The patient with chronic heart failure undergoing surgery

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Purpose of review
Congestive heart failure (CHF) is one of the most common diseases of the elderly patient. The underlying pathophysiology varies considerably and approximately 50% of the patients suffer from CHF with reduced left ventricular ejection fraction. Mortality in the perioperative period is increased in patients with CHF and this holds true for both minor and major surgeries. This review will summarize recent literature in the field of CHF and perioperative outcome in patients undergoing surgery with a special emphasis on actual guidelines, preoperative assessment and appropriate perioperative therapy.

Recent findings
In the past 18 months, new insights in the short and long-term effects of CHF in the perioperative period have been published. The role of left ventricular ejection fraction has been studied in noncardiac surgical patients and it has been demonstrated that an ejection fraction less than 30% is associated with a significant increase in mortality and myocardial infarctions. Moreover, in 25% of patients, acute exacerbation of heart failure takes place in the perioperative period. The European Society of Anesthesiology published new guidelines on the preoperative evaluation of patients with CHF. The role of adequate preoperative evaluation and preparation of patients with CHF is discussed widely. It becomes clear that parameters like brain natriuretic peptide play a crucial role in risk stratification and prediction of outcome. Also, the treatment of patients with low cardiac output was a topic, and it became clear that established therapies including the use of β-mimetics and PDE-III inhibitors should only be initiated in very selected patient groups. However, adequately powered studies in patients with CHF are still missing and the majority of knowledge is based on patient undergoing cardiac surgery.

Summary
CHF is a source of considerable perioperative morbidity and mortality and in contrast to coronary artery disease, knowledge is very limited and additional research urgently needed.

Keywords
brain natriuretic peptide, congestive heart failure, diastolic dysfunction, ejection fraction, NT-pro-BNP

INTRODUCTION

Chronic heart failure (CHF) is one of the most common diseases in the Western population. In the USA and in Germany, the number of patients with diagnosed CHF is in the range of 5–6 million and 1.8 million patients, respectively [1▪▪,2▪]. CHF is a disease of the elderly and it can be expected that approximately 8–15% of patients above the age of 65 suffer from the disease [1▪▪]. In particular, the risk of perioperative mortality in patients with CHF is two-fold to four-fold higher compared with patients with isolated coronary artery disease, clearly demonstrating the need for optimal perioperative management of these patients [2▪].

As more surgical procedures take place in elderly patients, anesthesiologists will more often face patients with diagnosed or even suspected CHF in the perioperative period. Therefore, knowledge of the different forms of CHF, adequate diagnosis and optimization of patients before exposure to surgery and anesthesia is of paramount relevance for the perioperative period.

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KEY POINTS

- CHF contributes significantly to perioperative mortality.
- Given the ageing population, it can be expected that the incidence of patients with CHF will increase over time.
- Echocardiography and BNP are helpful in diagnostics and control of the therapy.
- In patients with newly diagnosed CHF, elective surgery should be postponed for 3 months

DEFINITION

Heart failure is a complex clinical syndrome caused by impaired ventricular performance. It is the final common pathway for a variety of cardiovascular disease processes. CHF can result from any structural or functional cardiac disorder that impairs the ability of the ventricle to fill or eject blood. Traditionally, CHF has been subdivided into diastolic heart failure (DHF) with unimpaired left ventricular ejection fraction (LVEF) [described as DHF or heart failure with preserved ejection fraction (HFpEF)] and systolic heart failure (SHF) with decreased LVEF [heart failure with reduced ejection fraction (HFrEF)]. In this review we will use the terms DHF and SHF. The prognosis of both types of CHF is disappointing; 25–50% of patients die within 5 years after the diagnosis [1▪▪,2▪].

Approximately 50% of patients suffer from SHF. In two recent reviews in this journal, the pathophysiological differences, diagnosis and therapy of DHF and SHF have been described in detail [3,4]. Briefly, risk factors for developing CHF are coronary artery disease, cardiac valve diseases, arterial hypertension, atrial fibrillation and idiopathic cardiomyopathies. Additional risk factors are the use of cardiotoxic medication, particularly cancer therapeutics, viral myocarditis and drug or alcohol abuse. Whereas coronary artery disease forms the major risk factor for developing CHF with reduced LVEF, arterial hypertension and atrial fibrillation are more often present in patients with DHF [4]. The latter population is more often women, older and obese. The perioperative 30-day mortality of symptomatic heart failure patients is approximately 9% whether the underlying cause is ischemic or nonischemic [2▪,5]. In contrast, perioperative 30-day mortality rate of patients with atrial fibrillation or isolated coronary artery disease is approximately 4.8 and 2.8% [2▪]. Interestingly, patients undergoing minor surgical procedures still exhibit a mortality rate of approximately 8% [2▪].

Table 1. NYHA classification of heart failure

NYHA class	Symptoms
I	Structural myocardial changes (e.g. left ventricular hypertrophy)
II	Small decrease in exercise tolerance
III	Significant decrease in exercise tolerance
IV	Symptoms of heart failure in rest or during small exercise

NYHA, New York Heart Association.

The clinical symptoms of heart failure are classified according to the New York Heart Association classification (Table 1).

PREOPERATIVE ASSESSMENT

The diagnosis of CHF is based on clinical symptoms, cardiac ultrasound and laboratory testing. Clinical symptoms of CHF are fatigue, dyspnea, orthopnea and reduced exercise tolerance often combined with signs of peripheral and/or lung edema [4–6]. In contrast to patients with coronary artery disease, CHF is often not adequately diagnosed and clinical signs should therefore be carefully evaluated [1▪▪,2▪,4,5,7–9,10▪]. Increased risk of death and/or major adverse cardiac events (MACEs) among patients undergoing noncardiac surgery has been demonstrated in patients with a history/signs of heart failure (relative risk 3.4) [6,11]. Other factors associated with preoperative MACE are a decreased LVEF with the highest risk group being those with an LVEF $< 30\%$ [6,11]. Preoperatively, most commonly measured laboratory tests are brain natriuretic peptide (BNP) or NT-pro-BNP and both are found to predict perioperative and in-hospital MACEs as well as short-term mortality [11]. These patients should be discussed together with surgeons, internists and cardiologists on a regular case conference to decide which patients may benefit from a preoperative optimization [1▪▪,5].

In the actual guidelines of the European Society of Cardiology (ESC) and the European Society of Anaesthesiology recommendations [1▪▪] have been published for the preoperative assessment and treatment of noncardiac surgical patients with CHF (Fig. 1). In this guideline there is a strong recommendation (Class 1, Level A) to adequately examine patients with suspected or already diagnosed CHF scheduled for noncardiac surgery using transthoracic echocardiography and to measure the actual BNP or NT-pro-BNP preoperatively [1▪▪,2▪,10▪].

Studies on the prognostic value of B-type natriuretic peptides were recently analysed [10▪].

Recommendations	Class[a]	Level[b]
It is recommended that patients with established or suspected heart failure, and who are scheduled for non-cardiac intermediate or high-risk surgery, undergo evaluation of lV function with transthoracic echocardiography and/or assessment of natriuretic peptides, unless they have recently been assessed for these.	I	A
It is recommended that patients with established heart failure, who are scheduled for intermediate or high-risk non-cardiac surgery, be therapoutically optimized as necessary, using beta-blockers, ACEIs or ARBs and mineralocorticoid antagonists and diuretics, according to ESC Guidelines for heart failure treatment.	I	A
In patients with newly diagnosed heart failure,it is recommended that intermediate-or high-risk surgery be defferred, preferably for at least 3 months after intiation of heart failure therapy, to allow time for therapy up-titration and possible improvement of LV function.	I	C
It is recommended that beta-blockade be continued in heart failure patients throughout the perioperative period, whereas ACEIs/ARBs may be omitted on the morning of surgery, taking into consideration the patient's blood pressure. If ACEIs/ARBs are given, it is important to carefully monitor the patient's haemodynamic status and give appropriate volume replacement when necessary.	I	C
Unless there is adequate time for dose-titration, intiation of high-dose beta-blockade before non-cardac surgery in patients with heart failure is not recommended.	III	B

FIGURE 1. Recommendations on heart failure. Adapted with permission from [1▪▪]. ACEI, angiotensin converting enzyme inhibitor; AREI, angiotensin receptor blocker; ESC, Europeon Society of Cardiology; LV, left venticular. [a]Class of recommendation, [b]Level of evidence.

Preoperative increased BNP/NT-pro-BNP predict death or nonfatal myocardial infarction (MI) with an odds ratio (OR) of 1.90, whereas postoperatively elevated BNP/NT-pro-BNP is strongly associated with an increased mortality or nonfatal MI (OR 3.70), emphasizing the relevance of both measurements. The prognostic value of B-type natriuretic peptides in patients undergoing noncardiac surgery is increased compared with the established Revised Cardiac Risk Index (Lee-Index, RCRI) [10▪]. Therefore, a pragmatic option seems to measure B-type natriuretic peptides preoperatively and in the first 3 days after surgery, which do have an increased risk according to the RCRI. If other patient populations, like those with diabetes, pre-existing renal failure or atrial fibrillation, experience benefit from widespread screening using B-type natriuretic peptides remains unknown and merits further investigation. A limitation of natriuretic peptides in preoperative risk assessment is the wide range of reported cutoffs. Additionally, the ability of natriuretic peptides to discriminate risk among CHF patients who may have chronically elevated levels has not yet been examined [11].

Therapeutic optimization using β-blockade, ACE/AT-1 inhibition and diuretics is strongly recommended (Class A) by the ESC guidelines. For patients newly diagnosed with CHF, it is recommended to postpone surgery for 3 months to allow adequate titration of medication for therapy, in particular if LVEF is already decreased [1▪▪]. However, this recommendation is only supported by Class C evidence, as not enough conclusive study data is available now. With respect to existing medication, there is a wide consensus that the standard CHF therapy should be continued throughout the whole perioperative period [1▪▪]. In the case of stable CHF, we generally recommend continuing baseline medication. In individual cases, the use of ACE/AT-1 inhibitors at the morning of surgery can be discontinued to avoid severe arterial hypotension after induction of anesthesia [1▪▪] (Fig. 2).

Decompensated or untreated heart failure is a major predictor of risk. In case of emergent surgery and evidence of preoperative acute heart failure and congestion the surgical procedure should be postponed whenever possible until cardiac recompensation and euvolemia are achieved. Patients with a diagnosis 4 weeks prior to surgery do have an increased risk compared with those with long-lasting CHF [2▪].

INTRAOPERATIVE MANAGEMENT

In patients with CHF, intraoperative systemic hemodynamics must be carefully monitored and adequately treated. There is no adequately powered study in which the course of patients with SHF vs. DHF is investigated in patients undergoing noncardiac surgery. van Diepen *et al.* [2▪] stratified a CHF patient population to nonischemic and ischemic heart failure patients, the latter more likely to suffer from SHF. In this study [2▪], the OR for nonischemic vs. ischemic heart failure was 1.47. However, the study was not designed to analyse

Recommendations on use ACEIs and ARBs

Recommendations	Class[a]	Level[b]
Continuation of ACEIs or ARBs, under close monitoring should be considered during non-cardiac surgery In stable patients with heart failure and LV systolic dysfunction.	IIa	C
Initiation of ACEIs or ARBs should be considered at least 1 week before surgery in cardiac-stable patients with heart failure and LV systolic dysfunction.	IIa	C
Transient discontinuation of ACEIs or ARBs before non-cardiac surgery in hypertensive patients should be considered.	IIa	C

FIGURE 2. Recommendations for the discontinuation of angiotensin converting enzyme inhibitors/blockers in patients undergoing noncardiac surgery. Adapted with permission from [1▪▪]. ACEI, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker; LV, left ventricular. [a]Class of recommendation, [b]Level of evidence.

the perioperative course of patients with SHF compared to DHF [6] and therefore the results should be analysed with caution [2▪].

Published data provide incomplete information about the effectiveness of invasive perioperative hemodynamic monitoring using pulmonary artery catheter (PAC) vs. standard surgical care in heart failure populations [5,11]. Recent studies found no evidence supporting routine use of the PAC [11].

Recently, Chiulli *et al.* [8] studied the association between medical comorbidities, the incidence of medical complications and failure to rescue in non-cardiac surgery. The authors observed a relation between pre-existing CHF and end-organ failure resulting in sepsis, respiratory failure and/or renal failure [8]. The results of this study are in line with the observation of Wakeam *et al.* [9] that patients with pre-existing comorbidities experience a significantly increased mortality if a clinical complication like pneumonia, wound and urinary infection, transfusion of blood and MI occurs. In particular patients with CHF based on coronary artery disease form a distinct risk group to develop such complications which may necessitate increased care level, organ replacement therapy and ultimately contribute to mortality [2▪,5].

Perioperative outcome and long-term mortality are strongly associated with LVEF. In a retrospective analysis of 174 patients undergoing intermediate to high-risk surgery, Healy *et al.* [6] observed a strong relation between a LVEF < 30% and perioperative events, deaths within 30 days, MI and exacerbation of heart failure. The long-term mortality was high, resulting in only 58% survival at 3 years. Patients with cancer were excluded from this analysis. Moreover, the majority of patients had vascular and orthopedic surgery. In addition to this small study [6], there is little knowledge on acute exacerbation of CHF in the perioperative period. Only the subpopulation of patients with myocardial ischemia and/or infarction is adequately studied [9]. As already mentioned, coronary artery disease contributes to a large proportion of patients ultimately developing CHF, however approximately 50% of CHF patients do not have significant coronary artery disease [2▪].

In summary, preoperative functional capacity together with cardiac diagnostic (transthoracic echocardiography) and serial measurements of BNP or NT-pro-BNP form the mainstay of preoperative assessment in this patient population [1▪▪]. As functional capacity is of outstanding importance in risk assessment, an approach to accurately measure metabolic equivalents is of value, as both patient self-reporting and subjective functional capacity estimation by physicians is prone for error in particular in the low range of metabolic equivalents [7,11,12,13▪,14]. It seems if the combination of objective measures of functional capacity combined with echocardiography and serial measurements of BNPs are the most appropriate methods for adequate risk assessment. The effects of optimization are not studied yet; from a pathophysiological point of view it seems logical that adequate medical therapy can reduce perioperative morbidity and mortality. A BNP-orientated treatment approach has not been tested in the perioperative setting.

PERIOPERATIVE MANAGEMENT OF PATIENTS WITH CHRONIC HEART FAILURE

To date, there is no consensus on the use of a certain anesthetic technique for patients with CHF. Therefore, the use of individual anesthetic drugs are commonly based on expert opinion and pathophysiological considerations. In particular, the perioperative role of DHF is poorly understood. It can be expected that a relevant amount of patients with DHF already have pulmonary hypertension and concomitant right ventricular dysfunction. As already mentioned, the risk of acute decompensation of pre-existing CHF is not necessarily related to the degree of the surgical trauma [2▪,5].

The clinical signs of CHF cannot be easily monitored in patients during anesthesia, therefore the use of adequate monitoring represents a cornerstone

in the intraoperative and postoperative detection of exacerbation of CHF. Therefore, widespread use of invasive blood pressure monitoring, also in patients undergoing minor procedures, is commonly accepted. The role of filling pressure monitoring (central venous pressure and pulmonary artery pressure) is a matter of continuous discussion. To date, there are no studies available which demonstrate an outcome benefit of invasive filling pressure monitoring. One potential exception is the patient with severe pulmonary hypertension and at risk for acute exacerbation of right ventricular dysfunction [5].

The gold standard is intraoperative and postoperative monitoring of ventricular morphology and function by echocardiography [15]. In most centres, patients at risk for acute exacerbation of CHF will be monitored either by transesophageal echocardiography (TEE) or transthoracic echocardiography. In particular, in patients with a relevant risk of volume shifting (blood loss) and/or rapid changes of systemic vascular resistance, the use of TEE is strongly recommended, however, adequately powered randomized controlled trials which support this hypothesis are not available [5].

Monitoring of cardiac output (*CO*) and stroke volume index in patients at risk are also strongly recommended. However, when comparing different measuring techniques, we recently observed a clinically relevant and unacceptable bias of uncalibrated *CO* devices in high risk patients with decreased left ventricular function [16]. Therefore, we conclude that the use of techniques which allow frequent re-calibration using intermittent thermodilution *CO* are strongly recommended, as the noncalibrated approach can be misleading [16].

Volume management using dynamic preload indicators like pulse pressure ventilation (PPV) and stroke volume variation (SVV) are often recommended and indeed these parameters showed superior results when compared with classical preload indicators like CVP or PCWP. However, in a small scale clinical study, Montenij *et al.* [17] showed that these parameters failed to accurately discriminate between volume responders and nonresponders in a group of patients with decreased LVEF undergoing cardiac surgery. It can be expected, that in patients with small changes in *CO* after volume loading because of decreased cardiac function, SVV and PPV does not respond appropriately and should be used with caution and ideally in combination with other techniques like echocardiography. We aim to monitor these patients using transthoracic echocardiography throughout the perioperative process including the postanesthesia care unit and the early postoperative days.

CONSEQUENCES OF ANESTHESIA ON SYSTEMIC HEMODYNAMICS IN PATIENTS WITH CHRONIC HEART FAILURE

Induction of general anesthesia leads to vasodilation, loss of sympathetic tone and a shift of volume from the intrathoracic to the extrathoracic compartment. Moreover, mechanical ventilation influences the normal heart–lung interaction. Taken together, blood pressure is often decreased after induction and during maintenance of anesthesia. When comparing induction agents, propofol will have the most pronounced effects on systemic vascular resistance. Recent studies have demonstrated that *CO* is not really different when comparing etomidate, propofol or midazolam as induction agent [5]. However, the reduction in arterial pressure may lead to reduced end-organ perfusion resulting in organ failure which significantly contributes to morbidity and mortality in patients with CHF [2▪].

Historically, synthetic β-mimetics like dobutamine and dopexamine were used to reach adequate *CO* levels in patients with CHF. The recent guidelines of the American Heart Association and the ESC still include the use of short term continuous intravenous inotropic support (Level IIb, Level IIa recommendation). However, there is a growing body of evidence demonstrating that the use of β-mimetics and also of PDE-III inhibitors like milrinone or enoximone are associated with worse long-term outcome in patients with low *CO* states [18▪,19,20▪,21]. Recently, Nielsen and Algotsson [19] published an updated overview on the dilemmas associated with the use of inotropes in patients with CHF in this journal suggesting that the use of inotropes should be limited to patients with organ dysfunction. However, outcome data are mainly available for the subgroup of patients undergoing cardiac surgery or during hospitalization for heart failure and not for patients undergoing noncardiac surgery [20▪,21]. When summarizing the available evidence, it seems that inotropes may be used only in a situation of heart failure combined with signs of end-organ hypoperfusion [19]. Some studies and expert opinion suggest that levosimendan may be superior to classic inotropes in this situation [20▪]. Mechanical short-term support may be a useful alternative, however, the use of mechanical assist systems is not well investigated and data in patients undergoing noncardiac surgery are scarce and only available as case reports demonstrating the potential benefit in an individual patient. These results cannot be easily extrapolated to the general population. Moreover, the widespread use of the different mechanical circulatory assist systems will

have significant economical and logistical impact for healthcare.

CONCLUSION

Patients with CHF form a distinct risk population, which is associated with increased risk in the perioperative period. Today, there is increasing knowledge that careful evaluation and optimal medical treatment are prerequisites for adequate treatment. Preoperatively, assessment of cardiac function via cardiac echocardiography and measurement of brain natriuretic proteins are paramount. Elective surgery should be postponed if adequate medical treatment has not been established.

Despite this, perioperative mortality is high and particularly patients with low ejection fractions (LVEF $< 30\%$) need careful monitoring throughout their hospital stay. The measurement of BNP/NT-pro-BNP is also useful for additional risk assessment in the postoperative period. In case of decreased *CO* and associated end-organ failure, the use of levosimendan seems to be superior to other positive inotropic drugs.

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Conflicts of interest

W.F.B. is a member of the advisory board of Medtronic/Covidien, Ventinova B.V. and has received honoraria from AbbVie. V.S.-F. reports no conflicts of interest.

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