'Connor, D.J. Whellan, K.L. Lee, et al., Efficacy and safety of exercise training in patients with chronic heart failure. HF-ACTION randomized controlled trial, *Journal of the American Medical Association* 301 (2009) 1439–1450.
- [38] D. Rosen, F.J. Roux, N. Shah, Sleep and breathing in congestive heart failure, *Clinics in Chest Medicine* 35 (2014) 521–534.
- [39] R.L. Grayburn, Y. Kaka, W.H. Tang, Contemporary insights and novel treatment approaches to central sleep apnea syndrome in heart failure, *Current Treatment Options in Cardiovascular Medicine* 16 (2014) 322.
- [40] J.M. Beattie, Implantable Cardioverter Defibrillators in Patients who are Reaching the End of Life, *British Heart Foundation*, London, 2007.
- [41] N.E. Goldstein, D. Mehta, S. Siddiqui, et al., 'That's like an act of suicide' patients' attitudes toward deactivation of implantable defibrillators, *Journal of General Internal Medicine* 23 (Suppl. 1) (2008) 7–12.
- [42] T. Rutledge, V.A. Reis, S.E. Linke, et al., Depression in heart failure a meta-analytic review of prevalence, intervention effects, and associations with clinical outcomes, *Journal of the American College of Cardiology* 48 (2006) 1527–1537.
- [43] W. Jiang, M. Kuchibhatla, G.L. Clary, et al., Relationship between depressive symptoms and long-term mortality in patients with heart failure, *American Heart Journal* 154 (2007) 102–108.
- [44] D.B. Bekelman, S.M. Dy, D.M. Becker, et al., Spiritual well-being and depression in patients with heart failure, *Journal of General Internal Medicine* 22 (2007) 470–477.
- [45] S.A. Murray, M. Kendall, K. Boyd, A. Sheikh, Illness trajectories and palliative care, *British Medical Journal* 330 (2005) 1007–1011.
- [46] S.J. Goodlin, Palliative care in congestive heart failure, *Journal of the American College of Cardiology* 54 (2009) 386–396.