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The intensive care management of patients following heart transplantation at the Deutsches Herzzentrum Berlin

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Abstract

Today heart transplantation (HTx) is accepted worldwide as a treatment option for terminal cardiac failure. In approximately 90% of HTx patients the indication is ischemic or dilative cardiomyopathy. Seventy-five percent of the organ recipients are more than 40 years old and most of them are men (1). At the Deutsches Herzzentrum Berlin a total of 1637 HTx were carried out between April 1986 and July 2010. The age of the organ recipients ranged between 3 months and 71 years, with an average age of 50 years. Male organ recipients (n=1320) were about four times more frequent than female recipients (n=317).

Postoperative observation and treatment of patients on the intensive care unit (ICU) after HTx are essentially similar to those required after other heart operations. Nevertheless, HTx patients require special care, because not only must the immediate results of the operation be treated, but also immunological processes influence the clinical course and the necessary treatment. In the early phase after HTx the stabilization of organ functions and the introduction of immunosuppressive therapy are in the foreground.

The cardiovascular circulation requires intensive and continuous monitoring. Measures for hemodynamic optimization by means of volume substitution, inotropes and vasoactive substances must take into account specific features of the transplanted organ. Compensatory mechanisms to stabilize the hemodynamics can be applied only restrictedly on account of the ischemia, the reperfusion damage and the autonomic denervation with the subsequent chronotropic and inotropic failure. Stimulation by a pacemaker and catecholamine treatment are important.

The heart-transplanted patient is endangered in particular by right ventricular dysfunction, which can become life-threatening. The aims of postoperative therapy are therefore individually tailored preload conditions and ensuring contractility and an adequate reduction in the pulmonary vascular resistance. Mechanical ventilation serves to maintain adequate gas exchange and enables the right ventricular afterload to be specifically influenced.

Further important components of the intensive therapy after HTx are immediate immunosuppressive therapy and rejection monitoring. The intensive medical care after transplantation is always an interdisciplinary task.

In the following, treatment standards are given for the perioperative intensive medical management of HTx patients at the Deutsches Herzzentrum Berlin.

Key words: heart transplantation, intensive care

Transfer of the patient from the operating room to the ICU

The intensive care units of the Deutsches Herzzentrum Berlin more than 44 beds for artificial respiration. The patients are received from the operating area under sedation, intubated and artificially ventilated. Isolation of the patients and strict asepsis or sterility are necessary; therefore, patients who have undergone HTx are assigned to single or double-bedded rooms with double doors and reverse isolation. For these purposes four single rooms and four double rooms are available in our ICU. The doors must always remain closed to avoid contamination by air from the corridor.

In accordance with the recommendations of the Robert Koch Institute of Hygiene the medical staff must disinfect their hands and put on germ-free gloves before performing any procedure or maneuver on the patient (2). In addition, a mask and cap must be worn by people staying in the patient's room and also by visitors, who should be restricted in numbers. Individuals with an infection of any kind are prohibited entrance to the ICU.

Hemodynamic monitoring and standard medication

The first steps after arrival of the patient on the ICU are connection to the equipment for monitoring the arterial, central-venous, left atrial and pulmonary arterial blood pressure, the peripheral oxygen saturation, the ECG and the body temperature. Immediately after transplantation careful supervision of the hemodynamic parameters is necessary because, before the end of the organ recovery period (approx. 7-14 days), even slight changes in the preload and afterload can lead to serious developments that can be difficult to treat later on. The aim is to achieve adequate cardiac output and preload and afterload conditions suitable for the transplanted heart, while at the same time ensuring adequate organ perfusion and organ recovery.

The arterial pressure is measured invasively, usually by means of a catheter in the radial artery or, more seldom, in the femoral artery. Every patient who has undergone HTx receives hemodynamic monitoring by means of a pulmonary arterial catheter (Swan-Ganz catheter) that was already placed during surgery by the anesthesiologist through a venous sluice in the internal jugular vein.

Use of the pulmonary catheter is recommended for high-risk patients with complex surgical interventions, for the diagnosis and treatment of pulmonary hypertension and for the differentiation and treatment of severe right and left ventricular dysfunction. It enables monitoring of a number of hemodynamically significant parameters such as the cardiac output (CO), cardiac index (CI), peripheral vascular resistance, pulmonary vascular resistance (PVR), pulmonary-capillary wedge pressure (PCWP) and the mixed-venous oxygen saturation (SvO₂), so that prompt action can be taken if problems occur (3).

The standard postoperative medication includes nitroglycerin to lower pre- and afterload and adrenalin (Suprarenin) to increase inotropy and chronotropy. To increase cardiac inotropy and simultaneously reduce the afterload, dobutamine (Dobutrex) and the phosphodiesterase-III inhibitors milrinon (Corotrop) and enoximon (Perfan) are given.

Catecholamine administration is always necessary after HTx due to the autonomic denervation and the associated chronotropic and inotropic failure (4,5). In combination with volume therapy the target central venous pressure (CVP) is ≤ 12 mmHg and target mean arterial pressure (MAP) ≥ 65 mmHg. The infusion rates of vasoactive and inotropic substances are adapted accordingly.

The pressure values in the left atrium (LA) (target: 8-12 mmHg), measured via an LA catheter, should show no large discrepancy to the CVP. In particular the transplanted heart needs a carefully controlled balance between the LA pressure or PCWP and CVP.

The mixed-venous oxygen saturation should not fall below 65%.

In the case of hypertensive blood pressure regulation, nitroglycerine and urapidil are first given intravenously. The antihypertensive medication is extended in the further course by the addition of ACE inhibitors or AT-1 inhibitors and calcium antagonists.

Ischemia and reperfusion often cause diastolic dysfunction with rather restrictive filling of the ventricles. Because of the reperfusion damage the Frank-Starling mechanism of increased stroke output in the presence of raised preload is limited (6); therefore adequate chronotropic stimulation is important to achieve sufficient cardiac output. This is usually done by external pacing via temporary epicardial pacemaker leads placed during surgery. With sinus rhythm and intact atrial-ventricular conduction we stimulate via epicardial leads with a rate of 100/min. In the case of a high-grade atrial-ventricular block, sequential pacing is required.

Volume substitute therapy, kidney function and renal monitoring

The volume management is a central part of the intensive treatment of the patient and is of great importance for the further course. When choosing the volume substitute, not only the normalization of hypovolemia-related hemodynamic changes are to be considered. Side effects on the acid/alkali balance, the coagulation system and kidney and liver function are also important. We currently favor a standard crystalloid infusion regime. Above all to minimize postoperative renal complications due to hyperoncotic kidney failure, the application of HAES has to be restricted (7). From physiological considerations arises the need to use balanced colloid and crystalloid solutions. The volume substitute therapy is given under strict monitoring of the preload parameters (CVP, LAP/PCWP) and repeated echocardiographic controls.

The indication for transfusion of fresh-frozen plasma is made generously. Many of our heart-transplanted patients have received a left ventricular or biventricular assist device (LVAD, BVAD) as "bridge to transplant"; accordingly the preoperative coagulation situation is difficult due to the patients taking anticoagulant substances such as phenprocoumon or coumadin to increase the INR, and the danger of bleeding is clearly elevated (8).

All patients receive a urinary catheter for urine collection. The aim is, by moderate volume therapy taking into account the filling pressure (CVP, LAP, PCWP) and the application of diuretics (furosemide or torasemide), to keep the uric output ≥ 0.5 ml/kg/h.

In patients who develop oligoanuric or polyuric kidney failure with inadequate urine concentration and serum urea values > 200 mg/dls or hyperkalemia and/or increased preload as in hypervolemia, kidney replacement procedures are applied without delay. Early postoperatively we prefer continuous veno-venous hemofiltration (CVVHF), which is able to achieve an optimal volume balance.

The retention values (creatinine, urea) are monitored by daily blood tests. In case kidney replacement therapy remains necessary in the postoperative course and the patient's hemodynamics are stable without or with only slight catecholamine support, the change is made to intermittent dialysis (three times weekly). In the case of acute renal failure the dosage of nephrotoxic substances, for example antibiotics, has to be reduced. A reduction of the cyclosporin dose is also necessary.

In a study urodilatin was used from November 1990 to January 1992 and showed a significant improvement in nephritic function and therefore a positive influence on the hemodynamics in patients who had undergone heart transplantation. Urodilatin diminishes cyclosporin-associated nephrotoxicity and lowers pulmonary pressure. Currently clinical trials of urodilatin for the treatment of heart failure are underway; it is not yet officially approved (9).

Imaging procedures and laboratory diagnostics

Directly after arrival of the patient on the intensive care unit a chest X-ray is taken to check the position of drains, intravascular catheters, pacemaker leads and the intubation tube. The heart, lung, mediastinum and bony thorax are monitored. Thoracic X-ray examinations every 24 hours are necessary after heart transplantation.

Arterial, central-venous and mixed-venous blood is closely monitored; the parameters measured are listed in Table 1. Arterial blood gas analysis is generally carried out every 2 hours. Mixed-venous or central-venous blood gases are analyzed three times a day or if there are relevant changes in therapy.

The everyday routine laboratory tests included the blood count, the coagulation values and the blood chemistry, with electrolytes. Further, the drug levels (cyclosporin, antibiotics, antiarrhythmics) are identified once a day, in the morning before medication is given. Twice a week a T-cell count is taken, regulation of the pp65 antigen is checked and samples of the tracheal secretion and urine are taken for microbiological testing. Once a week the lipid profile and fungal serology are provided.

Echocardiography

Heart transplantation is a complex intervention with a specific spectrum of problems that occur in the intensive care setting. In

identifying and solving these problems echocardiography is a firmly established tool.

If unclear hemodynamically unstable situations occur after heart transplantation, in addition to the key question of the systolic and diastolic myocardial function, the possibility of graft rejection, the quality of the valve function, the anastomosis relations and pericardial effusion or tamponade have to be taken into account (10). In the early postoperative period our heart transplant patients undergo echocardiography daily.

This strategy of repeated echocardiographic examinations seems to be currently the most exact method of identifying right ventricular dysfunction. Although the concepts of right ventricular strain, dysfunction and decompensation are not strictly defined in the literature, right ventricular dysfunction may be identified by echocardiographic findings of limited wall motion of the right ventricle, right ventricular dilatation, disturbed motion of the ventricular septum and tricuspid valve insufficiency. Echocardiography should be generously used so that hemodynamic deterioration can be treated quickly and effectively.

Artificial respiration and respiratory weaning

Controlled artificial respiration is the central element in ensuring adequate oxygen saturation and carbon dioxide elimination. Artificial respiration usually continues until the patient's hemodynamic condition stabilizes and immunosuppressive therapy is started. Pres-

Table 1: Laboratory blood tests

Blood count	Coagulation	Chemistry	Serology
Hemoglobin Hematocrit Leucocytes Platelets	PTT INR TPZ	Troponin I, CK, CK-MB, gGT, albumin, creatinine, urea, glucose, bilirubin, lactate, electrolytes, anorganic phosphate, lipase, cholinesterase	Hepatitis A, B, C TSH, fT3, fT4

sure-controlled ventilation is the standard concept for early postoperative artificial respiration.

On the basis of recent discussions, the use of low tidal volumes and limited inspiratory artificial respiration pressures is recommended, to protect the lungs (11). However, if acute lung failure occurs, artificial respiration is performed in accordance with more traditional concepts. The question of how protective artificial respiration should be performed in patients with healthy lungs has not yet been adequately answered. With limited pressure and volume, attention should be given to the possible effects of hypercapnia and acidosis on the pulmonary vascular resistance, the renal blood flow and the myocardial function.

Controlled mechanical artificial respiration decreases the biventricular preload and in the left ventricle also decreases the afterload. Right ventricular pressure is influenced as a function of the pulmonary conditions in a different and often not predictable manner. Mechanical ventilation with positive endexpiratory pressure (PEEP), like any other active or passive ventilatory maneuver, primarily affects cardiac function by changing lung volume and intrathoracic pressure (ITP).

In order to minimize the effects of high ITP on right and left ventricular function the following target parameters are focused on:

- Adequate oxygenation by increasing FiO_2 , $\text{paO}_2 > 80 \text{ mmHg}$, $\text{SaO}_2 > 90\%$
- Avoidance of peak pressures $> 35 \text{ mbar}$
- Careful recruitment of non-ventilated lung areas
- Application of a moderate PEEP level ($< 10 \text{ mbar}$)
- Avoidance of hypercapnia, $\text{pCO}_2 \text{ 35-40 mmHg}$.

An imbalance between pulmonary vascular resistance and right ventricular function is a frequent complication after transplantation (12). In addition to already well established therapy options, inhalative therapy with vasodilators can lead to a significant clinical improvement of the hemodynamics by re-

ducing the right ventricular afterload. The inhalative application to reduce the right ventricular afterload increases the local effectiveness and so minimizes systemic side effects.

The indication for perioperative use of inhalable vasodilators such as nitrogen monoxide and iloprost (Ventavis) has been well supported by studies, and at the Deutsches Herzzentrum Berlin it is a clinical therapy option within the scope of a multimodal treatment concept. However, treatment with nitrogen monoxide requires complex delivery and measurement apparatus and in clinical practice is limited to special respirators. The dose given in the hemodynamic management after heart transplantation is initially 20-40 ppm.

As an alternative to the selective vasodilators the prostacyclin (PGI₂) analog iloprost has gained in importance. A possible advantage of the more stable prostanoid iloprost is the possibility of discontinuous use and its application independently of artificial ventilation.

In general the aim is to end the analgosedation and wean the patient from the respirator as soon as possible. Once the hemodynamics are stable without catecholamine therapy and iNO can be discontinued with normal filling pressures and pulmonary artery pressures, weaning from the respirator begins. The criteria for the weaning attempts and extubation do not differ from those applied in other cardio-surgical patients. Specially qualified respiration therapists accompany all transplanted patients during weaning from invasive respirator therapy and also from non-invasive respiratory support. In addition, timely mobilization of the patients in cooperation with our physiotherapy department is important.

Reasons for delayed weaning are varied and among them can be unstable hemodynamics (left and/or right ventricular failure) with a high catecholamine and extended NO requirement, partial or global respiratory failure with bronchopulmonary infection or acute respiratory distress syndrome (ARDS), or a neurological deficit with delayed awak-

ening due to anaesthesia surplus or an ischemic insult. In this case the respiratory weaning is performed in accordance with specific concepts and in cooperation with our respiratory therapists.

In patients with delayed weaning, in whom primary extubation is not possible, a percutaneous dilatation tracheostomy is normally carried out.

Postal-surgical coagulation disorders

Different factors increase the risk of postoperative bleeding in patients who have received heart transplantation. One cause may be postoperative treatment with anticoagulants (warfarin, coumarin), for example in patients with assist devices, or mediastinal scarring caused by previous operations. Close monitoring of the plasma and thrombocyte coagulation and substitution treatment, as required, is important.

For thrombocyte transfusion in the presence of acute bleeding the guidelines stipulate an intervention threshold for prophylaxis of bleeding of $<100,000/\mu\text{l}$ for the intervention. With manifest bleeding that is co-caused by coagulopathy, with Quick values of $< 50\%$, aPTT > 45 sec or a fibrinogen level < 1 g/l, fresh-frozen plasma is recommended (13).

In the case of postoperative hemorrhaging of ≥ 400 ml in the first hour or 200 ml/h during the first 4 hours after the operation and normal coagulation parameters, rethoracotomy becomes necessary.

A further indication for rethoracotomy is clinically suspected acute pericardial tamponade without confirmatory diagnostic results or clinically and diagnostically established pericardial tamponade with the typical indicators: ceasing of diuresis, an increase in the CVP, fall in cardiac index, enlargement of the heart silhouette in the chest X-ray, echocardiographic evidence, abrupt ending

of mediastinal bleeding and increasing metabolic acidosis.

If there is no unusual postoperative bleeding, administration of intravenous heparin is begun 12 h after the end of the operation. The target PTT is between 45 and 50 sec.

Patients with heparin-induced thrombocytopenia (HIT II) receive argatroban for anticoagulation. Nevertheless, each case should be decided upon individually.

Cardiac rhythm disorders

Bradyarrhythmia and supraventricular arrhythmia are among the most frequent rhythm disturbances occurring after heart transplantation. Sinus bradycardia is treated by adequate doses of adrenalin/epinephrine and by means of external atrial stimulation through the epicardial pacemaker cables. Severe AV block mostly requires sequential atrioventricular pacing. Stable sinus rhythm is often established within the first week. If patients are dependent on the pacemaker after this time, the implantation of a permanent pacemaker system should be considered. Patients who receive an IMEG (intramyocardial electrogram) system intraoperatively can receive stimulation by means of this system.

Supraventricular arrhythmias are often associated with the administration of large amounts of inotropic and chronotropic substances. Otherwise, variations in the electrolyte balance may be the cause. In the case of atrial fibrillation an acute rejection reaction should also be considered. The diagnostic procedure of choice is echocardiographic examination. If rejection is suspected, 500 mg urbason i.v. is given once as a bolus.

If pharmacological therapy of the atrium fibrillation is indicated, amiodaron (Cordarex) is our medicine of choice. Cardiac glycosides such as digoxin and digitoxin are also used successfully, despite frequent opinions to the contrary. If medicinal treatment does not lead to conversion into stable sinus rhythm, biphasic electrocardioversion is carried out without further delay.

With ventricular arrhythmias xylocain is preferred to amiodaron and ajmalin.

Beside these measures it is necessary to monitor the electrolyte metabolism, especially the potassium and magnesium levels, and to optimize them if necessary.

Infection control and antimicrobial therapy

After heart transplantation only one form of perioperative antibiotic prophylaxis is initially necessary. In our intensive care unit cefuroxim (Zinacef) 3 x 1500 mg i.v. is given for 7 days. Extension of the antibiotic therapy with regard to its duration and the spectrum of pathogens depends on the results of microbiological examinations of the graft transport medium, the tracheal secretion, the urine and smears taken intraoperatively as well as on the extent and the duration of the intervention.

Patients with assist devices and an existing wound infection receive vancomycin and meropenem as standard antibiotic therapy. The vancomycin level is measured daily and the dosage is adapted, if necessary, in view of the kidney function.

Graft recipients are at risk from a large number of infections. Their immunosuppressive treatment increases their susceptibility to infections, reduces their clinical symptomatology and may entail severe problems. Special attention should be paid to infection control in contacts with the patients, indications should be restrictive, and special care is necessary with invasive technologies. Early diagnosis and preventive therapies are especially important in patients with immunosuppression. In view of the danger of infections due to immunosuppressive therapy, different prophylaxis regimens have been established. Topical, antibiotic, virostatic and antimycotic prophylaxis should be given early postoperatively.

Once a week a microbiological ward round takes place on the intensive care unit at which the latest findings are discussed and

specific therapies based on a patient's antibiotic sensitivity profile are prescribed.

Immunosuppression

Four hours after the end of the operation heart transplant patients receive the start of induction therapy with antithymocyte globulin (ATG 1.5 mg/kg i.v.) on the intensive care unit, followed by further doses at 24 and 48 hours after the first dose.

In patients who are unstable, have a body temperature of > 39°C or present a contraindication, induction therapy is carried out with simulect (20 mg i.v.). In this case the second dose is given 96 hours after the first. Thirty minutes before the induction 1000 mg urbason, 8 mg fenistil and 100 mg ranitidin i.v. are infused. In the further course the patient receives urbason i.v. and decortin H p.o. in a descending dosage in accordance with an agreed cortisone scheme.

The following immunosuppressive agents are used: cyclosporin A (Sandimmune), tacrolimus (Procount), everolimus (Certican) or mycophenolate mofetil (Cell-Sept). The individual treatment is decided upon in close cooperation with the colleagues from the transplantation ward.

Nutrition and metabolism

During the stay of heart-transplanted patients on the intensive care unit, low-calorie enteral nutrition is given. Early postoperatively the patients are fed via nasogastric tube and receive drugs such as metoclopramide (Paspertin) (3x10 mg i.v. per day) to counteract gastrointestinal paresis. After evacuation of the bowels the amount of nutrition given by tube is gradually increased. A daily calorie supply of 25-30 kcal/kg is the target (14). If the patient's evacuation is disturbed or there is increased reflux, parenteral nutrition is given to achieve the calorie target. An adequate supply of vitamins and trace elements is important.

Following procedures with cardiopulmonary bypass and during parenteral nutrition and steroid administration, changes in the serum electrolytes, especially in the potassium, magnesium and inorganic phosphate levels, are frequent. Because of their significance for energy metabolism, cerebral excitation and neuromuscular signal transmission, as well as for erythrocyte function, normalization is necessary.

With terminal heart failure and after use of the heart-lung machine, functionally relevant hypothyreosis often occurs. In comparison with primary thyroid insufficiency with decreased fT3, the TSH is also clearly reduced. So that the graft function can recover, substitution with T3 should be begun early (15).

To avoid hyperglycemia or hypoglycemia, the comprehensive blood analysis includes the blood glucose values. The target blood glucose lies between 100 and 150 mg/dl. In the case of hyperglycemic values, old insulin is given.

Right ventricular failure

The treatment of pulmonary hypertension after heart transplantation is an essential component of the perioperative management. Often secondarily raised pulmonary vascular resistance (16) is found in graft recipients before the operation. Elevation of the pulmonary vascular resistance as a result of chronic heart failure with congested pulmonary circulation represents one of the main risk factors for primary graft failure (17,18). Pulmonary hypertension and right ventricular failure have a considerable influence on the postoperative morbidity and mortality rates (19).

Because a donor heart must first adapt to an often raised pulmonary vascular resistance, the danger of right ventricular dysfunction or failure threatens. Perioperatively the tendency toward pulmonary pressure elevation is increased by the use of the heart-lung machine, blood transfusions and protamin

administration (20,21). In addition there may be ischemia-reperfusion damage after lengthy ischemia and influences of pretreatment of the organ donor. Pharmacological treatment of the pulmonary hypertension is essential for the prognosis of patients after heart transplantation. After evaluation of the possibility of influencing the pulmonary circulation by pharmacological treatment, the maximal possible reduction in the right ventricular afterload in the early postoperative phase is a central aim of the hemodynamic management. Avoiding and treating right ventricular dysfunction includes optimizing the preload, maintaining adequate perfusion pressure, increasing contractility and reducing the right ventricular afterload. Different systemic approaches and inhalative therapy options are available.

Both the medicinal support of contractility by means of catecholamines and other inotropes, such as phosphodiesterase III inhibitors, and the systemic treatment with vasodilative agents are limited in their use post-transplant on account of the side effects to be expected.

The selective application of inhaled nitrogen monoxide (iNO) enables effective pulmonary vasodilatation by its quick effect and good compatibility. The therapeutic aim of iNO treatment is to prevent the development of pulmonary hypertension or to treat it. A number of publications have reported the use of iNO to lower the right ventricular afterload after heart transplantation (22-24). Inhalative NO has been used at the Deutsches Herzzentrum Berlin for many years to avoid or treat perioperative right ventricular heart failure after transplantation.

We studied a cohort of 164 heart transplant patients who were treated with iNO early postoperatively. As potentially advantageous effects we found a significant increase in the cardiac output of about 28% in the mean values. With a reduction in the pulmonary vascular resistance (PVR) of more than 40%, we can confirm the results of earlier studies of the application of nitrogen monoxide after heart transplantation. The he-

modynamic effects of the inhalative therapy were within the range that we expected and remained during the whole observation period. Alternatively, or in addition, the prostacyclin analogon iloprost (Ventavis 6x5-10 µg) can be given.

In 1999 it was pointed out for the first time that the phosphodiesterase-5 inhibitor sildenafil lowers the pulmonary vascular pressure, with only slight influence on the arterial systemic pressure. Initial studies showed that sildenafil lowers the raised pulmonary arterial blood pressure to an extent that is equal to the effects of prostaglandins and inhaled NO (25). Administration of sildenafil 3 x 20 mg p.o. seems to augment the hemodynamic effects of iNO, in line with the concept that these substances activate different regulatory systems of the vascular tone (26). This combination might also facilitate gradual weaning from iNO and reduce rebound phenomena.

In addition, controlled volume therapy using diuretic agents to avoid pulmonary hyperhydration, differentiated artificial respiration therapy (target: PaO₂: 100 mmHg, PCO₂: 30 mmHg, pH > 7.5, PEEP < 6) and the administration of inotropic substances are necessary. If the target values are not reached, an attempt to optimize the therapy is made using the intraaortic balloon pump. If the combination of all therapeutic options fails to restore satisfactory right ventricular function, the implantation of a temporary right ventricular support system, e.g. of a centrifugal pump (Lexitronix), should be considered (27).

With left ventricular insufficiency there is a significant increase in the LA pressure compared with the CVP. In addition there are signs that are similar to those of right ventricular insufficiency: falling cardiac output and CI, declining diuresis and increasing metabolic acidosis. Echocardiographic evidence of left ventricular insufficiency consists of LV hypokinesis, a reduction in the systolic wall motion velocities and a diastolic malfunction with increased relaxation time.

Therapeutic measures are, on the one hand, an increase in the dose of adrenalin to

> 25 ng/kg/min and, on the other hand, with raised peripheral vascular resistance of > 1000 dyn x sec x cm, the administration of phosphodiesterase inhibitors. In addition, a heart rate of 100-120 bpm should be aimed at by means of atrial stimulation under monitoring of the cardiac output. With low MAP (< 65mmHg), persistent oliguria and acidosis refractory to therapy in spite of high-dose catecholamine support, the implantation of an intraaortic balloon pump is indicated. Mechanical circulatory support would also be the final option.

Proposal for an algorithm of treatment for pulmonary hypertension and right ventricular dysfunction

- diagnosis and surveillance of the pulmonary hypertension and right ventricular dysfunction by means of a pulmonary artery catheter (CVP, MPAP, PCWP, CO, SvO₂) and transeophageal echocardiography
- avoidance of potentially PVR raising substances - ketamine, histamine-releasing muscle relaxants (mivacurium, atracurium)
- ensuring sufficient oxygenation (paO₂ 100 mmHg) by raising the FiO₂
- careful recruitment of nonventilated lung areas, use of a moderate PEEP level (< 10 mbar), avoidance of high peak pressure during artificial respiration
- avoidance of respiratory acidosis, moderate hyperventilation (pCO₂ 30-35 mmHg)
- neutralization of existing metabolic acidosis/ alkalization with sodium bicarbonate
- careful volume therapy under strict monitoring of the preload parameters/optimization of the cardiac filling pressures (CVP 10-12 mmHg, PCWP 12-15 mmHg)
- administration of systemic intravenous vasodilators (nitroglycerin, sodium nitroprusside, the prostacyclin (PGI₂) analogon iloprost (Ilomedin) with starting dose of 2 ng/kg/min)

- differentiated catecholamine therapy (with right ventricular dysfunction and pulmonary hypertension the contractility should be increased by giving dobutamin or adrenalin to ensure adequate systemic pressure and myocardial perfusion)
- infusion of inodilators such as the phosphodiesterase III inhibitors, the calcium sensitizer levosimendan, perhaps in combination with noradrenalin to maintain the right coronary perfusion pressure
- pharmacological treatment by inhalation: nitrogen monoxide 10-40 ppm, prostacyclin (PGI₂) analogon iloprost (Ventavis) 4-6 x 5-10µg
- start of iNO therapy for pulmonary arterial hypertension and clear right ventricular dysfunction occurring already when CPB is terminated
- intraindividual dose titration of iNO for optimal therapy effect with minimum dose (titration steps: 5, 10, 20, 30, 40 ppm iNO)
- early combination of iNO with phosphodiesterase V inhibitor (sildenafil - Revatio 3 x 20 mg p.o.) to augment the hemodynamic effects and avoid rebound phenomena.

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