South African Family Practice 2019; 61(6):6-8

Open Access article distributed under the terms of the
Creative Commons License [CC BY-NC-ND 4.0]
http://creativecommons.org/licenses/by-nc-nd/4.0

S Afr Fam Pract
ISSN 2078-6190 EISSN 2078-6204
© 2019 The Author(s)
REVIEW

Burning issues in acute heart failure management

JA Ker,[1] K Outhoff[2]

[1] Department of Internal Medicine, School of Medicine, Faculty of Health Sciences, University of Pretoria, South Africa
[2] Department of Pharmacology, School of Medicine, Faculty of Health Sciences, University of Pretoria, South Africa
Corresponding author, email: kim.outhoff@up.ac.za

In general, heart failure is the end-stage manifestation of cardiovascular disease and is an important and increasing cause of morbidity worldwide. Acute heart failure, whether of new onset or an exacerbation of chronic heart failure, causes sudden congestion, typically presenting as pulmonary oedema. The mortality associated with acute heart failure is extremely high. Potentially life-saving treatments and other burning issues are highlighted in this review.

Keywords: Acute heart failure, pulmonary oedema, N-terminal pro-brain-type natriuretic peptide (NT-proBNP), loop diuretics, ivabradine, angiotensin receptor-neprilysin inhibitor (ARNI)

Introduction

Heart failure is regarded as a heterogeneous syndrome of symptoms such as dyspnoea, orthopnoea, oedema of ankles, fatigue/limited exercise capacity, and signs such as elevated jugular venous pressure, pitting oedema, crackles in the lung and a gallop heart rhythm. The heart itself has a structural or functional abnormality leading to elevated intracardiac pressures or reduced cardiac output at rest or during effort.[1]

Importantly, acute heart failure may comprise distinct entities with different pathophysiologies, treatments and clinical outcomes. Currently two different phenotypes, including new onset acute heart failure and recurrent or severe worsening of existing previously well-controlled heart failure, are encountered. Most patients with acute new-onset heart failure present to a primary health care provider or an emergency room facility with acute dyspnoea, fatigue and occasionally swollen legs, the latter more common in acute exacerbations of chronic heart failure. People with acute heart failure have a poor prognosis with high rates of hospital admission that carry mortality rates of 25% or more per year.[2] In fact, in-hospital mortality of acute heart failure can be greater than that of acute myocardial infarction, and mortality remains high for more than a year after discharge compared to stable outpatient heart failure.[3] Early readmission within 30–90 days after discharge is common, affecting almost one quarter of acute heart failure patients. The clinical course and prognosis of chronic heart failure patients who have an acute episode of heart failure is worse.[4] One study demonstrated that although the 30-day mortality between the two phenotypes was the same, the 1-year mortality was significantly higher in the acute exacerbation group.[5]

Most patients present with congestion, predominantly pulmonary (crackles), peripheral oedema and elevated jugular venous pressure. Poor perfusion due to low cardiac output is seen in about 5% of acute heart failure cases. Renal dysfunction, due to a multitude of mechanisms, but mainly due to elevated central venous pressure increasing afterload on the kidneys is usually associated with a poor outcome. Declining renal function accompanied by persistent congestion despite treatment has a bleak outlook, and this combination presents a dilemma for the clinician: limiting diuretics to preserve renal function may prolong congestion, whereas aggressive diuresis may worsen renal dysfunction. Cardiac biomarkers that remain elevated, such as troponins, natriuretic peptides and transaminases, correlate with poor survival.[1]

Therapeutic approach

Clinical congestion

Decongestive therapy is the major goal in acute heart failure management to control clinical congestion such as dyspnoea and oedema.[6] As there is a paucity of hard evidence, the pharmacotherapy of acute heart failure remains largely empiric and consensus-driven.[1] Intravenous administration of furosemide, torsemide or bumetanide is recommended to relieve congestion, and these potent loop diuretics are the mainstay of treatment. There appears to be no real difference in outcomes between intermittent intravenous doses of a loop diuretic versus continuous infusions, but it has been shown that the earlier intravenous diuretic is initiated, the better the in-hospital mortality.[7,8]

Haemodynamic congestion

This phase of congestion usually occurs without clinical signs of congestion but with elevated pulmonary wedge pressures and elevated N-terminal pro-brain-type natriuretic peptide (NT-proBNP) levels, the latter much easier for a clinician to evaluate.[9]

If *cardiogenic shock* is present then mechanical and pharmacological circulatory support including non-invasive positive pressure support is necessary for survival.

Intravenous therapy for all

a. Systolic blood pressure > 100 mmHg: This pragmatic cut-off blood pressure indicates possible early danger to the kidney. In practice, it denotes a level above which only a diuretic is

Table I. Recommended intravenous loop diuretic dosing in acute heart failure with systolic blood pressure > 100 mmHg

Level	Previous oral dose of furosemide*	Administer intravenous furosemide* bolus	Followed by furosemide* infusion mg/hour	Add hydrochlorothiazide (HCTZ) if poor response
Level 1	< 80 mg	40 mg bolus	5 mg/hour	
Level 2	81–160 mg	80 mg bolus	10 mg/hour	50 mg twice daily
Level 3	161–240 mg	80 mg bolus	20 mg/hour	50 mg twice daily
Level 4	> 240 mg	80 mg bolus	30 mg/hour	50 mg twice daily

* Furosemide 40 mg is equivalent to bumetanide 1 mg or torsemide 20 mg

necessary. Therefore, administer intravenous diuretics, by either bolus or constant infusion, as there seems to be no difference in response between these regimens. The response goal of diuretic therapy is a urine output of 3–5 litres daily until euvolemia is reached. There is a convenient stepped-care approach to diuretic dosing in acute heart failure, which is dependent on the level of previous diuretic use (see Table I).[10] Vasodilator therapy is also part of treatment in this group of patients with relatively elevated blood pressures, especially in those with systolic blood pressures of 140 mmHg or higher.

b. Systolic blood pressure < 100 mmHg: Administer either diuretics if congestion is present, or intravenous fluid if there are no signs of congestion. Inotropes are recommended if there is no response to the intravenous fluid challenge. The use of inotropes has been of concern due to their association with increased mortality as shown in the Acute Decompensated Heart Failure National Registry (ADHERE).[11] Despite these concerns, short-term positive inotrope therapy (dobutamine) is often unavoidable, especially when the systolic blood pressure is below 90 mmHg.[12] Vasopressors are used if there is no response to inotropes.

Identify and treat significant co-morbidities

Several co-morbidities have been shown to contribute to the development and exacerbation of heart failure with reduced ejection fraction (HFrEF) specifically. These conditions include coronary artery disease, hypertension, myocardial disease, pericardial disease, cardiac electrical abnormalities (atrial fibrillation of specific worse outcome), valvular disease, renal disease, iron deficiency, lung disease (especially COPD with patients complaining of dyspnoea), diabetes mellitus and as well as non-adherence to treatment.[13]

Avoid potentially harmful therapies

A study has shown that when 1 litre of normal saline is given early in the treatment of acute heart failure compared to intravenous diuretic only, there is an increased risk of intubation, ICU admission and mortality. Opiates are also generally avoided because of their adverse effects on respiratory and cognitive function. Calcium channel blockers due to their negative inotropic properties should not be used. Other drugs to avoid in acute heart failure include antiarrhythmic drugs (except amiodarone), nonsteroidal anti-inflammatory drugs, and any drug that has an effect on renal function.

Therapy on discharge from hospital to prevent readmission

a. A pre-discharge NT-proBNP level is useful for determining prognosis and is recommended by guidelines.[14] Patients with an NT-proBNP decline of > 50% from hospital admission to pre-discharge had a similar mortality to those admitted with low levels of NT-proBNP in the ASTRONAUT study.[15] Soluble suppression of tumorigenicity 2 (ST2), a biomarker of cardiac stress, and the tumour marker cancer antigen 125 (CA125), widely used in ovarian cancer therapy monitoring, are increased in heart failure patients with effusions, ascites and peripheral oedema and are therefore increasingly used as biomarkers in heart failure. In future, they may prove useful as prognostic markers.

b. Planning and considering prevention of readmission strategies after discharge from hospital is essential as about 1 in 4 patients are readmitted within 30–90 days.[15]

c. Continue the use of or begin therapies known to decrease hospital readmissions.[13] It has been shown that initiation of guideline-directed-medical-therapy of heart failure in hospital rather than post-discharge leads to higher adherence to prescribed medications, at least for 60 days of follow-up evaluations.

Temporary further worsening of renal function caused by decongestive therapy or initiation of renin-angiotensin-aldosterone-system (RAAS) inhibitors is associated with cessation of proven angiotensin converting enzyme inhibitor (ACE-inhibitor) or angiotensin receptor blocker (ARB) medications, which then negatively affects not only prognosis, but also readmissions due to worsening heart failure. Do not stop these drugs and initiate them if not already in use.

Digoxin use is associated with a reduction in hospitalisation, but not improved mortality, and can be used for the purpose of reduced hospitalisations.

Torsemide could be a more effective diuretic as it has a better bioavailability and longer duration of action. The ongoing TRANSFORM-HF trial is comparing it to furosemide to determine clinical outcomes.

A thiazide diuretic added to furosemide is an important method to potentiate the action of the loop diuretic in controlling congestion, which is a critical issue as it determines prognosis.

Mineralocorticoid receptor antagonists have also been shown to be underused in pre-discharge of patients with acute heart failure. These drugs reduce mortality in heart failure with

reduced ejection fraction and may even be of value in those with preserved ejection fraction.

Ivabradine, the selective sinoatrial node inhibitor, has been shown to reduce hospital readmissions and death in patients with low ejection fraction heart failure with a resting heart rate of more than 70 beats/minute on beta-blockers in the SHIFT trial.

d. Initiation of the combination of the ARB, valsartan, plus the neprilysin-inhibitor, sacubitril, led to a greater reduction in NT-proBNP levels compared to enalapril in patients with heart failure admitted to hospital due to acute worsening of heart failure in the PIONEER trial.[16] The rates of worsening renal function, hyperkalaemia, symptomatic hypotension and angioedema did not differ significantly between the 2 groups. This angiotensin receptor-neprilysin inhibitor (ARNI) combination was initiated at a low dose (suggested 50 mg twice daily) in patients who had the following criteria: systolic blood pressure ≥ 100 mmHg, no ACE-inhibitor or ARB for at least 36 hours, no increasing dose of intravenous diuretic for 6 hours, no vasodilators for preceding 6 hours, and no inotropes for the preceding 24 hours. In the PARADIGM-HF randomised trial, ARNI reduced important clinical outcomes including mortality significantly more than enalapril in heart failure with reduced ejection fraction.[17]

Concluding summary

1. Acute heart failure often presents to an emergency facility, either *de-novo* or due to acute worsening of previous stable chronic heart failure.
2. Congestion is the main clinical problem.
3. Intravenous diuretic therapy is the mainstay of treatment.
4. It is important not to stop proven life-saving therapies, and if patients are not already receiving them, to initiate them, including the new ARNI combination, prior to discharging the patient.

References:

1. Metra M, Teerlink JR. Heart failure. Lancet. 2017;390:1981-1995.
2. Crespo-Leiro MG, Anker SD, Maggioni AP, et al. European Society of Cardiology Heart Failure Long-Term Registry (ESC-HF-LT): 1-year follow-up outcomes and differences across regions. Eur J Heart Fail. 2016;18:613-25.
3. Kristensen SL, Jhund PS, Kober L, et al. Comparison of outcomes after hospitalization for worsening heart failure, myocardial infarction and stroke in patients with heart failure and reduced and preserved ejection fraction. Eur j Heart Fail. 2015;17:169-76.
4. Ponikowski P, Voors AA, Anker SD, et al. European Society of Cardiology, European Society of Intensive Care Medicine. Guidelines for the diagnosis and treatment of acute and chronic heart failure. Eur J Heart Fail. 2016;37(27):2129-00.
5. Younis A, Mulla W, Goldkorn R, et al. Differences in mortality of new-onset (De-Novo) acute heart failure versus acute decompensated chronic heart failure. Am J Cardiol. 2019;124:554-9.
6. Mentz RJ, Kjeldsen K, Rossi GP, et al. Decongestion in acute heart failure. Eur J Heart Fail. 2014;16:471-82.
7. Kuriyama A, Urushidani S. Continuous versus intermittent administration of furosemide in acute decompensated heart failure: a systematic review and meta-analysis Heart Fail Rev. 2019;24:31-9.
8. Matsue Y, Damman K, Voors A, et al. Time-to-Furosemide treatment and mortality in patients hospitalized with acute heart failure. J Am Coll of Cardiol. 2017;69:3042-51.
9. Solomon SD, Dobson J, Pocock S, et al. Influence of non-fatal hospitalization for heart failure on subsequent mortality in patients with chronic heart failure. Circulation. 2007;116:1482-7.
10. Ellison DH, Felker GM. Diuretic treatment in heart failure. New Engl J Med. 2017;377:1964-75.
11. Abraham WT, Adams KF, Fonarow GC, et al. In-hospital mortality in patients with acute decompensated heart failure requiring intravenous vasoactive medications: an analysis from the Acute Decompensated Heart Failure National Registry (ADHERE). J Am Coll Cardiol. 2005;46:57-64.
12. Francis GS, Bartos JA, Adatya S. Inotropes. J Am Coll Cardiol. 2014;63(20):2069-78.
13. Njoroge JN, Cheema B, Ambrosy AP, et al. Expanded algorithm for managing patients with acute decompensated heart failure. Heart Fail Rev. 2018;23:597-607.
14. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA Focused update of the 2013 ACCF/AHA Guideline for the management of heart failure. J Am Coll Cardiol. 2017;70(6):776-803.
15. Palazzuoli A, Evangelista I, Ruocco G, et al. Early readmission for heart failure: An avoidable or ineluctable debacle? Int J Cardiol. 2019;277:186-95.
16. Velazquez EJ, Morrow DA, DeVore AD, et al. Angiotensin-Neprilysin inhibition in acute decompensated heart failure. New Engl J Med. 2019;380(6):539-48.
17. McMurray JJ, Packer M, Desai AS, et al., for the PARADIGM-HF Investigators and Committees. Angiotensin-neprilysin inhibition versus enalapril in heart failure. New Engl J Med. 2014;371:993-1004.