CURRENT OPINION

Management of perioperative heart failure

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Purpose of review
In the perioperative period, acute heart failure can result from a variety of conditions, and treatment may vary considerably depending on its mechanism. This review aims to provide conceptual framework by selectively presenting recent knowledge and advances in acute heart failure therapies including drugs (inotropes, diuretics) and devices (mechanical assistance, biventricular pacing, ultrafiltration).

Recent findings
The calcium sensitizer levosimendan, showed a mortality benefit in cardiac surgery patients in a recent meta-analysis. A study involving patients with cardiogenic shock complicating myocardial infarction for which early revascularization was planned, intra-aortic balloon support did not reduce 30-day mortality. A novel study showed that ultrafiltration was inferior to pharmacologic therapy in acute heart failure in nonsurgical patients. Biventricular pacing provided a significant clinical benefit over right ventricular pacing in nonsurgical patients with left ventricular dysfunction and atrioventricular block. Two recently published meta-analyses confirmed the prognostic role of natriuretic peptides in the perioperative setting.

Summary
Poor data exist in the perioperative setting concerning acute heart failure therapies. Large trials are needed to support the use of levosimendan, mechanical assistance, utrafiltration and biventricular pacing in the perioperative setting. The prognostic role of natriuretic peptides was confirmed in the perioperative period.

Keywords
acute heart failure, B-type natriuretic peptide, inotropes, mechanical assistance

INTRODUCTION

Heart failure is one of the most frequent cardiac complications of noncardiac surgery. In the perioperative period, acute heart failure can result from a variety of conditions. It often occurs in patients with underlying chronic heart failure; however, it may occasionally present in patients with preserved left ventricular ejection fraction and possibly left ventricular diastolic dysfunction [1]. With such prevalence and complexity, acute perioperative heart failure management is a major challenge for physicians.

EPIDEMIOLOGY AND OUTCOME

Based on recent American Heart Association statistics, incidence of heart failure has remained stable over the past several decades with more than 650 000 new cases of heart failure diagnosed annually. Approximately, more than 5 million persons in the USA clinically manifest heart failure and the prevalence continues to rise [2]. Hence, the number of patients with heart failure presenting for surgery is growing significantly.

Incidence of major cardiac complications after major noncardiac surgery is between 2 and 3.5% [3]. In cardiac surgery, the incidence rises to 20% or more [4].

Contemporary data showed that the cumulative total mortality rate of acute heart failure at 1 year was between 24 and 33% [5,6▪]. Although there have been no recent reports of mortality from acute perioperative heart failure, it would be well tolerated to assume that it would at least approach the previously mentioned statistics.

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Curr Opin Anesthesiol 2014, 27:140–145

DOI:10.1097/ACO.0000000000000056

KEY POINTS

- Recently published studies and meta-analyses confirmed the role of natriuretic peptides in risk stratification in the perioperative setting.
- The use of calcium sensitizer levosimendan, showed a mortality benefit, mainly in cardiac surgery patients with acute heart failure.
- Insufficient recent data exist in the perioperative setting concerning the use of mechanical assistance, ultrafiltration or biventricular pacing in acute heart failure patients, and large trials are more than needed to support their use.

DEFINITION AND CAUSE OF ACUTE PERIOPERATIVE HEART FAILURE

Heart failure is a complex clinical syndrome that results from various structural or functional impairment of ventricular filling or ejection of blood [2]. Acute heart failure presents frequently as pulmonary oedema, or left/right/biventricular congestive heart failure, sometimes as cardiogenic shock [4]. The majority of acute perioperative heart failure occurs in patients who have decreased cardiovascular reserve prior to surgery. In the perioperative period, patients may be faced with numerous triggers of acute heart failure, including hypertension, tachyarrhythmias, anemia, hypercoagulability, inappropriate fluid management, pain, surgical stress and myocardial ischaemia. Other possible causes of perioperative heart failure include acute or chronic valvular heart disease, pulmonary or fat emboli, which can be presented as acute right ventricular failure.

Cardiac surgery may lead to some unique causes of heart failure. Indeed, mechanical complications including spasm or occlusion of a coronary graft, prosthetic paravalvular regurgitation, cardiac tamponade, and pneumo or hemothorax may be seen after cardiac surgery.

DIAGNOSIS AND MONITORING

For years, the diagnosis of acute heart failure was based on clinical signs and was confirmed by echocardiography. Recently, the use of plasma biomarkers (mainly natriuretic peptides) has shown great diagnostic value. The diagnosis of acute perioperative heart failure is still principally based on history and clinical findings. In the perioperative setting, acute heart failure patients present with orthopnea related to increased left-sided filling pressures, and abdominal discomfort, nausea and vomiting caused by right-sided overload. The physical examination may demonstrate signs of heart failure severity: hypotension, tachycardia, dyspnea, hepatic congestion, oliguria, cyanosis, mottling and disorder of consciousness. The association of low cardiac output and tissue hypoxia in the absence of hypovolemia define cardiogenic shock. The diagnosis can be supported by appropriate investigations such as electrocardiogram, chest radiograph, echocardiography, pulmonary artery catheter and biomarkers.

Intraoperative and postoperative transoesophageal echocardiography (TOE) and postoperative transthoracic echocardiography should be performed as early as possible in patients suspected of perioperative heart failure. Echocardiography quickly provides data on regional or global, right and/or left ventricular dysfunction, the presence of tamponade, cardiac thrombi, valvular dysfunction and preload estimation. The role of TOE is important for perioperative haemodynamic monitoring and the assessment of the optimal volume status. Preload estimation through the measurement of left ventricular end diastolic area, and estimation of fluid responsiveness by dynamic indicators enables real time guidance for volume therapy. Continuous monitoring in the postoperative period can be obtained by a single-use miniaturized TOE probe that can be left in place 72 h in ventilated patients [7,8].

Although the role of pulmonary artery catheterization is contentious, it can be very useful for explaining a complex perioperative haemodynamic situation. The diagnosis of severe acute heart failure is suspected by the association of low cardiac index ($<2.2 l/min/m^2$), low mixed venous saturation ($<60\%$) and elevated pulmonary capillary wedge pressure (>18 mmHg).

Biomarkers are very useful in less severe acute heart failure when the mechanism of postoperative acute dyspnea is unclear, and when there is an urgent need to discriminate pulmonary infection and pulmonary oedema. Currently, the diagnostic role of B-type natriuretic peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP) in the perioperative period remains to be demonstrated. These biomarkers have the potential to strengthen the diagnosis of acute perioperative heart failure when used in conjunction with history, physical exam and other diagnostic tools.

MANAGEMENT OF PERIOPERATIVE HEART FAILURE

Management of acute heart failure in the perioperative period requires rapid diagnosis and treatment to prevent further myocardial and organ dysfunction. Risk stratification may be a valuable tool in the setting of acute perioperative heart failure. Patients identified at high risk may benefit from aggressive optimization of drug or device therapy, avoiding known triggers of acute heart failure, and identifying the appropriate postoperative care setting.

How to detect high-risk patients?

The goals of preoperative evaluation in noncardiac surgery are to gather information concerning the risk for cardiac events pertaining to surgery (urgency, type, magnitude, duration and blood loss), the functional capacity measured in metabolic equivalents (METs) and the Lee Revised Cardiac Risk Index, which contains five independent clinical determinants of major perioperative cardiac events: a history of ischaemic heart disease, heart failure, cerebrovascular disease, insulin-dependent diabetes mellitus and impaired renal function.

According to the 2009 ESC guidelines, noninvasive testing of ischaemic heart disease (physiological exercise, stress echocardiography and myocardial perfusion imaging) are indicated before noncardiac surgery in patients with a stable cardiac condition scheduled for an intermediate or high-risk surgery, with a poor functional capacity (MET ≤ 4) and a Lee Index of at least 3. Patients without stress-induced ischaemia can proceed with the planned surgical procedure. It is recommended that statin therapy and a titrated low-dose β-blocker regimen be initiated. In patients with extensive stress-induced ischaemia, as assessed by noninvasive testing, individualized perioperative management is recommended, taking into consideration the potential benefit of the proposed surgical procedure compared with the predicted adverse outcome. Also, the effect of medical therapy and/or coronary revascularization must be assessed.

Routine rest echocardiography is not recommended in the preoperative evaluation of left ventricular function, but may be performed in asymptomatic patients undergoing high-risk noncardiac surgery [3].

In cardiac-surgery patients, indicators of major clinical risk in the perioperative period are: unstable coronary syndromes, decompensated heart failure, significant arrhythmias and severe valvular disease. The European system for cardiac operation risk evaluation (EuroSCORE) is widely used for predicting in-hospital mortality after cardiac surgery. Because of the therapeutic advances, the EuroSCORE slightly overestimates the perioperative risk, which is why an updated version of the score, the EuroSCORE II, is under assessment [9,10]. EuroSCORE II is better calibrated than the original model yet preserves powerful discrimination.

In addition to noncardiac and cardiac surgery scoring systems, BNP and NT-pro-BNP levels at admission could be an additional risk stratification factor. In coronary artery bypass graft surgery patients, increased perioperative BNP concentrations independently associate with heart failure hospitalization or heart failure death during the 5 years after surgery [11■]. In another study including patients undergoing emergency noncardiac procedures, preoperative NT-pro-BNP $\geq 1740\,\text{pg}\,\text{ml}^{-1}$ was associated with a 6.9-fold univariate relative risk (95% CI: 3.5–13.4) for in-hospital major adverse cardiac events, but did not remain significant in a multivariate logistic regression model [12■]. In a recent systematic review and meta-analysis in noncardiac surgery patients, increased postoperative BNP and NT-pro-BNP are independently associated with increased risk of mortality, myocardial infarction (MI), and cardiac failure at 30 days and more than 180 days after surgery [13■].

General considerations

In the perioperative acute heart failure, a differential diagnosis for the cause must be established as resuscitation measures are initiated. Indeed, the good aetiologic diagnosis may allow definitive treatment through the use of specific therapies. For example, patients with perioperative acute heart failure secondary to an acute MI, reperfusion via angioplasty, stenting or bypass grafting will be necessary. Acute mitral regurgitation from a MI causing acute heart failure might require urgent surgical repair.

At the same time, appropriate resuscitation measures must be undertaken. The concept of the golden hour for acute heart failure management is essential, and drugs administration must be started within minutes of diagnosis. The list below highlights the general approach to perioperative acute heart failure management (modified from [14]).

(1) Develop differential diagnosis for cause, treat repairable lesions.
(2) Initiate resuscitation measures: maximize oxygenation/ventilation, control postoperative pain/tachycardia, correct acid-base and electrolyte abnormalities.
(3) Evaluate and optimize preload, afterload, contractility, heart rate and rhythm
    (a) Preload – volume load vs. diuresis based on evaluation of volume status

   (b) Afterload – if high, consider dilation with nitrogycerine, sodium nitroprusside; if low consider augmentation with norepinephrine
   (c) Contractility – utilize inotropic agent
   (d) Establish stable heart rate and rhythm.
(4) Utilize mechanical assistance for patients resistant to above measures.

THERAPEUTIC APPROACHES: YEAR IN REVIEW 2012

In the setting of the failing ventricle with clear clinical and pathological signs of low cardiac output, inotropes often act as the first-line agents to improve contractility and haemodynamics. Although the use of inotropes is a mainstay of treatment in acute heart failure, a recent meta-analysis, including 14 studies with 673 participants, found that dobutamine was not associated with improved mortality in patients with acute heart failure, and a trend towards an increase in mortality with use of dobutamine compared with placebo or standard care, although this did not reach statistical significance. In this meta-analysis, the estimate of the odds ratio for mortality for patients with severe heart failure treated with dobutamine compared with control was 1.47 (95% CI = 0.98–2.21, $P = 0.06$) [15].

The authors concluded that dobutamine is not associated with improved mortality in patients with heart failure, and there is a suggestion of increased mortality associated with its use without statistical significance. It was also pointed out that studies had a poor level of methodological reporting.

In another recent meta-analysis evaluating the effects of levosimendan on mortality and hospitalization, data from 45 randomized clinical trials were analyzed in 5480 cardiac surgery, cardiology and septic patients [16].

The overall mortality rate was 17.4% among levosimendan-treated patients and 23.3% in the control group [risk ratio 0.80 (0.72; 0.89), $P < 0.001$]. Reduction in mortality was confirmed in studies with placebo [risk ratio 0.82 (0.69; 0.97), $P = 0.02$] or dobutamine [risk ratio 0.68 (0.52–0.88); $P = 0.003$] as a comparator. This meta-analysis suggests that the use of levosimendan in lieu of usual therapies is associated with a significant reduction in mortality mainly in cardiac surgery patients.

In situations in which the use of pharmacologic therapy alone is insufficient and catecholamines have to be used at a high dose to improve ventricular performance, mechanical support is an appropriate option. Currently, three methods are employed: the intra-aortic balloon pump (IABP), percutaneous cardiopulmonary bypass system and mechanical assist devices. Most of these techniques are restricted to use in specialized cardiac surgery centres. Many review articles of the currently available devices for mechanical support, their indications, outcomes and complications were recently published [17–19].

In the IABP-SHOCK II Trial, a randomized controlled study involving patients with cardiogenic shock complicating MI for whom early revascularization was planned, IABP support did not reduce 30-day mortality. Indeed, 119 patients in the IABP group (39.7%) and 123 patients in the control group (41.3%) died (relative risk with IABP, 0.96; 95% CI, 0.79–1.17; $P = 0.69$). There were no significant differences in secondary end points or in process-of-care measures, including the time to hemodynamic stabilization, the length of stay in the ICU, serum lactate levels, the dose and duration of catecholamine therapy, and renal function [20].

The authors concluded that the results of the study cannot be generalized to the subgroup of patients with the most severe form of cardiogenic shock that are most likely to receive benefit from IABP support.

In patients with atrioventricular block, right ventricular versus biventricular pacing was assessed. Curtis *et al.* [21▪] investigated whether biventricular pacing might reduce mortality, morbidity and adverse left ventricular remodelling in patients who had indications for pacing with atrioventricular block, New York Heart Association class I, II, or III heart failure, and a left ventricular ejection fraction of 50% or less. Patients received a cardiac-resynchronization pacemaker or implantable cardioverter-defibrillator (ICD) and were randomly assigned to standard right ventricular pacing or biventricular pacing. The primary outcome was the time to death from any cause, an urgent care visit for heart failure that required intravenous therapy, or an increase in the left ventricular end-systolic volume index of 15% or more. Biventricular pacing patients had a significantly lower incidence of the primary outcome over time than did those assigned to right ventricular pacing (hazard ratio, 0.74; 95% CI, 0.60–0.90).

It was concluded that biventricular pacing provided a significant clinical benefit over right ventricular pacing in patients with left ventricular dysfunction and atrioventricular block who require ventricular pacing. More trials are needed to support the use of biventricular pacing in the perioperative setting, mainly in cardiac surgery patients.

Ultrafiltration may be useful for diuretic-refractory patients who have acute heart failure, and some investigators have advocated its early and more widespread use. Potential advantages of ultrafiltration include adjustable fluid-removal volume and neutral effect on serum electrolytes. Two recent studies raise concerns about the efficacy and safety of using ultrafiltration as a rescue strategy in acute heart failure patients with persistent congestion and renal failure.

In an observational study, Patarroyo *et al.* [22] evaluated the outcome of 63 patients with acute heart failure and refractory congestion undergoing slow continuous ultrafiltration. Although 48 h of ultrafiltration improved haemodynamic parameters, renal function did not improve in this high-risk population, and 59% required hemodialysis during their hospitalization.

The Cardiorenal Rescue Study in acute Decompensated Heart Failure (CARRESS-HF trial) randomly assigned 188 patients with acute heart failure, worsened renal function and persistant congestion to a strategy of stepped pharmacologic therapy (94 patients) or ultrafiltration (94 patients). Ultrafiltration was inferior to pharmacologic therapy with respect to the bivariate end point of the change in the serum creatinine level and body weight 96 h after enrolment ($P = 0.003$), owing primarily to an increase in the creatinine level in the ultrafiltration group. In addition, a higher percentage of patients in the ultrafiltration group than in the pharmacologic-therapy group had a serious adverse event (72 vs. 57%, $P = 0.03$) [23].

Therefore, at present, it is reasonable to use ultrafiltration in treating the diuretic-refractory patient, but widespread or pre-emptive use in the patient with acute heart failure will require more evidence of benefit and safety.

The emerging data suggest that biomarkers may be useful for the diagnosis and the prognosis of surgical patients with acute heart failure. The results of four recent studies evaluating BNP and NT-pro-BNP in this case are summarized in Table 1 [11▪,12▪,24,25]. Two recently published meta-analyses confirmed these results. The first showed that increased postoperative BNPs are independently associated with adverse cardiac events after noncardiac surgery [13▪], and the latter demonstrated that additional postoperative natriuretic peptides measurement enhanced risk stratification for the composite outcomes of death or nonfatal MI 30 days and at least 180 days after noncardiac surgery as compared with a preoperative measurement alone [26▪]. However, whether or not biomarker-guided therapy improves outcome in the setting of perioperative acute heart failure has not been determined.

Table 1. Characteristics of recent studies evaluating B-type natriuretic peptide and N-terminal pro-B-type natriuretic peptide in the perioperative period

Study	Type of observational study	Number of patients	Nature of surgery	Biomarker	Timing of perioperative NPS samples	Biomarker cut-off	Primary outcome
Mercantini *et al.* [24]	Prospective	205	Elective major abdominal surgery	BNP	Preoperative and postoperative day 1	Preoperative >36 pg/ml	Adverse cardiac events until 30 days after discharge
Fox *et al.* [11▪]	Prospective	1025	Isolated primary coronary artery bypass graft	BNP	Preoperative and peak postoperative	–	HF hospitalization or HF death during the 5 years after surgery
Farzi *et al.* [12▪]	Prospective	297	Emergent non-cardiac procedure	NT-pro-BNP	Preoperative once between POD 3 and 5 and on the day of discharge	Preoperative ≥725 pg/ml Postoperative ≥160 pg/ml	Composite endpoint of nonfatal MI, acute HF and all cause mortality between index surgery and 3 years follow-up
Park *et al.* [25]	Prospective	97	Elective orthopedic surgery	BNP	Postoperative day 1	≥217.5 pg/ml	Length of hospital stay ≥ 30 day

BNP, B-type natriuretic peptide; HF, heart failure; MI, myocardial infarction; NPS, natriuretic peptides; NT-pro-BNP, N-terminal pro-B-type natriuretic peptide; POD, postoperative day.

CONCLUSION

Perioperative acute heart failure represents a major problem for physicians. Currently, the best option for patients is prevention through risk stratification and adequate perioperative management. The role of natriuretic peptides measurement in the perioperative setting was demonstrated in the diagnosis and prognosis of acute heart failure.

Recently, completed trials answered questions regarding the safety and efficacy of inotropes, ultrafiltration and mechanical assistance. Although advances have been realized, attempts should be made to determine the optimal place and timing of each of the treatments in perioperative acute heart failure patients.

Acknowledgements

None.

Conflicts of interest

There are no conflicts of interest.

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