Palliative Care for Advanced Heart Failure: An Overview

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Background

As in many parts of the world, hospital admissions in Hong Kong due to heart failure is both common and on the rise, and heart failure is a final common pathway of various cardiac conditions leading to death. In fact, advanced heart failure (AHF) was described as more ‘malignant’ than cancer because of its poor one-year survival rate and its prognosis worse than for most common forms of cancer. However, patients with AHF are disadvantaged as compared with cancer patients, as they are less likely to have an understanding of their illness, to receive supportive care, and to have the opportunity to plan for care with regard to death and dying. Quality of life assessment of patients with AHF revealed worse physical role function and higher pain scores than patients with end-stage renal failure or respiratory failure.

Prognosis and disease trajectory in advanced heart failure

It has been reported that mortality of patients with heart failure at New York Heart Association (NYHA) functional class IV would be up to 40% to 50% in one year. Other demographic and clinical powerful predictors associated with a poor prognosis in heart failure include advanced age, ischaemic aetiology, hypotension, prior heart failure hospitalization, hyponatraemia, wide QRS complex, low left ventricle ejection fraction (LVEF) and reduced work with low peak VO₂. The list of poor prognostic conditions also includes renal dysfunction, diabetes, raised uric acid, anaemia, COPD, sleep-related breathing disorders and depression. Yet, quite a number of these published model predictors are only important to ambulatory patients or specific target groups. Prognostigation to patients with AHF, who commonly suffer from multiple co-morbidities, remains difficult.

There are conceptual models of disease trajectories commonly quoted in literatures in geriatric and palliative medicine, describing typical patterns of decline of functional status over time. These models are helpful in planning and delivery of palliative care as well as in communication with patients and their families. While cancer patients are more likely to sustain a relatively stable functional state until a short period of evident decline before death, patients with heart and lung failure are commonly depicted to share a slower decline with long-term limitations and intermittent serious (and usually sudden) episodes until a lethal one. However, the course of AHF in reality is likely to be even more unpredictable. A prospective study looking at the dying trajectories in heart failure delineates the functional state of twenty-seven patients for 24 months prior to death. It turns out that no ‘typical’ dying trajectory could be identified, and only a minority of patients conformed to the theoretical trajectory of dying in heart failure. Such unpredictable clinical trajectory often results in patients dying before they are deemed eligible for palliative care.

Palliative care for advanced heart failure

For the definition of advanced heart failure, besides the presence of severe symptoms, the position statement from the European Society of Cardiology (ESC) has recommended the inclusion of objective evidence of severe cardiac dysfunction, severe impairment of functional capacity, history of heart failure hospitalization and presence of these features despite optimized guideline-recommended therapies. In order to provide due care to patients with heart failure, the first step is to confirm the diagnosis of heart failure and to understand its aetiology, such that appropriate, guideline-recommended and evidence-based therapies can be given. Guidelines on diagnosis of heart failure are available in detail. Although current knowledge in specific symptoms management for AHF is still limited, the following discussion
the following discussion will address on a small number of studies on palliative interventions which can be beneficial. Issues related to implantable cardiac devices will also be discussed.

Active communication with patients with AHF and their families is essential, and liaison with palliative care specialists in a shared care approach is encouraged, to address and coordinate patient’s care need optimally. Education for patients and their care-givers on principles of self-care maintenance and heart failure management should be provided. Explanation on disease progression and change in treatment emphasis is a sensitive issue and must be approached with care and empathy. Advanced care planning should be initiated and reviewed regularly, with discussion on preferences on future treatment options. Decision on device management (including deactivation) and resuscitation orders must be clear for patient with end-stage heart failure. End-of-life care should include plans for crises, spiritual support and bereavement support. To maintain hope for patients with AHF, Davidson and colleagues suggested the following issues as important: 1. acknowledgement of the changing life circumstances, 2. restructuring of reality, 3. dealing with vulnerability, 4. achieving normalization and 5. resolving uncertainty.

Medical management of advanced heart failure

It is important that evidence-based guideline-recommended treatment of heart failure is optimized because this has major benefits not only on survival but also on symptom control and quality of life. Such treatment is made on basis of improving the symptoms of sodium and water retention, modifying on-going cardiovascular risk and targeting neurohormonal activation. Yet we have to be aware that the benefits from such evidence-based strategy are based on extrapolation of the study findings in heart failure as a whole. At present there is limited evidence specifically addressing AHF, and it is uncertain whether such benefits could be translated to these patients, who are typically elderly, complex, symptomatic and with multiple co-morbidities.

The most desirable approach is to use proven agents in the proven dosage regimens in accordance with contemporary clinical guidelines and not to assume a ‘class effect’. Lack of adherence to guidelines has been found to be an independent negative predictor of outcome in chronic heart failure. However patients with AHF may not tolerate the recommended regimens. Individualized therapy with realistic targets should be attempted, and some drug is better than none.

Angiotensin-converting enzyme inhibitors (ACEI) have a pivotal role across the entire spectrum of heart failure severity. The landmark Co-operative North Scandinavian Enalapril Survival (CONSENSUS) Study, which included only patients with NYHA Class IV, has shown the benefits from ACEI not only on reduction in mortality and hospital admissions, but also on improvement on symptoms and functional capacities. ACEI should be initiated at a low dose, and doubled slowly, with careful monitoring of renal function and blood pressure. Pre-existing renal dysfunction (with serum creatinine below 220 micromol/L) is not considered a contraindication by ESC, and rise of creatinine level is not considered clinically important if the increase in creatinine is less than 50% or its absolute value less than 265 micromol/L, whichever is lower. Complete intolerance to ACEI due to haemodynamic or renal cause is uncommon but a particularly poor prognostic indicator in patients with AHF.

Beta-blockers provide incremental benefits in addition to ACEI in terms of outcome and reversal of the detrimental remodeling process in heart failure. For patients without asthma and significant atrioventricular conduction defects, beta-blockers should be initiated as early as tolerated. The effective agents include a slow-release preparation of metoprolol, bisoprolol and carvedilol. The concern for negative impact of beta-blockers on quality of life especially on initial phase was not supported by a meta-analysis addressing this issue. The nine randomized controlled trials identified have included patients with NYHA Class III, and quality of life was found to improve more often in patients taking beta-blocker, although the standardized mean difference did not reach statistical significance.

Other therapeutic agents which have studies involving patients with NYHA Class III to IV include angiotensin receptor blockers.
(spironolactone\textsuperscript{23}) and hydralazine plus isosorbide dinitrate (in dosage of hydralazine 75mg/ isosorbide dinitrate 60mg three times daily\textsuperscript{24}). Digoxin has also been found to decrease hospitalization when being used on top of diuretic and ACEI therapy in patients with symptomatic heart failure and low LVEF\textsuperscript{25}.

**Symptom palliation in advanced heart failure**

The principles in symptom management are the same irrespective of diagnosis. A holistic assessment of aetiology of symptoms (including relevant investigations), intervention to reverse any reversible factors and palliation of irreversible situations would be a system applicable to both cancer and heart failure patients\textsuperscript{26}.

Dyspnoea is common and its severity is the criterion for NYHA classification. Besides pulmonary edema, dyspnoea in patients with AHF can be due to pleural effusion, pneumonia, pulmonary embolism, underlying obstructive airway disease or cachexia. There are a few randomized controlled trials\textsuperscript{27-29} with small sample size suggesting the effectiveness of opioids for palliation of dyspnoea in heart failure. A randomized placebo controlled crossover pilot study conducted in out-patient setting has shown that low dose oral morphine lowered breathlessness score by day two while sedation score increased until day three, with both reaching statistical significance\textsuperscript{27}. Another randomized controlled study has shown that low dose intravenous diamorphine significantly improves aerobic exercise capacity for patients with chronic heart failure performing cardiopulmonary exercise\textsuperscript{28}. For non-pharmacological measures, a low-level leg muscle strengthening exercise has been found to improve strength and endurance of lower limb muscles in patients with moderate to severe heart failure, along with improvement in both dyspnoea and functional state in \textsuperscript{30}.

Heart failure patients commonly experience pain, and it has been reported to affect up to 78\% of patients dying of AHF\textsuperscript{31}. Besides angina, pain can be due to edema and claudication as well as from conditions not confining to cardiovascular system, like musculoskeletal pain, osteoarthritis, diabetic neuropathy, shingles and chest drains. If angina is refractory to optimal conventional antianginal treatment, opioids can be considered\textsuperscript{26}, and there is some evidence for the use of transcutaneous electrical nerve stimulation (TENS)\textsuperscript{32}, acupuncture and spinal cord stimulation\textsuperscript{33}. For arthritic pain, joint injection, joint-sparing exercise and local therapy (e.g. topical NSAIDs or lignocaine) are potential measures. Systemic non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided as they precipitate decompensation by fluid retention.

Sleep disturbances are frequently reported in heart failure. Sleep-disordered breathing is associated with sleep disturbance in over 50\% of ambulatory patients with heart failure\textsuperscript{34}. Oxygen desaturation and apnoea result in marked elevation of noradrenaline, which is associated with general malaise, anxiety and depression. Screening with overnight-oximetry should be considered for patients with AHF. For sleep apnoea in left ventricular dysfunction, continuous positive airway pressure (CPAP) ventilation has been shown not only to reduce apnoea and improve oxygenation, but also to improve LVEF and functional status\textsuperscript{35}.

Depression has been reported in 20-30\% of patients with chronic heart failure\textsuperscript{36}. Serotonin-specific re-uptake inhibitors (SSRIs) are the first-line treatment for major depressive disorder and for dysthymia in patients with heart failure. SSRIs have relatively favorable cardiac profile, but there is potential risk of hyponatraemia and worsening of heart failure, likely due to increased antidiuretic hormone\textsuperscript{37}. Tricyclics should be avoided for their risks of arrhythmias and postural hypotension. For patients with end-stage heart failure and limited life expectancy, psychostimulants such as methylphenidate can be considered as it has few adverse effects and a quick onset of action\textsuperscript{38}.

**Management of implantable cardiac devices at the end of life**

Implantable devices that treat potentially lethal arrhythmias and support cardiac function have become standard therapies. These devices include implantable cardioverter defibrillators (ICDs) and bi-ventricular pacemakers for cardiac resynchronization therapy (CRT) and ventricular assist devices (VADs). According to ESC guidelines\textsuperscript{6}, ICD therapy is recommended for survivors of ventricular fibrillation (VF) and
symptomatic ventricular tachycardia (VT) as primary prevention, and for patients with LVEF <35% and NYHA class II or III as secondary prevention. CRT is recommended for patients with NYHA class III to IV with LVEF <35% to improve symptoms and to reduce hospitalization and mortality.7 Besides bridging to transplantation and managing patients with acute severe myocarditis, now VADs are also indicated for long-term use (as destination therapy) when no definitive procedure is planned for end-stage heart failure.8

Issues related to deactivation of implantable cardiac devices should be discussed with patients with end-stage heart failure. At the end of life, there are severe electrolyte and homeostatic disturbances which will result in VT or VF refractory to ICD shocks. Patients with AHF may prefer arrhythmic death to their symptoms or to invasive therapy,9 and this follows ethical and legal principles which permit competent adults to forego potentially life-saving medical interventions. Delivery of ICD shocks can be avoided without affecting backup pacemaker function by computer reprogramming. The shock function can also be turned off by taping a doughnut-shaped magnet at the chest over the generator. In fact, on maintaining pacemaker function without defibrillation, ICDs can alleviate symptomatic arrhythmia; and they have shown to be not prolonging life for pacing dependent patients. On the other hand, if patients want to keep defibrillation function, options include use of amiodarone and sotalol to prevent ventricular arrhythmia, electrophysiological study to ablate arrhythmic foci in selected patients, or reprogramming of devices to enhance anti-tachycardia pacing (ATP).10

Different from ICDs, CRT devices improve quality of life by inducing favorable reverse remodeling of the left ventricle, leading to improvements in ejection fraction and reduction in amount of mitral regurgitation. CRT reduces mortality in a different fashion as do ICDs, and de-activation of CRT may worsen symptoms. On the other hand, instead of de-activation, function of the devices can be optimized using electrocardiographic and echocardiographic measures to direct the settings. These may not only reduce the number of CRT non-responders, but it may also help to alleviate refractory symptoms.12

De-activation of VAD is technically and ethically distinct from that of ICD or CRT. De-activation of VAD should be regarded as a terminal event, as this will lead to back flow and thrombosis within the device or the heart, inducing worse cardiac dysfunction. Detailed discussion must be conducted with patients and families. Standard VAD management is complex, including handling of backup system, wound care, assessment of dysfunction and complications, and most patients with VADs probably die in the acute setting.13

Conclusion

Because of its unpredictable clinical course, AHF poses specific challenges to providers of palliative care. To improve the quality of life of patients with AHF, knowledge on both evidenced-based medical treatment and symptom palliation is essential. Education and support for patients and caregivers as well as timely communication on advanced directives and end-of-life issues are important, and often need a multidisciplinary approach. Further research in this area is imminently needed, so is the awareness of the suffering and uncertainties faced by these patients.

References


