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Review Article

Non-Cardiac General Surgery in Patients with Pulmonary Hypertension: Particularities of Perioperative Management

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Abstract

Pulmonary hypertension is a major reason for elevated perioperative morbidity and mortality, even in non-cardiac surgical procedures. Patients more often experience serious complications, such as right-ventricular failure, arrhythmias, and early postoperative death. Preoperatively patients should be thoroughly prepared for the intervention and allowed plenty of time for consideration. All specialty disciplines involved in treatment should play a role in these preparations. After selecting each of the suitable individual anesthetic and surgical procedures, intra operative management should focus on avoiding all circumstances that could contribute to exacerbating pulmonary hypertension (hypoxemia, hypercapnia, acidosis, hypothermia, hypervolemia, and insufficient anesthesia and analgesia). Due to possible induction of hypotension, intravenous vasodilators (milrinone, dobutamine, prostacyclin, Na-nitroprusside, and nitroglycerine) should be administered with the greatest care. A method of treating elevations in pulmonary pressure with selective pulmonary vasodilation by inhalation should be available intraoperatively (iloprost, nitrogen monoxide, prostacyclin, and milrinone) in addition to invasive hemodynamic monitoring. During the postoperative phase, patients must be monitored continuously and receive sufficient analgesic therapy over an adequate period of time. All in all, perioperative management of patients with pulmonary hypertension presents an interdisciplinary challenge that requires the adequate involvement of anesthetists, surgeons, pulmonologists, and cardiologists alike.

ABBREVIATIONS

NYHA: New York Heart Association; **PH:** Pulmonary Hypertension; **RA:** Right Atrium; **SVV:** Stroke Volume Variability; **TEE:** Trans Esophageal Echocardiography; **MAC:** Minimal Alveolar Concentration; **NO:** Nitric Oxide; **cAMP:** Cyclic Adenosine Mono Phosphate

INTRODUCTION

Patients with severe pulmonary hypertension are at increased risk for perioperative morbidity and mortality when undergoing all kinds of cardiac and non-cardiac surgery. Stress, pain, intra-/postoperative mechanical ventilation, and trauma-induced inflammation can further increase pressure and resistance within the pulmonary arteries and cause right heart failure. Available data show a perioperative mortality of 7-24% – depending on the primary disease and the type of surgical intervention – with the highest risk for pregnant women and patients undergoing emergency interventions [1-6]. Conditions that cause one or more perioperative complications in 42% of all patients were heart failure of NYHA class II or higher, a history of pulmonary embolism, high-risk surgery (e.g., thoracic or major abdominal surgery), and an anesthesia duration of more than 3 hours [1,2]. Risk factors for major complications in these patients were an elevated right atrial pressure, a six minute walking distance <399 m, the need for emergency surgery and the perioperative use of vasopressors, show by Meyer et coworkers in a large international prospective survey [6]. Even postoperatively PH patients have significantly increased risk for hemodynamic instability, heart failure, post-operative sepsis, and respiratory failure; and required significantly prolonged postoperative ventilation and a longer intensive-care stay [7].

The perioperative management of patients with major pulmonary hypertension presents a great challenge to both anesthesiologists and surgeons. Little is known about the special management and outcome of orthopedic patients with severe pulmonary hypertension, therefore the aim of our paper is to present our clinical experiences with these special surgical patients and to formulate experience-based recommendations for the perioperative management. An interdisciplinary team with anesthesiologists, surgeons, pulmonologists, and cardiologists will play a central role to play in achieving the best outcome for this high-risk population.

MATERIALS AND METHODS

Interdisciplinary preoperative evaluation and diagnostics

Pulmonary hypertension affects several organ systems simultaneously (lung, heart, vascular system), therefore preoperative evaluation should be considered as a joint task of anesthesia, surgery, pulmonology, and cardiology [8]. The purpose of these preparations should be, on the one hand, to evaluate the functional state of the heart and lung organ systems as good as possible. On the other hand the patient's initial conditions should be optimized as far as possible by adjusting the current specific medication and treatment of comorbidities. Both approaches are appropriate to minimize the individual risk of complications. The diagnostics listed below are not obligatory

for all patients, but should compose individually dependent from basic disease and functional state.

Clinical examination: The clinical symptoms of pulmonary hypertension are largely unspecific, often overlooked or misinterpreted in early stages of the disease (Table 1) [9]. The most common but very unspecific symptom is stress-induced dyspnea. In addition to obtaining a detailed medical history, the clinical investigation should focus on symptoms for right-sided heart failure. In late-stage diseases in particular, obstruction of the jugular veins, peripheral edema, hepatomegaly, hepato-jugular reflux, and ascites are probable. The functional classification of pulmonary hypertension is similar to the criteria of NYHA (Table 2) [10].

Depending from origin of pulmonary hypertension, functional state and invasiveness of the surgical intervention, more diagnostics may be necessary: Thoracic X-ray, ECG, pulmonary function examination including arterial blood gas analysis, spiroergometry, echocardiography, and right heart catheterization [8]. Before surgical intervention, medication should be critically examined from a pulmonological and cardiological perspective with a view to possible optimization. At the time of surgery, the patient should ideally have been in a stable condition for an extended period of time.

Intraoperative monitoring

The intraoperative monitoring should be adapted individually to the severity of the disease and the invasiveness of the surgical procedure. To date, there is no evidence to suggest that any specific type of monitoring has an influence on patient morbidity and mortality. However, the authors believe that early recording of deviations from the initial conditions (in particular in relation to right heart function) can make a decisive contribution to recognizing and avoiding severe complications from the outset.

Whereas basic monitoring can be considered sufficient for minor and medium procedures in functional state II, all major interventions and those in functional state III should be carried out under extended monitoring (Table 3) [10]. For intraoperative fluid management stroke volume variability (SVV) is an appropriate method of evaluating volume responsiveness,

Table 1: Clinical findings in patients with pulmonary hypertension (mod. [9]).

1	Dyspnea (during stress/at rest) / Cyanosis
2	Fatigue
3	Dizziness
4	Synkope
5	Thoracal pain
6	Palpitations
7	Orthopnea
8	Cough
9	Croakiness
10	Abdominal tension
11	Peripheral Edema / Ascites
12	Hepatomegaly

Table 2: Functional classification of pulmonary hypertension (WHO 1998) [10].

Class I	Patients with pulmonary hypertension but without resulting limitation of physical activity. Ordinary physical activity does not cause dyspnea or fatigue, chest pain or near syncope.
Class II	Patients with pulmonary hypertension resulting in slight limitation of physical activity. They are comfortable at rest. Ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class III	Patients with pulmonary hypertension resulting in marked limitation of physical activity. They are comfortable at rest. Less than ordinary physical activity causes undue dyspnea or fatigue, chest pain or near syncope.
Class IV	Patients with pulmonary hypertension with inability to carry out any physical activity without symptoms. These patients manifest signs of right heart failure. Dyspnea and/or fatigue may even be present at rest.

Table 3: Intraoperative monitoring: recommendation for patients with PH (mod. [11]).

Basic monitoring	
	- ECG
	- SaO ₂
	- End-expiratory CO ₂
	- Invasive blood pressure
	- Optional: stroke volume variation (SVV)
Extended monitoring	
	- Pulmonary arterial catheter
	- Transesophageal echocardiography (TEE)

provided that the prerequisites for its use are fulfilled (sinus rhythm, ventilation) [11].

For all patients in the late stages of PH and existing or history of right-sided heart failure, pulmonary artery catheterization and/or transesophageal echocardiography (TEE) are the methods of choice for adequate intraoperative monitoring. The best method for evaluating preload and contractility is certainly TEE, even if it requires the presence of specifically trained personnel. The intraoperative use of pulmonary artery catheters is subject to controversial discussions in the current literature. However, all authors point out that the insertion of a pulmonary artery catheter is associated with certain risks, which must be considered when applying this monitoring method [4,10,12].

Selection of the anesthetic technique

Patients with late-stage pulmonary hypertension should be treated in medical centers that fulfill all conditions for qualified treatment in terms of their structure and personnel (Table 4). All standard anesthetic techniques can, in principle, be applied to patients with pulmonary hypertension [12]. Regional anesthetic techniques offer the advantage of not impairing spontaneous breathing and can be used for postoperative analgesic therapy. In general, continuous techniques should be preferred to bolus administration – especially for spinal or epidural analgesia – in order to avoid uncontrolled drops in blood pressure, which can endanger myocardial perfusion [10,12]. In our orthopedic,

gynecologic and abdominal surgical patients with PH, spinal and epidural catheter techniques are also preferred. By fractionated administration, the required dose can be delivered without any significant effects on hemodynamics. Plexus or nerve catheters (sciatic or femoral nerve) are recommended for surgical procedures involving the extremities in particular, as they do not affect hemodynamics, have a low failure rates, and ensure treatment of postoperative pain. Nearly all patients with pulmonary hypertension receive continuous anticoagulant therapy; this fact must be taken under consideration when planning the intervention and the regional anesthetic procedures. Recommendations in relation to this issue are provided in the current guidelines [13].

Particularly in the later stages of pulmonary hypertension or in diseases affecting the lung, patients cannot be subjected to remaining in a flat position over a long period of time. In these cases, regional anesthesia should be combined with careful general anesthesia to ensure adequate oxygenation [10,12].

In view to general anesthesia the main advantages are safe oxygenation and uncomplicated airway management, and intraoperative selective pulmonary vasodilation can – if necessary – easily be administered through the breathing circuit (Figure 1). Anesthesia-induced systemic vasodilation and mechanical ventilation can lead to a significant drop in mean arterial pressure, which has the potential to endanger myocardial perfusion and critically affect right-ventricular contractility [14]. All standard induction anesthetics can, in principle, be used in combination with opioids, as they have no influence on pulmonary vascular resistance and oxygenation [15]. Histamine-releasing relaxants (atracurium, mivacurium) should be avoided for patients with pulmonary hypertension, as they may further increase pulmonary resistance [15]. Volatile anesthetic agents of concentrations up to 1 MAC can be administered without any negative effects on pulmonary pressure and resistance [14]. We suggest a balanced technique, mixing higher doses of opioids and low-dose volatile anesthetic agents [10].

Intraoperative treatment of increased pulmonary arterial pressure

The most important requirement for intraoperative



Figure 1 Intraoperative selective pulmonary vasodilation with inhaled iloprost via ultrasonic nebulizer (m-neb®, nebutec/Elsenfeld, Germany) in the ventilatory circuit.

management and maintenance of anesthesia is to avoid anything that could increase right-ventricular after load or decrease contractility of the right ventricle, as both factors will ultimately lead to ischemia and right-sided heart failure (Figure 2).

Hypoxia is one of the strongest inducers of pulmonary vasoconstriction, therefore high inspiratory oxygen concentration should be used (FiO₂ 0.6-1.0) to minimize the risk of hypoxic phases. Carefully performed recruitment maneuvers are able to prevent inadequate ventilation-perfusion ratios [16]. It is not clear if an intraoperative low-tidal-volume ventilation offers any benefits over “conventional” pressure-controlled ventilation; the authors would recommend to set peak pressures as low as possible (6-8 ml/kg ideal body weight) to avoid alveolar over-inflation [16]. In addition to hypoxia, acidosis and hypercapnia may also aggravate existing hypertension. Therefore, moderate hyperventilation (target PaCO₂ of 30-35 mmHg) should be carried out under continuous blood gas analysis, but without allowing the pH value to fall below 7.4 [14,15]. Hypothermia and shivering can considerably increase pulmonary pressure and should therefore be strictly avoided (Table 5).

Perioperative fluid management should be carried out rather restrictively and in a targeted manner, with adequate hemodynamic monitoring to optimize right-ventricular preload. It is very difficult to indicate general target values for these therapy forms that take account of the individual needs of this

Table 5: Intraoperative “basic treatment” to avoid an increase of pulmonary arterial pressure (mod. [11,13,15]).

“Luxury”-oxygenation with inspiratory FiO ₂ 0.6 – 1.0
Moderate hyperventilation (goal: PaCO ₂ 30-35 mmHg)
Avoidance of metabolic acidosis (pH > 7.4)
Recruitment-manoeuver to avoid ventilation/perfusion-mismatch
Low-tidal-volume ventilation to avoid over-inflation of aveoli (goal: 6-8 ml/kg ideal body weight)
Temperature management to maintain body temperature of 36-37 °C
“Goal-directed” fluid- and volume-therapy with hemodynamic monitoring

particular patient population. The target values for right-sided heart failure – e.g., after heart transplantation – certainly cannot be applied to patients with chronic pulmonary hypertension [17]. One possibility, which is favored by the authors, would be to consider the initial values measured during preoperative evaluation (right heart catheter!) as target values and to initiate specific treatment in the event of deviations ±15-20%. Gille et al. also recommend carrying out intraoperative management in a way that allows mean pulmonary artery pressure to fluctuate in a range of 15% above or below the initial value [10]. However, clinical trials have not yet collected sufficient data to substantiate this “target corridor”.

In general, it should be considered that patients with PH have low arterial pressure as a result of their disease and the specific therapy, and that the possibilities for compensation are very limited due to right-sided heart failure. Therefore, if mean arterial pressure falls below the critical value of 50-55 mmHg, low doses of a vasoconstrictor (e.g., noradrenalin 2-5 µg) should be administered carefully [10,12,15].

Intraoperative vasodilator therapy

If an increase in pulmonary artery pressure cannot be controlled by the symptomatic measures described above, specific medication should be induced immediately to reduce right-ventricular after load and thus the risk of right-sided heart failure. The required vasodilators can be administered both intravenously and by inhalation.

Administration of nitroglycerin, sodium nitroprusside, milrinone, dobutamine, or prostacyclin is recommended for intravenous vasodilation (for dosage see table 6) [10,12,15]. As the effect of these substances is not limited to the pulmonary circulation and is accompanied by systemic vasodilation, a considerable decrease in systemic mean arterial pressure may involve the risk of right-ventricular perfusion pressure falling below a critical limit [18]. In the case of hypotonic blood circulation selective pulmonary vasodilator therapy by inhalation offers several advantages over intravenous vasodilation. As alveoli and pulmonary capillaries are located in close proximity, the effect of inhaled vasodilators is direct, immediate and – in case of short-acting drugs – limited to the pulmonary vascular bed; therefore avoiding systemic vasodilation and hypotension. In addition, substances that are administered by inhalation only have an effect on ventilated lung areas, and the consecutive vasodilation in the ventilated areas therefore leads to a decrease

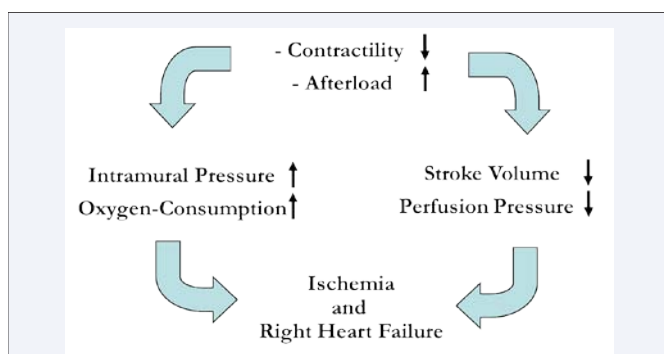


Figure 2 Mechanisms of acute right heart failure (adapted from [11]).

Table 4: Authors recommendations: human, structural and technical requirements for the perioperative management of patients with severe pulmonary hypertension.

Established cooperation with cardiologists und pulmologists
Access to specific medication for the treatment of pulmonary hypertension
Experiences in all procedures of general and regional anesthesia
Experiences in dealing with pulmonary arterial catheterization and the use of inhaled drugs for selective pulmonary vasodilation
Intraoperative transesophageal echocardiography
Hemodynamic monitoring in critical care
Specific educational program for “pulmonary hypertension”
Consultants with special experiences in the treatment of pulmonary hypertension
Regular pain visits and/or pain nurses for the perioperative pain therapy

of the pulmonary shunt and improved oxygenation [18]. Several substances are currently available for vasodilator therapy by inhalation in patients with pulmonary hypertension (Table 6).

Postoperative recovery and analgesic therapy

Patients with pulmonary hypertension are at risk of developing elevated pulmonary pressure and right-sided heart failure not only during the perioperative phase itself, but also in the postoperative course. These patients should therefore be placed under intense postoperative monitoring for a period appropriate to the degree of surgical trauma; the target monitoring time should be between 24 hours for small interventions and several days for major procedures (abdominal and thoracic surgery, major urological interventions). Depending on the patient's initial condition (functional classification), hemodynamic monitoring may need to be continued postoperatively until pulmonary pressures and right-sided heart functions have stabilized at the preoperative level. For our institution, the mean monitoring time in intensive or intermediate care is a ppr 36 hours.

In this phase, sufficient analgesic therapy can make a decisive contribution to the avoidance of pulmonary complications. In the ideal case, analgesic therapy in the form of continuous regional anesthesia can be organized in a way that avoids higher doses of opioid-based analgesics. The basic treatment of patients with pulmonary hypertension therefore includes daily visits by pain management nurses. The specific therapy for pulmonary hypertension should be resumed at the preoperative dosage as soon as possible. In the postoperative course, it is also advisable to treat pressure elevations with iloprost inhalation, which can also be administered intermittently due to its long half-life.

DISCUSSION

Pulmonary hypertension is a major reason for elevated perioperative morbidity and mortality, even in non-cardiac surgical procedures. Price et al. reported about 28 PH patients having non-cardiac and non-obstetric surgery under general or regional anesthesia: at the time of surgery, 75% of patients were in NYHA functional class 1–2. Deaths occurred in 7% of patients and perioperative PH-related complications occurred in 29% of patients [19]. In a smaller case series of 21 patients with moderate to severe PH, Minai et al. showed an 18% mortality rate [20].

Considering that most patients were throughout at functional class III, careful preoperative evaluation and optimization may contribute to minimize the perioperative risk. In a retrospective study of Kaw the mortality rate was very low with 1% [3]. But in this study population, there were a great number of patients with pulmonary hypertension due to left heart failure. The anesthetic management of patients with left heart disease differs significantly from those with pre-capillary forms of pulmonary hypertension; therefore the results are not comparable.

It is consensus in all reviews that patients with pulmonary hypertension should be thoroughly prepared for the intervention by an interdisciplinary team. Pilkington and coworkers support our concept, that the pre-operative evaluation of a patient with established pulmonary hypertension should be based on a risk assessment that takes into account their functional state, severity of the disease and type of surgery proposed [12]. Established PH therapies should be continued in the peri-operative period and when oral formulations cannot be used, temporary administration of inhaled (NO, nebulised prostacyclin) or intravenous (prostacyclin, sildenafil) therapy should be considered [12].

Various anesthetic techniques have been used in patients with pulmonary hypertension. Neuroaxial regional anesthesia was previously thought harmful in patients with PH because of the hemodynamic compromise following sympathetic blockade; however, as shown in our orthopedic patients, using a spinal or epidural catheter technique with low intrathecal dose or careful incremental epidural top-ups minimizes this potential drop in after load. Regional techniques have also been used in patients with PH in general surgery [1,21]. On the other hand, regional anesthesia may be inappropriate for many surgical procedures, as well as in emergency cases. Based on our experiences we recommend regional anesthesia techniques, alone or – if necessary – in combination with moderate general anesthesia as method of choice for patients with PH undergoing surgery.

The intraoperative management should focus on maintaining right ventricular cardiac output, avoiding systemic hypotension, and avoiding all circumstances that could contribute to exacerbating pulmonary hypertension (hypoxemia, hypercapnia, acidosis, hypothermia, hypervolemia). In this context, the intraoperative management should also pay attention to the fluid management: the balance between adequate right-ventricular filling and hyperhydration is often difficult to find and requires an extended intraoperative hemodynamic monitoring and the knowledge of preoperative hemodynamics. We prefer a restricted fluid substitution, adjusted to the individual needs and intraoperative hemodynamics. Hypotension should not be tolerated and treated with fractional or continuous low-dose vasoconstrictors to maintain an adequate myocardial perfusion.

A method of treating elevations in pulmonary pressure by inhalation of short-acting pulmonary-selective vasodilators should be available intra- and postoperatively. During the postoperative phase, patients must be monitored continuously and receive sufficient analgesic therapy over an adequate period of time.

It is important to emphasize that the selection of the anesthesia team is just as crucial as the selection of the anesthetic

Table 6: Specific interventions for therapy of intra- and/or postoperative increase of pulmonary arterial pressure (mod. [11,13,16]).
Reduction of right-ventricular afterload: - intravenous vasodilation
1) Milrinone - 50µg/kgBW bolus, followed by 0.5-0.75µg/kgBW/min continuously
2) Dobutamine - 2-5 µg/kgBW/min continuously
2) Prostacyclin - 4-10 ng/kgBW/min continuously
3) Na-Nitroprusside - 0.2-0.3 µg/kgBW/min continuously
4) Nitroglycerine - 2-10 µg/kgBW/min continuously
Pulmonary-selektive inhalative Vasodilatation
1) Iloprost - 5-10 µg for 10-15min (by ultrasonic nebulizer)
2) Stickstoffmonoxid - 0.5-20 ppm continuously
3) Prostacyclin - 30-40 µg/kgBW/min continuously
4) Milrinone - 2 mg for 10-15min (diluted in 10-15mL NaCl0.9%)

technique to be used. It is essential to have not only excellent anesthesiological expertise on hand, but also specific knowledge of the pathophysiology of pulmonary hypertension and right-sided heart failure, the interpretation of hemodynamic data, and the corresponding concepts of complex medical treatment.

CONCLUSION

All in all, perioperative management of patients with pulmonary hypertension presents an interdisciplinary challenge that requires the adequate involvement of anesthetists, surgeons, pulmonologists, and cardiologists alike. Current concept shows that general surgery is feasible with satisfactory outcome even in cases of severe pulmonary hypertension by an individualized, disease-adapted interdisciplinary treatment concept.

CONFLICT OF INTEREST

AS: honoraria for lectures and travel reimbursements from Bayer Healthcare, Actelion, Glaxo Smith Kline, CSL Behring, Boehringer Ingelheim; HJS: none; JG: honoraria for lectures from Pulsion Medical Systems; SG: none; MM: none; EC: none.

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