Therapeutic Strategy for a Patient with Advanced Heart Failure and Schizophrenia Without Cardiac Replacement Therapies

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Summary

We had a 58-year-old man with advanced heart failure and progressive end-organ dysfunction refractory to inotropes. Following detailed discussions, he decided not to receive ventricular assist device therapy considering his comorbidity of schizophrenia. A palliative care team initiated 2.5 mg of morphine together with low-dose anti-heart failure medications, which improved not only his heart failure symptoms but also the congestive heart failure itself. Aggressive commitments of the palliative care team might improve not only patients’ quality of life but also advanced heart failure itself.

Key words: Ventricular assist device, Morphine, Dyspnea

Survival in patients with advanced heart failure has improved, given the improvements in cardiac replacement therapy, including durable left ventricular assist device and heart transplantation, in addition to the sophisticated pharmacological therapy. However, given the shortage of donor hearts, high morbidities following cardiac replacement therapy, its expensiveness, and its extensive invasiveness, many patients with heart failure cannot be good candidates for such intensive therapies. However, thus far, an alternative approach for such cohorts, including palliative care, has not yet been established.

We had a patient with advanced heart failure and schizophrenia, who eventually decided not to receive cardiac replacement therapy. His heart failure was managed successfully using morphine-incorporated medical therapy.

Case Report

On admission: A 58-year-old man with a history of schizophrenia for 30 years was admitted to our institute, presenting dyspnea, appetite loss, and peripheral edema. His blood pressure was 119/83 mmHg, heart rate was 108 bpm, and oxygen saturation was 98% on 3 L/minute of nasal cannula support. His serum sodium was 131 mEq/L, serum total bilirubin was 0.9 mg/dL, serum creatinine was 1.1 mg/dL, and plasma B-type natriuretic peptide (BNP) was 3167 pg/mL. Dominant symptoms were negative symptom and auditory hallucination, but his cognitive function was preserved. He was taking medications to control schizophrenia: clozapine 150 mg, zopiclone 7.5 mg, zotepine 60 mg, and biperiden 3 mg.

A chest X-ray showed cardiomegaly and bilateral pulmonary congestion (Figure 1). Transthoracic echocardiography showed 71 mm of left ventricular end-diastolic diameter and 6% of left ventricular ejection fraction with left ventricular diffuse severe hypokinesis. He had mild mitral regurgitation and mild tricuspid regurgitation. He was hospitalized with a clinical diagnosis of congestive heart failure.

Initial course following hospitalization: Following the initiation of intravenous administration of dobutamine and oral diuretics, his dyspnea and peripheral edema improved (Figure 2). However, 0.625 mg/day of enalapril and 1.25 mg/day of carvedilol worsened his pulmonary congestion and hypotension, accompanied by increases in serum total bilirubin and creatinine up to 1.8 and 1.7 mg/dL, respectively. He was assigned to the INTERMACS profile 2 with worsening end-organ function refractory to inotropes therapy.

Following the detailed explanation of his current clinical condition and repeated discussions with him and his caregivers, they decided to decline any further invasive procedures and treatment, including endo-myocardial biopsy to diagnose etiology, mechanical circulatory supports, and heart transplantation, but rather to receive palliative care. We could not exclude the ischemic etiology because he refused to receive coronary angiography.

Palliative care intervention: From day 20, the palliative care team, consisting of multidisciplinary experts (medical
doctors, expert nurses, pharmacists, physical therapists, psychotherapists, nutritionists, and medical social workers), participated in the daily care, and 2.5 mg/day of intravenous administration of morphine was initiated to ameliorate his persistent dyspnea due to pulmonary congestion, with careful monitoring for its adverse effects. His dyspnea improved immediately and congestive heart failure was ameliorated following the initiation of morphine therapy (Figure 1), which further allowed us to attempt low-dose anti-heart failure medications again, including enalapril, carvedilol, and spironolactone, followed by a considerable decrease in plasma BNP (from 4835 to below 1000 pg/mL) as well as the recovery of end-organ dysfunction. Liaison psychiatrists committed to stabilize his mental health and anxiety for his disease. They discontinued clozapine and zopiclone and instead initiated quetiapine 75 mg. Cardiac rehabilitation was performed to improve his activities of daily living. Social workers sought external institutions appropriate for his unique medical features.

The morphine dose was reduced gradually, given the improvement of his symptoms. On day 82, the patient was transferred to another institute to continue palliative care with dobutamine infusion.

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**Figure 1.** Chest X-rays obtained on admission (A) and day 60 (B). Bilateral congestion improved following the morphine-incorporated optimal medical therapy.

**Figure 2.** Time course following the hospitalization. BNP indicates B-type natriuretic peptide.
**Discussion**

**Decision support:** Patients with advanced heart failure often have to make major decisions, such as continuous inotropes infusion via a central venous catheter, intracardiac defibrillator, and cardiac replacement therapy. Notably, these major interventions should be proposed with a balanced description of alternative approaches.

Decision making for cardiac replacement therapy is sometimes challenging, given that it requires complex assessments of the refractoriness of heart failure, relatively preserved end-organ function, the ability of self-management, and social support with appropriate caregivers. Given that destination therapy is not approved in Japan, candidates for durable left ventricular assist devices should also satisfy the indication of heart transplantation beforehand.

Following detailed discussions with multidisciplinary healthcare providers, the patient and his family eventually decided to decline such an intensive surgical therapy, instead preferring palliative care, predominantly because of his severity of schizophrenia. Such discussions should be repeated if necessary and the decision can be changed. The patient initially declined central venous catheter placement, but later accepted long-term palliative care with inotropes. Unfortunately, the palliative care team could commit only after the patient’s decision to decline cardiac replacement therapy, because rapid progression of his heart failure did not allow their early commitments. In principle, the palliative care team should intervene at an earlier stage before hemodynamic deterioration.

**Psychological support:** Psychological support is another important approach for those with advanced heart failure, given that they are at high risk of depression or other psychological disorders. Although large-scale randomized control trials could not demonstrate a significant advantage of medical interventions in improving depression and the cardiovascular status, pharmacological therapy using selective serotonin reuptake inhibitors and tricyclic antidepressants are attempted, if applicable, with the careful monitoring of their side effects, including QT prolongation, hypotension, and hyponatremia. Our patient was supported by the psychological support team during hospitalization to manage his schizophrenia and heart failure-related anxiety.

**Symptom management:** Symptom management is key to palliative care for those with advanced heart failure, and morphine plays a dominant role in the literature of cardiac palliative care. In this case, we initiated morphine at a low dose of 2.5 mg/day. Interestingly, morphine therapy improved not only his dyspnea but also heart failure congestion, with an improvement in plasma BNP levels. The detailed mechanism remains uncertain, but morphine therapy resulted in a decreased cardiac demand because of sympathetic nerve suppression, an afterload reduction due to peripheral artery dilatation, and a preload reduction due to venous dilatation, all of which ameliorated congestive heart failure and gave us a chance to attempt anti-heart failure agents again. The adverse effects of morphine, including hypotension and bradycardia, were not observed, probably because of concomitantly administered inotropes. In 10 outpatients with heart failure, Johnson and colleagues also observed that 4-day morphine therapy decreased plasma BNP levels significantly compared to the placebo. Further studies are warranted to construct optimal morphine-incorporated medical therapy for those with advanced heart failure.

**Disclosure**

**Conflicts of interest:** None.

**References**


