Anesthesia for non-cardiac surgery in patients with heart failure

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INTRODUCTION

Complications during and after non-cardiac surgery are a continuous concern for medical societies, as it was shown in the latest multi-center study with this topic that mortality after surgery in Europe is much bigger than expected and previously estimated - 4%.[1]

It is also estimated that 42% of the complications and deaths associated with non-cardiac surgery are due to cardiac complications.[2] Given the fact that there are approximately 19 million major procedures being performed in Europe each year[3], it can be assumed that 319000 deaths are caused by perioperative cardiac complications in Europe yearly.

Taking also into account the continuing ageing of the population, it becomes obvious that emphasis has to be put on preventing cardiac complications in non-cardiac surgery patients, by establishing an optimal and homogenous practice in anesthetic perioperative management of such cases.

DEFINITION OF HEART FAILURE

Heart failure (HF) represents a significant and growing health care burden. HF can be defined as an abnormality of cardiac structure or function leading to failure of the heart to deliver oxygen at a rate commensurate with the requirements of the metabolising tissues, despite normal filling pressures (or only at the expense of increased filling pressures).[4] Clinically, HF is defined as a syndrome in which patients have typical symptoms (e.g. breathlessness, ankle swelling, and fatigue) and signs (e.g. elevated jugular venous pressure, pulmonary crackles, and displaced apex beat) resulting from an abnormality of cardiac structure or function. The diagnosis of HF can be difficult as many of the symptoms of HF are not specific and, therefore, of limited diagnostic value. Many of the signs of HF result from sodium and water retention and resolve quickly with diuretic therapy, i.e. may be absent in patients receiving such treatment.

Identification of the underlying cardiac problem is crucial for the diagnosis and treatment of HF. The most frequent cause of HF is myocardial disease which impairs systolic ventricular function. However, one or more abnormalities of ventricular diastolic function or of the valves, pericardium, endocardium, heart rhythm, and conduction can also cause HF.[4]

HF can be systolic or diastolic, left-sided, right-sided or biventricular, acute or chronic, with high cardiac output or with low cardiac output, with preserved or reduced ejection fraction.

Chronic heart failure (CHF) is a disease that causes significant mortality and morbidity world-wide, with a prevalence that rises with age, ranging from 1-2% in the general population to >10% in persons older than 70 years.[5] It has a known impact on postoperative prognosis in non-cardiac surgery, and it is associated with higher mortality, but not with myocardial infarction.[6] A factor that worsens prognosis is reduced LVEF (<35%).[4] As for heart failure with preserved ejection fraction (HF-PEF), the prognostic impact on perioperative mortality is uncertain. Some studies found no difference in cardiac events between HF-PEF and heart failure with reduced ejection fraction (HF-REF) in patients undergoing non-cardiac surgery, while others find that only patients with severely depressed LVEF (<30%) have increased perioperative event rates, compared with other groups of HF patients.[7] Since no clear quality data is available, patients with HF-PEF and HF-REF should be managed perioperatively in a similar fashion.

Acute heart failure (AHF) is defined as a gradual or rapid change in heart failure (HF) signs and symptoms, resulting in the need for urgent therapy.[8] AHF is complex and encompasses multiple diagnoses and etiologies: coronary artery disease (CAD), hypertension, valvular heart

disease, and/or atrial fibrillation, as well as noncardiac conditions such as renal dysfunction, diabetes, anemia, and medications.

A nearly universal finding in AHF is pulmonary and systemic congestion due to elevated ventricular filling pressures with or without a decrease in cardiac output. The majority of AHF patients have worsening CHF.[8]

PREOPERATIVE EVALUATION

The new 2014 Joint Task Force European Society of Cardiology (ESC)/ European Society of Anesthesiology (ESA) guidelines on perioperative assessment and management of cardiac risk in non-cardiac surgery[7] has upgraded previous recommendations regarding preoperative evaluation of patients scheduled for non-urgent non-cardiac interventions.

It was previously widely accepted that the Lee index, or "revised cardiac risk" index is the gold standard for predicting cardiac complications after non-cardiac surgery.[9] The Lee index was designed to predict post-operative cardiac events, defined as myocardial infarction, pulmonary oedema, ventricular fibrillation or cardiac arrest, and complete heart block. The score is comprised of six independent factors, which all add 1 point to the risk index: type of surgery, history of ischaemic heart disease (IHD), history of HF, history of cerebrovascular disease, preoperative treatment with insulin, and preoperative creatinine > 2 mg/dl. The incidence of cardiac events is predicted to be 0.4%, 0.9%, 7%, and 11% for patients with an index of 0, 1, 2, and 3 or more points, respectively.[10] While still accepting its value as a good discriminator between patients with low vs. high risk for cardiac events after mixed non-cardiac surgery, it seems that it is not as viable as a predictor of death or cardiac events in vascular non-cardiac surgery.[11]

Therefore the need for a new predictive model has risen, and it has been met with the validation of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) MICA model, which was validated on a dataset containing more than 200000 patients.[12] Five independent predictors of perioperative myocardial infarction/ cardiac arrest were identified: type of surgery, functional status, elevated creatinine (>1.5 mg/dl), American Society of Anesthesiologists (ASA) class, and age.[7] This model is presented not as a scoring system, but as an interactive risk calculator (http://www.surgicalrisk-calculator.com/miorcardiacarrest). The model is a better choice for its designed endpoints, but it becomes obvious that some cardiac events are not included in the NSQIP predictor, for which the revised cardiac risk index remains the solid choice.

The clinician should, in fact, use these models in his decision-making algorithm as complementary, but, most importantly, they should be viewed as a tool, among others, to plan a non-cardiac surgical intervention.

Another important factor in the preoperative evaluation of the risk is the operation itself. Depending on the type of surgery to be performed, the risk for cardiac events (cardiac death and myocardial infarction) is divided into three categories: low (<1%), intermediate (1-5%), and high (>5%)[9] (see table 1).

The need for preoperative cardiac evaluation also depends on the urgency of surgery. Emergency surgical procedures (such as ruptured abdominal aortic aneurysms or major trauma) results or indications are not influenced by cardiac assessment, but perioperative management of such cases is crucial in these cases. Cardiac evaluation in urgent but non-emergency interventions will not influence the decision to perform the intervention, but can contribute to reducing periprocedural cardiac risk.[7]

Table 1. Estimating surgical risk for cardiac events (after ref 7, 9, modified)

Low risk < 1%	Intermediate risk 1-5 %	High risk > 5%
Breast surgery	Abdominal surgery (splenectomy, hiatal hernia repair, cholecystecomy)	Aortic and major vascular surgery
Dental surgery	Carotid surgery	Perypheral vascular surgery
Thyroid surgery	Peripheral arterial angioplasty	Duodeno-pancreatic surgery, perforated bowel repair
Eye surgery	Endovascular aneurism repair	Liver resection
Minor gynaecologic surgery	Head and neck surgery	Adrenal resection
Minor orthopedic surgery	Major neurosurgery/ orthopedic surgery	Total cystectomy
Reconstructive surgery	Non-major intrathoracic	Pneumonectomy
Minor urological surgery	Major urological/ renal transplant	Pulmonary/ liver transplant

Another important preoperative prognostic factor is the patient's functional capacity, which is measured in metabolic equivalents (METs). Measuring it is not usually necessary, as it can be approximated based on daily activities. One MET is equal to the basal metabolic rate (see table 2). The capacity to climb two flights of stairs or run a short distance (>4 METs) indicates a good functional capacity, which, by itself, offers a good postoperative prognosis, regardless of additional risk factors and even in the presence or stable IHD.[7,13]

Aside from risk stratification and functional capacity evaluation, cardiac assessment includes measuring biomarkers, performing noninvasive and invasive test of cardiac status.

Table 2. Estimated energy requirements for daily activities (MET = metabolic equivalent) (after ref. 7, 9)

1 MET ↓	Can you take care of yourself?	**4 METs** ↓	Climb two flights of stairs or walk up a hill?
	...eat, dress, or use the toilet?		Run on short distances?
	...walk indoors around the house?		Do heavy work around the house?
4 METs	...walk 100 m on level ground at 3-5 km/h?	**> 10 METs**	Participate in sports like swimming, tennis, football, skiing?

Pre- and post-operative measurement of cardiac troponins T and I (cTnT and cTnI) can be taken into consideration, as small increases in the perioperative period can translate into worsened cardiac prognosis and outcome.[14] Plasma B-type natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP) are important prognostic indicators in non-surgical settings, and they have been found to have prognostic value for long-term mortality also in major non-cardiac surgery, but universal pre-operative sampling is not justified. Conversely, it can be

considered in high risk patients (METs ≤4 or revised cardiac risk index >1 for vascular surgery and >2 for non-vascular surgery).[7,15,16]

Noninvasive preoperative testing aims for obtaining information on three markers of perioperative cardiac risk: left ventricle (LV) dysfunction, myocardial ischaemia and valvular anatomical anomalies. Heart function can be assessed at rest with various imagistic tools: radionuclide ventriculography, single photon emission computed tomography (SPECT), echocardiography, magnetic resonance imaging (MRI).[7] The most readily available in clinical practice is rest echocardiography, which is not routinely recommended for preoperative evaluation of ventricular function, but may be useful in patients with high surgical risk (IIb/C).[7] Perioperative major cardiac events occur more often in patients with preoperative LV systolic dysfunction, moderate-to-severe mitral regurgitation and aortic stenosis.[17]

Preoperative IHD is commonly evaluated with the 12-lead ECG, which offers important prognostic information,[18] but may be normal even in patients with ongoing myocardial ischaemia. It is, therefore, useful that in patients at risk for IHD additional test be performed, such as exercise ECG, or, in patients with limited exercise capacity, stress ECG or stress echocardiography, both of which have a high negative predictive value, but a low positive predictive value (25-45% positive predictive value for dobutamine stress echocardiography).[19]

In recent guidelines, pre-operative ECG is recommended for patients with risk factors (according to the pre-operative risk scores) if they must undergo intermediate-risk or high-risk surgery (I/C); it may be considered (IIb/C) for patients with risk factors and low-risk surgery or for patients with no risk factors but who are older than 65 years and must undergo intermediate-risk surgery.[7]

Guideline recommendations are that imaging stress testing should be performed in patients with poor functional capacity who are to undergo high risk surgery (I C recommendation) and should not be performed before low-risk surgery (III C recommendation).[7]

Coronary angiography is an invasive diagnostic procedure that is seldom used for assessing preoperative risk. Indications are similar to non-surgical patients and include acute coronary syndromes (ACS) - acute ST- segment elevation myocardial infarction (STEMI), non-STEMI or unstable angina.[20-22] Preoperative treatment of myocardial ischaemia is recommended whenever non-cardiac surgery can be delayed, but in stable patients, preoperative revascularization does not improve cardiac prognosis.[7,20]

Risk reduction strategies

In patients with newly discovered HF, if possible, non-cardiac surgery should be postponed so it can be performed under optimal medical therapy, in a stable patient.[7] Pharmacological reduction of perioperative cardiac risk in non-cardiac surgery is based mainly on the concept that surgical stress can trigger ischaemia by increasing myocardial oxygen demand or/and reducing myocardial oxygen supply.

The rationale for using *beta-blockers* perioperatively is that they decrease myocardial oxygen consumption by reducing heart rate, and they improve myocardial perfusion by a longer diastolic filling, additional protective factors being redistributing coronary flow and stabilizing plaques.[23] Clinical translation of these theoretical effects is somewhat controversial, after the concerns that have been raised over studies performed in the DECREASE family.[24]

The ideal in beta-blocker therapy is that treatment be initiated 30 days (or at least one week) prior to surgery in patients with clinical risk factors undergoing high risk surgery. Atenolol or bisprolol(beta-1 selective drugs) should be used with therapeutic targets: a heart rate of 60-70 bpm and a systolic blood pressure >100 mmHg.[25,26] Doses should slowly be up-titrated and high doses should be avoided, particularly before surgery.[7] In patients without clinical risk factors, perioperative beta-blockade does not decrease risk for cardiac complications and might expose patients to increased risk in mortality.[27] Nonetheless, in patients with ongoing beta-blocker therapy, treatment withdrawal is associated with increased mortality.[28] Therefore, beta-blockers should not be withdrawn in patients receiving this medication (see table 3), especially for IHD

or arrhythmias (I B recommendation).[7] The optimal duration of therapy is not well defined, but it is encouraged for several months postoperatively, especially in patients with positive preoperative stress tests.[9]

Contraindications to using beta-blockers are asthma, severe conduction disorders, symptomatic bradycardia and symptomatic hypotension.[29]

Table 3. Recommendations for perioperative use of beta-blockers (from ref. 7)

- Perioperative continuation of beta-blockers is recommended in patients currently receiving this medication (I B)
- Pre-operative initiation of beta-blockers may be considered in patients scheduled for high-risk surgery or who have ≥2 clinical risk factors or ASA status ≥3 (IIb B)
- Pre-operative initiation of beta-blockers may be considered in patients who have known IHD or myocardial ischaemia (IIb B)
- When oral beta-blockade is initiated in patients who undergo non-cardiac surgery, the use of atenolol or bisprolol as a first choice may be considered (IIb B)
- Initiation of peri-operative high-dose beta-blockers without titration is not recommended (III B)
- Pre-operative initiation of beta-blockers is not recommended in patients scheduled for low-risk surgery (III B)

Statins. 3-Hydroxy-3-methylglutaryl coenzyme A reductase inhibitors (statins) are prescribed in patients with IHD, but also in patients with non-coronary atherosclerosis, for secondary prevention. They induce plaque stabilization, which can prevent myocardial infarction in the perioperative period.[7] Guidelines recommend continuation of statins perioperatively in patients already on this treatment (I C), but also preoperative initiation of therapy in patients undergoing vascular surgery, ideally at least two weeks before surgery.[7] As for the concern that statins can induce myopathy and rhabdomyolysis, the risk is exacerbated by various factors perioperatively. That is why early introduction is advised, so potential side-effects can be better detected and addressed.[30]

Nitroglycerine is known for its anti-ischemic effects, but no effect to lower cardiac events has been proven; moreover, haemodynamic risks can be enhanced, as it can produce decreased preload, hypotension and tachycardia.[7]

Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) are proven to preserve organ function, irrespective of their antihypertensive effects. However, in high risk patients undergoing major vascular surgery, ACEIs do not decrease cardiac complications.[31] Guideline recommendations are that ACEIs/ ARBs be continued during non-cardiac surgery in stable patients with heart failure and LV systolic dysfunction (IIa C); initiation of such therapy should be considered at least one week prior to surgery in such patients (IIa C); transient discontinuation of therapy should be considered in patients treated for hypertension (IIa C).[7]

Heart rate-reducing *calcium-channel blockers* (verapamil and diltiazem) are used in patients who do not tolerate beta-blockers and can reduce the incidence of myocardial ischaemia and supraventricular tachycardia (SVT).[32] This class of drugs should be continued perioperatively, both in patients who do not tolerate beta-blockers, but also in patients with vasospastic angina.[7]

Diuretics are frequently used as treatment of heart failure or arterial hypertension. Generally, antihypertensive drugs should be continued to the day of the surgery and resumed as soon as possible, either intravenously, if needed, or orally. In heart failure patients, diuretic administration might be needed to maintain euvolemia, but care should be given to possible side effects-electrolyte disturbances, mainly hypokalemia and hypomagnesaemia, which are to be treated promptly, in order to minimize the risk of ventricular fibrillation or cardiac arrest.[7,9]

Surgery and coagulation-altering

Aspirin (ASA) is a widely used antithrombotic agent, and its cessation perioperatively is somewhat controversial. Firsly, it has been shown that aspirin treatment raises bleeding risk perioperatively by up to 50%.[33] On the other hand, due to the results of the POISE-2 trial, which concluded that in non-cardiac surgery, aspirin does not reduce the 30-day risk of myocardial infarction, while augmenting the risk of bleeding,[34] some support aspirin being discontinued if the bleeding risks outweigh the potential benefits. However, the POISE-2 trial excluded patients undergoing carotid surgery, with less than six weeks after placement of a bare metal coronary stent (BMS), or less than one year after placement of a drug-eluting coronary stent (DES). The 2013 ESA Guidelines on management of severe perioperative bleeding recommend that aspirin be continued perioperatively in most surgical settings (1 C), with the exception of neurosurgery, where it suggests a thorough analysis of risk-benefit ratio.[35]

Dual anti-platelet therapy (DAPT) is most often used in patients with coronary stents, whether BMS or DES. Due to high risk for stent thrombosis, it is recommended to postpone elective surgery for a minimum of 4 weeks and ideally 3 months in BMS, and up to 12 months in DES and after percutaneous coronary interventions (PCI) for ACS. In an urgent setting, current guidelines, both ESC and ESA[35,37] recommend withdrawal of clopidogrel and ticagrelor 5 days before surgery and prasugrel 7 days, with aspirin treatment continued, unless there is a high risk of thrombosis (1 C), when DAPT should be continued perioperatively.

Anticoagulant therapy is linked with higher risk for bleeding during non-cardiac surgery.[7] Nonetheless, in selected patients the risks are greater than the benefits of anticoagulation.

Vitamin K antagonists (VKA) are commonly used to treat patients with need for anticoagulation, but risks of thrombosis are not similar in all categories of patients. In patients at low risk for thrombosis (patients with CHADS2 score $\leq$2 and atrial fibrillation [AF], patients treated for a non-recurrent venous thromboembolism [VTE]) VKA antagonists should be stopped 5 days prior to surgery, with no brigding needed; safe surgery can be performed with an INR <1.5.[35]

High risk patients pose a different challenge, as they often need permanent anticoagulation. Such patients are those with AF and CHADS2 >2, patients with a mechanical prosthetic heart valve or patients with recurrent VTE treated for <3 months.[3,35] These patients need bridging therapy, which can be done with unfractioned heparin (UFH) or low-molecular weight heparin (LMWH).[38] In patients with a high thromboembolic risk, therapeutic doses of LMWH are given subcutaneously, twice-daily, on a weight adjusted regimen.[39] Recommendations are that bridging therapy should be handled as follows: day 5- last VKA dose, day 4- no heparin, days 3 and 2- therapeutic subcutaneous LMWH twice daily, day 1- hospitalization and INR measuring, day 0- surgery (1C).[35] In patients treated with VKA and emergency non-cardiac surgery, treatment options are prothrombin complex concentrate (PCC) or fresh-frozen-plasma (FFP).[7,35]

Novel oral anticoagulants (NOACs) - dabigatran (a direct thrombin inhibitor), rivaroxaban, apixaban or edoxaban (factor Xa inhibitors), due to their short biological half-lives do not impose a bridging strategy before surgery.[7] However, in patients with high risk for thromboembolic disease bridging should be done on a similar protocol to that described for VKAs, except for dabigatran usage in patiens with a creatinine clearance <50 ml/min, where therapy should be stopped 5 days prior to surgery, with no bridging.[35] Currently, there are no specific antidotes for NOACs, but PCC seems to help to some degree in factor Xa inhibitors reversal, and haemodialysis is an effective method of eliminating dabigatran from circulation.[7]

Revascularisation

Indications for pre-operative coronary angiography and revascularization in patients with known or suspected IHD are similar to those in the non-surgical setting, and there is no indication for routinely searching for silent ischaemia before non-cardiac surgery.[7,40]

The indications for revascularisation in patients with stable coronary artery disease are persistence of symptoms despite medical treatment and/or improvement of prognosis.[20, 40] All patients considered for revascularization should receive optimal medical therapy and non-cardiac

surgery should be postponed for several months up to a year.[7,40] The type of revascularization, PCI vs. coronary artery bypass grafting (CABG), depends on the extend of CAD and technical difficulties of performing each procedure and the decision should be taken in a multidisciplinary team.[40]

In patients with NSTE-ACS in the setting of non-cardiac surgery, if non-cardiac surgery can be postponed, patients should be referred to a cardiologist and treated according to NSTE-ACS guidelines (I A). If there is a life-threatening condition requiring non-cardiac surgery and NSTE-ACS revascularization, an expert team should discuss the priority of surgery, case by case (IIa C). In patients who have had non-cardiac surgery and have suffered an NSTE-ACS aggressive medical treatment and revascularization are recommended following surgery (I B).[7,22,40]

In patients that have suffered previous revascularization by CABG and are stable, perioperative risk of a cardiac complication is lower in the event of non-cardiac surgery.[41] Therefore, asymptomatic patients may undergo surgery without preoperative stress testing. In the case of revascularization by PCI, it is recommended to postpone surgery until 12 months after DES implantation and 4-12 weeks after BMS.[7]

Valvular heart disease (VHD)

Patients with VHD are at increased risk of complications during non-cardiac surgery. The risk is higher for patients with severe aortic stenosis, severe symptomatic mitral stenosis or with pulmonary artery pressure >50 mmHg, primary severe aortic and mitral regurgitation.[7]

In symptomatic patients, severe aortic stenosis should be addressed prior to elective non-cardiac surgery either by open-heart surgery, or by balloon aortic valvuloplasty or TAVI (transcatheter aortic valve implantation), in patients not suitable for surgery due to high risks.[7,38]

In patients with severe mitral stenosis, with pulmonary artery pressure (PAP) <50 mmHg, there is no need for preoperative correction of the VHD, but care must be taken to avoid tachycardia or fluid overload, as there is a risk of pulmonary oedema. In patients with symptoms or PAP >50 mmHg, ther might be benefit in percutaneous mitral commissurotomy, particularly prior to high risk non-cardiac surgery.[7,38]

In emergency settings, non-cardiac surgery should be performed in patients with VHD, even severe, albeit with advanced intraoperative hemodynamic monitoring.[9]

Algorithm for evaluating and management of cardiac patients

The 2014 ESC/ESA Guidelines on non-cardiac surgery offers a 7 step algorithm that can be summarized:[7]

1. In **urgent surgery** there is no time for cardiac testing or specific treatment. The cardiologist should provide recommendations for managing perioperative risk, monitoring cardiac events and continuation of chronic cardiovascular therapy.
2. In the case of **unstable cardiac conditions** (unstable angina, AHF, arrhythmias, symptomatic VHD, recent MI), treatment options should be discussed by a multidisciplinary team, involving all perioperative care physicians.
3. The **risk of the surgical procedure** should be estimated (see table 1); if the risk is low, surgery should be done as planned, taking into consideration patient risk factors and starting therapy according to cardiologist's recommendation;
4. If the risk is moderate to high, **functional capacity assessment** should be performed**,** based on which further decisions are to be made; if it is >4 MET, the overall prognosis is good, and procedures should be continued;
5. If the functional capacity is ≤4 MET, and intermediate-risk surgery is planned, a **non-invasive stress-**testing is indicated**.**
6. If high risk surgery is planned, the **revised cardiac risk** index is helpful; if the Lee index is ≤2, in addition to the above, rest echocardiography and biomarkers should be considered.

7. If the Lee index is >2, a **non-invasive testing** should be done; interpretation should be done in a multidisciplinary team and preoperative invasive interventions should be undergone if necessary, as described hereinabove.

ANAESTHESIA

Although the role of the anaesthesiologist in the development of postoperative cardiac complications cannot be denied, so far there is no strong evidence leading to preferring one anaesthetic agent over another in non-cardiac surgery. Most anaesthetic techniques reduce sympathetic tone and produce vasodilation, leading to hypotension.[42] Therefore, the anaesthesiologist must be vigilent for maintaining end-organ perfusion pressure throughout the procedure. In the past it was considered that anaesthetic agents do not influence outcomes, but recent data, especially from cardiac surgery suggests that volatile techniques using sevoflurane have a better outcome.[43] Administering quality anaesthesia is not only choosing an anaesthetic agent, but also preoperative evaluation and optimisation, adequate monitoring, smart volemic and transfusion strategies and postoperative analgesia.[9]

The main perioperative objective in cardiac patients is to prevent myocardial ischemia by optimizing oxygen delivery and oxygen consumption, and treating accordingly if such an imbalance should occur. This is much more important than the type of anaesthesia or the anaesthetic agent choice. For example, tachycardia is deleterious both by increasing the myocardial oxygen demand and by lowering oxygen transport and thus heart rate should be maintained within 20% limits of normal values. Similarly, it has been shown that decreases by >20% in mean arterial pressure or mean arterial pressure (MAP) values <60 mmHg for durations of >30 minutes pose a greater risk for postoperative complications that include myocardial infarction, stroke and death.[44,45]

Therefore, avoidance of arterial hypotension (a process more complex than mere correction of arterial pressure values through infusion of vasoconstrictors) has been recently recommended (IIb/B).[7] Avoidance covers different approaches from anticipation/ diagnosis/correction of hypovolaemia to diagnosis and correction of anaesthetic drug overdose (detected most easily through cortical electroencephalography (EEG) or EEG-based depth of anaesthesia monitors).[7]From the recent literature, it is impossible to assert that correction of intra-operative arterial hypotension through the use of different vasconstrictors will affect the direction of the relationship between intra-operative arterial hypotension and post-operative outcome. However, diagnosis/correction of anaesthetic drug overdose is part of the process of 'avoidance' of intra-operative arterial hypotension.

The benefits of neuraxial anaesthetic techniques (spinal or epidural) are also debatable, as it can also induce sympathetic blockade.[42] A recent systematic review showed that compared with general anaesthesia, neuraxial anaesthesia may reduce the 0-to-30-day mortality for patients undergoing a surgery with an intermediate-to-high cardiac risk.[46] Neuraxial anaesthesia alone (but not when associated with general anaesthesia) can therefore be considered as the anaesthetic technique of choice following careful assessment of the risk/benefit ratio for each patient. [7] Similarly, neuraxial analgesia is also associated with better post-operative outcome and should therefore be considered as the technique of first choice (following careful assessment of individual risk/benefit profile). [7] Care should be given to frequent association in cardiac patients of drugs that impede coagulation; complications can be tragic, so risk-benefit ratio should be calculated.[47]

Perioperative monitoring includes, routinely, continuous ECG monitoring for all patients (I C)[7], but ischaemic episodes are not always detected. Normally, 2-lead monitoring is employed, and for a long time leads II and V5 have been the standard of care for detecting intra and postoperative ischaemia.[48] It seems that the best sensitivity (greater than 95%) is given by using leads II, V4 and V5 simultaneously.

Intraoperative transoesophageal echocardiography (TOE) is rarely used, as it is not routinely indicated for perioperative monitoring in non-cardiac surgery.[7] TOE is recommended if acute

and severe haemodynamic instability or life-threatening abnormalities develop perioperatively. Its use is indicated in patients with newly discovered wall-motion abnormalities, severe valvular lesions and it can guide volemic management in critical patients with dereased LV function.[7]

Monitoring patients by pulmonary artery catheters (PACs) is associated with a series of complications that can outweigh its benefits.[49] An elevated pulmonary capillary wedge pressure (PCWP) can indicate myocardial ischaemia and a wide *v* wave can indicate mitral regurgitation secondary to a papillary muscle dysfunction induced by ischaemia. Although widely used in the 1980s, monitoring PCWP has not been found to change outcomes and interest for it has decreased.[50]

Goal-directed therapy aims to optimise cardiovascular function by following flow variables, such as pulse-pressure variation, stroke volume variation, fluid responsiveness, in order to establish a normal delivery of oxygen to tissues. This strategy can be used intraoperatively in high risk surgery/patients, but its use is most prominent in the postoperative setting.[51] It also has the advantage of being less invasive than a PAC, by using transpulmonary thermodilution measurements or transoesophageal Doppler. Based on several meta-analyses, recent guidelines recommend that patients with high cardiac and surgical risk should be considered for goal-directed therapy (IIa/B). [7]

Anaesthesia in patients with heart failure

In preparing for surgery, preoperative transthoracic echocardiography (TTE) is paramount in patients with known or suspected HF. It can give information regarding LFEF, LV and atrial volumes, heart valve function and diastolic function, and inferior vena cava diameter for assessing volume status, all of which are of use in approaching such a patient successfully. Routine pre-operative TTE should be performed in high-risk cardiac patients.[7]

Natriuretic peptides dosing in known or suspected patients with HF is of significance also, as their levels correlate well with perioperative morbidity and mortality (I A).[7] ACEIs can be transiently discontinued in patients susceptible to hypotension, but all HF medicine should be reinstituted as soon as clinical conditions allow postoperatively (I C).[7] Diuretics are useful for patients with signs of congestion and digitalis can be added to patients remaining symptomatic despite on maximal treatment, especially in those with AF.[52] Vasodilators, inotropes and inodilators are indicated in advanced stages of CHF or in patients with AHF (see below). Current ESC guidelines on heart failure recommend that patients with CHF use optimal doses of ACEIs/ARBs, beta-blockers and aldosterone antagonists as primary strategies in patients with HF-REF, in order to reduce morbidity and mortality (evidence-based heart failure medicine) (I A).[7] All patients with HF who are scheduled for non-cardiac surgery are to be treated optimally according to these guidelines. HF-REF patients with LVEF <35% and left bundle branch block with QRS >120 ms should be evaluated for resynchronization therapy or implantable defibrillator placing.[4,7]

The principles of anesthetic management in patients with HF are synthesized in table 4. Specific considerations concerning patients with hypertrophic cardiomyopathy (HCM) and pulmonary heart disease (PHD) are shown in table 5.

Intraoperative use of inotropes is justifiable only in patients with low cardiac output. Perioperative circulatory assist device use is advised only in experienced centres.

In patients with newly diagnosed severe systolic HF, it is recommended that medical therapy be optimal before attempting non-urgent non-cardiac surgery, and the proposed time interval for achieving that status is three months, during which LV function and remodeling can improve.[53] Rapid preoperative initiation of high doses of beta-blockers or ACEIs, without careful titration is not recommended, as it can increase the risk for intraoperative hemodynamic instability and hypontension.[7]

Table 4. Principles of anesthetic management in patients with HF (modified from ref.52)

Preoperative	Continuing preoperative HF medication (except for aldosterone antagonists) ECG Recent echocardiography Diagnosing and correcting electrolyte dysturbances Premedication for reducing anxiety Disabling ICD and availability of external defibrillator
Intraoperative	Any type of general anesthesia No formal contraindication for neuraxial anesthesia Avoid sudden afterload drop and tachycardia Invasive arterial pressure monitoring Blood gas and acid-base status monitoring Right heart catheterization in selected cases TTE monitoring when available Volemic monitoring Avoid hypothermia Aggressive treatment of malignant arrhythmias
Postoperative	ICU monitoring Keep intraoperative monitoring tools until stable Extubate when hemodynamically stable Aggressive pain therapy

Table 5. Considerations concerning patients with hypertophic cardiomyiopathy (HCM) and pulmonary heart disease (PHD) (modified from ref.52)

Patients with HCM	**Patients with PHD**
Aggressive correction of hypovloemia	Preoperative optimization is focused on controlling infection, reversal of bronchospasm, improving mucus drainage, hidrating and reversal of athelectasis.
Avoid high-pressure mechanical ventilaton and PEEP	Adequate depth of anesthesia during induction to avoid bronchospasm.
Volatile agents, beta-blockers and calcium blockers are prefered for reducing contractility	Volatile agents are prefered for bronchodilator effect.
Hypotension is treated with an alfa-adrenergic agonist	Avoid high dose opioids.
Avoid drugs that increase risk of left-ventricle outflow tract obstruction (digitalis, nitrates, vasodilators, cathecolamies)	Humidified anesthetic gases for preserving muco-ciliary function
	Avoid high motor block and decreased systemic vascular resistance in patients with fixed pulmonary hypertension

Perioperative acute heart failure (AHF) is a challenge for the surgical team and it sometimes is difficult to diagnose, in absence of proper monitoring tools. It can present itself frequently as pulmonary oedema, or left/right/biventricular congestive heart failure and sometimes as cardiogenic shock. In the perioperative period, patients with preoperative decreased cardiac reserve may be faced with numerous triggers of AHF, including hypertension, tachyarrhythmias, anemia, hypercoagulability, inappropriate fluid management, pain, surgical stress and myocardial ischaemia.

Essential in the perioperative period is to be able do differentially diagnose the etiology of AHF, and, in this endeavor, all necessary monitoring techniques should be used, including physical examination, ECGs, serial biomarker measurements for ischaemia or natriuretic peptides, X-ray, echocardiography, right-heart catheterization and even PACs (which can, in these cases, provide unique insight into complex monitoring scenarios).[9,54] At the same time, a stepwise approach should be taken to manage these patients (see table 6).

Table 6. Stepwise approach to perioperative heart failure (after ref 55).

1) Develop differential diagnosis for cause, treat repairable lesions.
2) Initiate resuscitation measures: maximise oxygenation/ventilation, control postoperative pain/tachycardia, correct acid-base and electrolyte abnormalities.
3) Evaluate and optimise preload, afterload, contractility, heart rate and rythm
   a) Preload- volume load vs. diuresis based on evaluation of volume status
   b) Afterload- if high, consider dilation with nytroglicerine, sodium nitroprusside; if low consider augmentation with norepinephrine
   c) Contractility - use inotropic agents
   d) Establish stable heart rate and rhythm
4) Use mechanical assistance for patients refractory to above measures.

AHF therapy which is associated with low cardiac output is most frequently treated with iv inotropes, of which only two have been found not to increase mortality in this group of patients: dobutamine and levosimendan.

The recommendation in the ESC HF guidelines is that an i.v.infusion of an inotrope (e.g. dobutamine) should be considered in patients with hypotension (systolic blood pressure <85 mmHg) and/or hypoperfusion to increase cardiac output, increase blood pressure, and improve peripheral perfusion. The ECG should be monitored continuously because inotropic agents can cause arrhythmias and myocardial ischaemia (IIa C).[7] However, recent studies have found no benefit in mortality after use of dobutamine in AHF, and a trend towards increased mortality has been noticed in a recent meta-analysis of studies comparing dobutamine with placebo, although it was not statistically significant.[54]

Levosimendan, an inodilator, shows promise in treating AHF and, with the addendum that it has vasodilator effects and might require adding norepinephrine in order to maintain MAP >60 mmHg, it could be a treatment option in perioperative AHF in non-cardiac surgery. Data from cardiac surgery suggest improvement in outcome when using levosimendan for cardiogenic shock.[55,56]

Problems can occur in patients that develop a clinical picture of ACS intra or postoperatively. Every effort should be made to reduce the patient's exposure to prolonged myocardial ischaemia, and, if possible, the surgical team should discuss aborting the procedure.[57] Intraoperatively, aside for the principles discussed above, care should be given to instituting aspirin therapy as soon as possible (possibly by gastric tube), given that the bleeding risk is acceptably low.

In patients with cardiogenic shock, which is defined as low blood pressure unresponsive to fluids in the setting of elevated filling pressures, low cardiac output and signs of tissue hypoperfusion, pharmacologic positive inotropic support should be instituted, alongside with proper monitoring tools.[58,59] In refractory patients, placement of an intraaortic balloon pump (IABP) is mandatory and urgent.[57,60]

Other options of mechanical circulatory support include: extracorporeal membrane oxygenation (ECMO) and left/right ventricular assist devices, used either as bridge to recovery, but more often as bridge to decision, in patients where full evaluation has not been possible and in whom death could occur without this treatment.[7] Patients with such indications need referral to a cardiac surgery center.

In patients with severe conduction abnormalities, such as complete atrioventricular block, temporary or permanent endocavitary pacing should be performed urgently. Outcomes are better if biventricular pacing is used.[61]

For patients with AHF and anuria or congestion that is refractory to diuretic therapy, ultrafiltration is a therapeutic alternative as a rescue strategy. It has theoretical advantages, as it has no potential for causing dyselectrolytemias, while allowing for precisely tailoring fluid-removal from patients. However, in clinical practice, results are inconclusive, as recent studies have not shown better outcomes in ultrafiltrated patients despite improved hemodynamics.[54]

The fact that intra-operative haemodynamic instability is associated with post-operative complications allows for risk stratification at the end of surgery. This has been the result of the use of the surgical Apgar score.[62] The benefit of immediate post-operative risk stratification could be related to better identification of patients who may require special attention in the post-operative period (e.g. measurement of cardiac-specific troponin or natriuretic peptides, or continued observation in the ICU).

Patients who develop HF have a significantly increased risk of rehospitalization and hospital discharge should be optimally planned preferably in a multidisciplinary team, thoroughly evaluating residual congestion and signs of HF.[7]

In conclusion, the perioperative role of anaesthesiologists (physicians trained in anaesthesia and intensive care medicine) has changed, increasing the workload and responsibility. The anaesthesiologists have a leading role in perioperative management of patients with heart failure by identifying patients who require pre-operative evaluation and optimisation by a team of integrated multi-disciplinary specialists including anaesthesiologists, cardiologists and surgeons, and when appropriate an extended team (e.g. internists, pulmonologists or geriatricians).

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