

Heart failure for the anaesthetist

L Gilliland

Department of Anaesthesia, School of Clinical Medicine, Faculty of Health Sciences, Chris Hani Baragwanath Academic Hospital, University of the Witwatersrand, South Africa

Corresponding author, email: lizilg@gmail.com

Patients with heart failure have increased risk for adverse cardiac events including death, following non-cardiac surgery. The necessity of surgery needs to be determined along with appropriate preoperative evaluation and risk stratification. The anaesthetic should be tailored to specific haemodynamic goals with careful fluid management and appropriate use of vasoactive therapies.

Keywords: heart failure, anaesthetist, adverse cardiac events, risk

Introduction

Cardiovascular disease (CVD) and stroke are the leading causes of death from noncommunicable diseases in South Africa (SA). Almost one in six deaths (17.3%) can be attributed to CVD. Hypertension is the largest contributor to CVD and is prevalent in one of three South Africans older than 15 years, with half being unaware of their condition. Nearly eight out of 10 South Africans older than 50 years are diagnosed with hypertension, ranking SA the highest for any country in the world.¹

The main causes for heart failure in SA include hypertension, dilated cardiomyopathy (DCM), valvular heart disease related to rheumatic heart disease (RHD), coronary artery disease (CAD) and HIV-associated heart disease.²

Recent data from nearly 20 000 heart failure patients in the United States undergoing ambulatory non-cardiac surgery, confirmed increased 30-day postoperative morbidity as well as 90-day postoperative mortality with the risk progressively increasing with decreased systolic function. Symptomatic heart failure patients had a greater risk of mortality.³

Definitions

Heart failure is a complex clinical syndrome in which the heart undergoes structural and functional abnormalities resulting in an impaired ability to fill or eject. This leads to the symptoms of heart failure, namely exertional dyspnoea, fatigue, and signs of pulmonary and systemic congestion. Neurohormonal adaptations of the renin-angiotensin-aldosterone system (RAAS) and the autonomic nervous system can improve cardiac output initially but result in a sustained haemodynamic burden on an already failing heart leading to progression of the heart failure due to apoptosis of myocardial cells.^{3,4} The European Society of Cardiology (ESC) published a universal definition of heart failure in 2021 as illustrated in Figure 1.

Heart failure used to be classified based on symptoms as left- or right-sided. It can present as compensated or decompensated, acute or chronic and pathophysiologically, it can be from systolic or diastolic dysfunction. Systolic heart failure is termed heart failure with reduced ejection fraction (HFrEF), whereas symptoms of heart failure with preserved ejection fraction caused by diastolic dysfunction is known as heart failure with preserved ejection fraction (HFpEF) as shown in Table I.²

The American College of Cardiology/American Heart Association (ACC/AHA) classifies disease progression using well-recognised stages as seen in Table II. All stages of heart failure are dynamic and applicable to patients with HFrEF or HFpEF, based on symptoms with or without evidence of structural heart disease. Stages A and B include pre-symptomatic patients. A recent published position statement proposed some revisions included in Table II to enhance patient and clinician understanding.⁵

Treatment should be initiated for HFrEF and HFpEF as soon as diagnosed and reversible causes of LV dysfunction should be excluded.²

Precipitating factors should be sought and the patients can be classified according to the New York Heart Association (NYHA) functional classification (Table III). It is important to specify

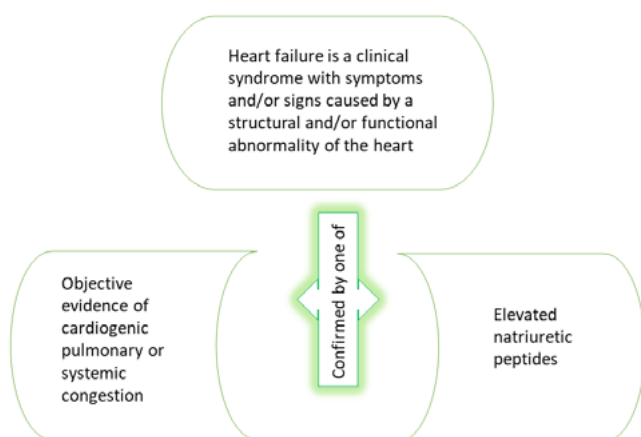


Figure 1: Universal definition of heart failure⁵

current symptoms as a worsening NYHA class is associated with a worse prognosis.⁵

Recognised clinical syndromes can be complicated by heart failure and these include:⁵

- Right heart failure: This commonly occurs secondarily to left heart failure. Other causes include pericardial disease; primary right ventricular (RV) conditions such as arrhythmogenic right ventricular cardiomyopathy, ischaemia and infarction as well as congenital heart disease or valvular pathologies causing pulmonary hypertension.⁷ Primary pulmonary hypertension (WHO groups 1.3 and 4) leading to isolated heart failure should not be categorised under heart failure, as the signs and/or symptoms are not caused primarily by a structural and/or functional cardiac abnormality.⁵ Intraoperative myocardial ischaemia or acute pulmonary hypertension can cause

acute right heart failure after non-cardiac surgery leading to prolonged hospitalisation and increased mortality.⁷

- ACS: Acute myocardial infarction is often complicated by heart failure.
- Cardiogenic shock: This refers to severe cardiac dysfunction causing organ hypoperfusion requiring definitive therapy such as intravenous inotropes, vasopressors, or mechanical circulatory support.
- Hypertensive emergencies: Can lead to end-organ damage that includes acute left ventricular dysfunction, pulmonary oedema, myocardial infarction and/or aortic dissection.
- Valvular heart disease: RHD contributes significantly to the heart failure burden in South Africa. Outcomes remain poor with high mortality rates in admitted patients.²
- Congenital heart disease.

Table I: Revised classification of heart failure based on LV ejection fraction^{2,5}

Type of heart failure	Ejection fraction	Additional signs	Causes
HF_rEF	LVEF < 40%		CAD, DCM, hypertension, valvular disease
HF_{mr}EF	LVEF 40–49%	<ul style="list-style-type: none"> • Elevated levels of natriuretic peptide (NT-proBNP ≥ 125 pg/ml or BNP* ≥ 35 pg/ml) • At least one of: <ol style="list-style-type: none"> i. Structural heart disease (LVH and/or LAE) ii. Diastolic dysfunction 	
HF_pEF	LVEF ≥ 50%		Hypertension, CAD, diabetes, hypertrophic and obstructive cardiomyopathies
HF_{imp}EF	Baseline LVEF ≤ 40%, a ≥ 10-point increase from baseline LVEF, and a second measurement of LVEF > 40%		

*HF_{mr}EF – heart failure with mid-range ejection fraction, HF_{imp}EF – HF with improved EF, LVEF – left ventricular ejection fraction, NT-proBNP – N-terminal pro-B-type natriuretic peptide, BNP – brain natriuretic peptide, LVH – left ventricular hypertrophy, LAE – left atrial enlargement

Table II: Proposed revised staging of heart failure^{5,6}

Stage	Description
A (At risk for HF)	Patient at high risk for developing HF but who has no structural disorder of the heart and no symptoms or signs of HF.
B (Pre-heart failure)	Patient with a structural disorder of the heart or abnormal cardiac function or elevated natriuretic peptides but who has never developed symptoms of HF.
C (Heart failure)	Patient with past or current symptoms of HF associated with structural or functional heart disease.
D (Advanced HF)	Patient with end-stage disease and severe symptoms/signs at rest who requires specialised treatment strategies such as mechanical circulatory support, continuous inotropic infusions, cardiac transplantation, or hospice care.

Table III: NYHA functional classification of heart failure severity⁶

NYHA functional class	Description
I	Patients with cardiac disease but no limitations of physical activity. Activities of daily living do not cause dyspnoea, palpitations or fatigue.
II	Patients with cardiac disease resulting in slight limitation of physical activity, but comfortable at rest. Ordinary physical activity results in dyspnoea, palpitations or fatigue.
III	Patients with cardiac disease resulting in marked limitation of physical activity, but still comfortable at rest. Less than ordinary activity causes dyspnoea, palpitations or fatigue.
IV	Patients with cardiac disease resulting in inability to carry on any physical activity without discomfort. Symptoms are present even at minimal exertion.

- Peripartum cardiomyopathy: Heart failure in the last month of pregnancy or up to five months postpartum occurs in approximately 1 in 1 000 women in SA and is associated with a one-year mortality of 28%.
- High-output failure: Is caused by liver disease, arteriovenous shunts, lung disease, thiamine deficiency, anaemia, thyroid disease or myeloproliferative disorders. Presents with heart failure signs and symptoms, tachycardia and peripheral vasodilation.
- Some primary conditions are complicated by heart failure: Cardiac diagnoses include rapid atrial fibrillation (AF), prolonged ventricular tachyarrhythmias, pulmonary embolism, pericardial diseases, and acute valvular dysfunction. Non-cardiac diagnoses include renal failure, liver failure, morbid obesity with peripheral oedema and chronic respiratory failure hypoventilation syndrome that may present with symptoms and signs that mimic heart failure. The incidence of HIV-associated heart failure is on the increase. Diastolic dysfunction associated with inflammation and fibrosis appears to be the main contributor in patients on antiretroviral treatment. Lipid and metabolic derangements associated with antiretroviral treatment may contribute.²

Acute decompensated heart failure

Acute decompensated heart failure (ADHF) is the clinical presentation of symptoms and signs of congestion and poor organ perfusion due to heart failure requiring urgent treatment. Compensatory mechanisms are overwhelmed in the acute dysfunction of ADHF and this results in signs and symptoms of increased left and/or right ventricular filling pressures. Left ventricular failure leads to pulmonary vascular congestion, and increased right ventricular pressures lead to vascular congestion of the kidneys, liver, gastrointestinal system and heart resulting in end-organ damage. A small proportion of ADHF patients have cardiogenic shock. Diuretics, vasodilators and inotropes remain the main treatment for ADHF. Novel therapies include myotropes such as omecamtiv mecarbil, which improve cardiac function by increasing contractility without increasing myocardial oxygen demand or calcium but by increasing interaction of myosin heads with actin filaments.⁸ Patients with ADHF are prone to arrhythmias and a defibrillator with pacing function should be readily available with external pads preferably placed. An intra-aortic balloon pump can be considered in patients refractory to medical treatment.⁹

Arrhythmias

Arrhythmias occur frequently in patients with heart failure, irrespective of the LVEF, and may contribute to worsening symptoms. AF and flutter are common, and increase the risk of thromboembolic events. Correctable causes should be excluded and electrical cardioversion employed in haemodynamically compromised patients. A rate control strategy is advised in haemodynamically stable patients to achieve a heart rate < 100 bpm, using a beta blocker (BB). If a patient is unstable or has severe congestion, digoxin or amiodarone is recommended.

Anticoagulation is commonly used in patients with HFrEF and ablation therapy is a useful option. Calcium-channel blockers and class I anti-arrhythmic agents can lead to premature death in symptomatic heart failure patients and should be avoided.²

Perioperative cardiac risk assessment

A recent published review analysing eleven risk indices that involved over two million patients identified several risk factors predictive for adverse cardiac outcomes. Congestive heart failure, type of surgery, elevated preoperative creatinine levels, diabetes, history of stroke or transient ischaemic attack, and emergency surgery were all highly predictive for poor outcomes. Hypertension, patients' functional status, advanced age and American Society of Anesthesiology (ASA) physical status classification were additional risk factors as indicated in the review from larger studies.

The authors concluded that indices had limitations and clinical judgement should always accompany preoperative cardiac risk stratification. The combination of a high-accuracy National Surgery Quality Improvement Program-based risk index (NSQIP) with the Revised Cardiac Risk Index (RCRI) ensures a more accurate estimate of the risk of life-threatening cardiac outcomes and a broader assessment of cardiac risk involved.¹⁰

Natriuretic peptide levels are used to assist in the diagnosis or exclusion of heart failure in patients presenting with dyspnoea, with the proviso that an array of cardiac and non-cardiac conditions can lead to raised levels. These include severe burns, sepsis, anaemia, renal failure, pulmonary hypertension, pneumonia, obstructive sleep apnoea and advanced age. Non heart failure cardiac causes include ACS, LVH, AF, valvular heart disease, myocarditis, pericardial disease, cardioversion, cardiac surgery and myocardial insults, including chemotherapy for cancer.¹¹

There is increasing evidence that a preoperative N-terminal pro-B-type natriuretic peptide (NT-proBNP) level may improve risk prediction in adults undergoing major non-cardiac surgery when used in conjunction with recommended risk models such as RCRI. In multivariable analyses performed in a prospective cohort study of 10 402 patients who underwent non-cardiac surgery, preoperative NT-proBNP values were strongly associated with an increased risk of death and major cardiovascular events at 30 days after surgery. It was found that an NT-proBNP threshold of 200 pg/ml identified patients at higher risk.¹²

The addition of a postoperative natriuretic peptide measurement was found to aid in the identification of patients at risk for non-fatal myocardial infarction and was the strongest predictor of mortality in a review done by Rodseth et al.¹³

Preoperative functional capacity to determine metabolic equivalents (METs) forms an important part in risk assessment. It can be estimated by the ability of a patient to perform daily living activities. Climbing two flights of stairs require 4 METs and the inability to achieve this is associated with an increased incidence of postoperative cardiac events.^{14,15} Combining echo-

cardiography and serial measurements of natriuretic peptide levels can lead to appropriate risk assessment.¹⁶

Medical management update

Combination therapy is the mainstay treatment to provide symptomatic and prognostic benefits in HFrEF. Drugs used include beta blockers (BB), angiotensin-converting enzyme inhibitors (ACE-I), angiotensin receptor blockers (ARB) and mineralocorticoid antagonists (MRAs).² The aim of treatment is to control symptoms of heart failure and limit the progression, remodelling and complications of disease.^{4,9}

Sacubitril is a neprilysin inhibitor that prevents neprilysin from breaking down natriuretic peptides, bradykinin, adrenomedullin, substance P and calcitonin gene-related peptide which plays an important role in the progression and pathogenesis of heart failure. It is combined with an ARB (valsartan) and the combination angiotensin receptor-neprilysin inhibitor (ARNI) has a clear benefit on mortality and heart failure hospitalisation.¹¹ It is indicated for NYHA class II–IV patients and given in place of an ACE-I or ARB.¹⁷ Side-effects include hypotension, renal insufficiency and angioedema; therefore, ACE-Is should be stopped at least 36 hours before initialising therapy.²

Ivabradine is a new beneficial agent that reduces the heart rate by selectively inhibiting the I_f current in the sinoatrial node. It should be used in NYHA class II or III patients on maximum tolerated doses of BB, ACE-I and MRA that are in sinus rhythm with a rate > 70 bpm.¹⁷

Sodium-glucose cotransporter-2 inhibitors (SGLT2) in both diabetic and non-diabetic patients with HFrEF lead to lower hospitalisation and mortality. These agents decrease arterial pressure via an osmotic diuresis and natriuresis leading to a reduced preload and afterload which favours myocardial remodelling.¹⁷ A concern in the perioperative period is the occurrence of normoglycaemic ketoacidosis, and the potential for this critical diagnosis to be delayed or missed entirely. Although recommendations are to stop SGLT2 inhibitors at least 24 hours before elective surgery, it might be best to halt treatment approximately three days (or five half-lives) before major surgery or minor surgery that predisposes to a ketotic state (colonoscopies with bowel preparation). Patients requiring emergency surgery should stop treatment immediately. Treatment should be resumed once the patient is on a normal diet and euvolaemic postoperatively.¹⁸

Diuretics provide relief from fluid overload and congestion symptoms with no prognostic benefit.² Spironolactone, an MRA, reduces mortality but requires regular follow-up of electrolytes, especially potassium levels and renal function.^{9,17} Digoxin is usually reserved for patients with HFrEF and AF but can also be used for the treatment of refractory heart failure. Nitrates and hydralazine are underutilised despite their beneficial effects and are indicated for patients unable to take a RAAS inhibitor or symptomatic patients despite combination therapy.²

Cardiac resynchronisation therapy (CRT) can be indicated in select HFrEF patients with or without an internal cardioverter defibrillator (ICD). These include patients with an EF < 35% despite maximal medical treatment or QRS duration > 130 ms with a left bundle branch morphology.^{2,4} A left ventricular assist device (LVAD) is indicated in patients on optimal medical therapy with end-stage HFrEF as a bridge to transplantation, as it improves patient survival and reduces hospitalisation.²

Heart failure patients on existing medication should continue therapy throughout the perioperative period. ACE-Is and ARBs can be discontinued on the morning of surgery to avoid hypotension and resumed postoperatively, but this can be individualised. Newly diagnosed heart failure patients should ideally be managed medically for at least three months prior to surgery, especially if HFrEF is present.¹⁶

Anaesthetic management

Providing anaesthesia to patients with heart failure remains a challenge as heart failure is a well-established risk factor for postoperative mortality.³ Identifying the aetiology and precipitators of heart failure will guide intraoperative management. The severity of heart failure and the functional state of the patient need to be assessed and a multidisciplinary approach is needed to determine the necessity of surgery and the appropriate timing thereof.¹⁶

Irrespective of the anaesthetic technique chosen, the goals of anaesthesia are to:

- Maintain preload
- Avoid myocardial depression
- Avoid tachycardia
- Avoid increased afterload
- Prevent hypotension

Invasive monitoring to aid in the above-listed goals includes an intra-arterial catheter, and a central venous catheter if vasoactive drugs need to be infused. Transoesophageal echocardiography (TEE) can assist in guiding fluid and vasopressor therapy during major surgery. The use of a pulmonary artery catheter is not supported by research.^{4,16}

The choice of anaesthetic technique should be guided by the procedure, patient preference and individualised contraindications. Peripheral nerve blocks will cause the least haemodynamic changes. Neuraxial techniques cause hypotension secondary to sympathetic blockade but this is combined with a beneficial afterload reduction. Induction of general anaesthesia often leads to vasodilation with resultant hypotension; agents should therefore be carefully titrated. Etomidate has the least haemodynamic effects with propofol causing negative inotropy but with a beneficial decrease in systemic vascular resistance. Volatile agents in high concentrations will lead to myocardial depression. Opioids

reduce the need for anaesthetic agents and have minimal cardiovascular depressant effects.^{9,14,16}

Fluid management in heart failure patients should be goal-directed using a balanced solution with a well-defined transfusion trigger of haemoglobin level < 10 g/dl to ensure normal or even supernormal oxygen delivery. Euvolaemia should be maintained, although patients can present with hypovolaemia from excessive diuretic therapy or hypervolaemia secondary to underlying disease and precipitators. Advanced pressure waveform analysis (including pulse pressure and stroke volume variation) can be used as dynamic preload indicators with good results if the focus is on the trend rather than absolute readings. Ideally, it should be combined with TEE if expertise allows.^{14,16}

Vasodilators, vasopressors, inotropes and inodilators are agents that are utilised in selected heart failure patients. The choice of drug depends on the patients LVEF and level of organ hypoperfusion. Vasopressors like phenylephrine, ephedrine, adrenaline, dopamine, noradrenaline and vasopressin require very careful dose titration to treat hypotension in order to curb the decreased CO resulting from the increased afterload.⁹ Inotropes should be utilised if there are signs of organ hypoperfusion with calcitropes (inotropes that alter the myocardial calcium transients) presently the drugs of choice. Calcitropic drugs including dobutamine, dopamine, milrinone and adrenaline were associated with increased short-term mortality, arrhythmia, and end-organ damage without a reduction in CVS morbidity in patients with ADHF. The use of levosimendan, a calcium-sensitising inodilator, in patients with ADHF is controversial as recent minor studies demonstrated benefits, while evidence from larger trials bordered on detrimental results.⁸

Patients should be closely monitored postoperatively whilst haemodynamic and fluid therapy are optimised. Respiratory status and developing signs of acute heart failure should be pursued and treated.⁹ Non-invasive ventilation can be employed postoperatively as it decreases preload, afterload and intrapulmonary shunting. Care should be taken to avoid supplemental oxygen in heart failure patients that are not hypoxaemic as this could lead to impaired diastolic function, increased left ventricular filling pressures, and increased systemic vascular resistance resulting in decreased CO.⁸ Administering appropriate analgesia is critical in avoiding an increased systemic vascular resistance. Postoperative care can be best achieved within an intensive care unit.⁹

Conclusion

Patients with heart failure have increased risk for adverse cardiac events, including death, following non-cardiac surgery.^{3,4,9,16} The necessity of surgery needs to be determined along with appropriate preoperative evaluation and risk stratification. The anaesthetic should be tailored to specific haemodynamic goals with careful fluid management and appropriate use of vasoactive therapies.

References

- Heart and Stroke Foundation South Africa (HSFSA). Cardiovascular disease statistics reference document. Jessica Byrne RD (SA), Gabriel Eksteen RD (SA), Christelle Crickmore MSc (Nutrition). March 2016. Available from: <http://heartfoundation.co.za/wp-content/uploads/2017/10/CVD-Stats-Reference-Documents-2016-FOR-MEDIA-1.pdf>. Accessed 23 Aug 2021.
- Hitzerth J, Mpe M, Klug E, et al; Society of South Africa HF. 2020 Heart Failure Society of South Africa perspective on the 2016 European Society of Cardiology Chronic Heart Failure Guidelines. *S Afr Med J*. 2020;110(8b):13057.
- Lerman BJ, Popat RA, Assimes TL, et al. Association between heart failure and postoperative mortality among patients undergoing ambulatory noncardiac surgery. *JAMA Surg*. 2019;154(10):907-14. <https://doi.org/10.1001/jamasurg.2019.2110>.
- Prout J, Jones T, Martin D, editors. Oxford higher specialty training: Advanced training in anaesthesia the essential curriculum. Oxford (UK): Oxford University Press; 2014.
- Bozkurt B, Coats AJS, Tsutsui H, et al. Universal definition and classification of heart failure: a report of the Heart Failure Society of America, Heart Failure Association of the European Society of Cardiology, Japanese Heart Failure Society and Writing Committee of the Universal Definition of Heart Failure: Endorsed by the Canadian Heart Failure Society, Heart Failure Association of India, Cardiac Society of Australia and New Zealand, and Chinese Heart Failure Association. *Eur J Heart Fail*. 2021;23(3):352-80. <https://doi.org/10.1002/ehf.2115>.
- Yancy CW, Jessup M, Bozkurt B, et al. American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation*. 2013;128(16):e240-327. <https://doi.org/10.1161/CIR.0b013e31829e8776>.
- Konstam MA, Kiernan MS, Bernstein D, et al. American Heart Association Council on Clinical Cardiology; Council on Cardiovascular Disease in the Young; and Council on Cardiovascular Surgery and Anesthesia. Evaluation and management of right-sided heart failure: a scientific statement from the American Heart Association. *Circulation*. 2018;137(20):e578-e622. <https://doi.org/10.1161/CIR.0000000000000560>.
- Njoroge JN, Teerlink JR. Pathophysiology and therapeutic approaches to acute decompensated heart failure. *Circ Res*. 2021;128(10):1468-86. <https://doi.org/10.1161/CIRCRESAHA.121.318186>.
- Ibrahim RI, Sharma V. Cardiomyopathy and anaesthesia, *BJA Educ*. 2017;11:363-9. <https://doi.org/10.1093/bjaed/mkx022>.
- Wright DE, Knuessel SJ, Nagarur A, Philpotts LL, Greenwald JL. Examining risk: a systematic review of perioperative cardiac risk prediction indices. *Mayo Clin Proc*. 2019;94(11):2277-2290. <https://doi.org/10.1016/j.mayocp.2019.03.008>.
- 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: A Report of the American College of Cardiology/American Heart Association Task Force on clinical practice guidelines and the Heart Failure Society of America. *Circulation*. 2017;136(6):e137-61. <https://doi.org/10.1161/CIR.0000000000000509>.
- Duceppe E, Patel A, Chan MTV, et al. Preoperative N-terminal pro-B-type natriuretic peptide and cardiovascular events after noncardiac surgery: a cohort study. *Ann Intern Med*. 2020;172(2):96-104.
- Rodseth RN, Biccard BM, Le Manach Y, et al. The prognostic value of pre-operative and post-operative B-type natriuretic peptides in patients undergoing noncardiac surgery: B-type natriuretic peptide and N-terminal fragment of pro-B-type natriuretic peptide: a systematic review and individual patient data meta-analysis. *J Am Coll Cardiol*. 2014;63(2):170-80. <https://doi.org/10.1016/j.jacc.2013.08.1630>.
- Kristensen SD, Knuuti J, Saraste A, et al. 2014 ESC/ESA Guidelines on non-cardiac surgery: cardiovascular assessment and management: The Joint Task Force on non-cardiac surgery: cardiovascular assessment and management of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology (ESA). *Eur Heart J*. 2014;35(35):2383-431. <https://doi.org/10.1093/eurheartj/ehu282>.
- Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;130(24):2215-45. <https://doi.org/10.1161/CIR.000000000000105>.
- Smit-Fun V, Buhre WF. The patient with chronic heart failure undergoing surgery. *Curr Opin Anaesthesiol*. 2016;29(3):391-6. <https://doi.org/10.1097/ACO.0000000000000335>.
- Maddox TM, Januzzi JL Jr, Allen LA, et al. 2021 Update to the 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: Answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Solution Set Oversight Committee. *J Am Coll Cardiol*. 2021;77(6):772-810. <https://doi.org/10.1016/j.jacc.2020.11.022>.
- Milder DA, Milder TY, Kam PCA. Sodium-glucose co-transporter type-2 inhibitors: pharmacology and peri-operative considerations. *Anaesthesia*. 2018;73(8):1008-18. <https://doi.org/10.1111/anae.14251>.