Extracorporeal Circulation and Myocardial Protection in Adult Cardiac Surgery

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6.1 Conduct of Cardiac Surgery with Extracorporeal Circulation

Adult cardiac surgery can be performed in different ways. For the majority of cardiac surgical procedures, extracorporeal circulation is employed, i.e., a standard heart-lung machine is connected, whereas some operations such as off-pump coronary artery bypass surgery or the transcatheter aortic valve replacement (TAVR) can be carried out without it (see also ► Chapter «Minimally Invasive Surgery», Sect. 26.3.4). Minimized heart-lung machines basically consisting of a combined pump-oxygenator provide another tool, which is predominantly used for coronary artery bypass surgery and in a few centers for aortic valve replacement too.

6.1.1 Physiology During Extracorporeal Circulation

The purpose of extracorporeal circulation is the maintenance of peripheral perfusion and gas exchange during open-heart surgery and in cardiopulmonary failure. Therefore, extracorporeal circulation has a profound influence on the hemodynamic status and the oxygenation/acid-base status of the patient. The hemodynamic status is optimized via the pump flow, whereas the gas exchange is adjusted with the oxygenator. The blood flow over artificial surfaces necessitates anticoagulation and compromises end-organ function with time. A prolonged cardiac arrest requires cardioplegic myocardial protection.

6.1.1.1 Hemodynamics

The main task of circulatory support is the maintenance or reestablishment of a physiological systemic perfusion. As the required cardiac output (CO) is related to the patient's body size and shape, the necessary pump flow has to be normalized to the body surface (◘ Table 6.1).

The pump flow aimed at for standard adult open-heart surgery employing extracorporeal circulation is commonly defined to 2.4 L/min/m^2. In miniaturized systems, less hemodilution allows for a lower pump flow. The regulation of the mean arterial pressure is achieved by adjusting the pump output and the systemic vascular resistance (SVR). Under normal perfusion conditions, the central venous saturation (SvO_2) should be >65 %, and the serum lactate should be normal. A decreasing SvO_2 during extracorporeal circulation indicates insufficient circulatory support.

◘ **Table 6.1** Necessary pump flows related to the body temperature

Body temperature	Pump flow L/min/m^2
Normothermia	2.2–2.6
Mild hypothermia (32–35 °C)	2.0
Moderate hypothermia (26–31 °C)	1.5

Cerebral autoregulation keeps cerebral perfusion constant for an arterial blood pressure range of 50–150 mmHg. As brain metabolism decreases to as low as 40 % of normal during anesthesia, a perfusion pressure of 40–60 mmHg at full flow suffices during normothermia or mild hypothermia. In elderly hypertensive patients and those with significant carotid artery stenosis, however, one is inclined to maintain the perfusion pressure somewhat higher to prevent ischemic complications.

The oxygenator of the heart-lung machine usually contains a heat exchanger, which allows cooling and rewarming of a patient with a hypo-/hyperthermia system. Between 22 and 37 °C, cerebral perfusion remains constant, again due to autoregulation, and drops below 22 °C down to 15 % of normal. For that reason, the pump flow of the heart-lung machine can be lowered to 1.5 L/min/m^2 at a temperature of about 28 °C and even further with more pronounced hypothermia.

The benefit or harm of total body hyperperfusion is still unclear. In vasoplegic or septic patients, who normally present with high cardiac output and high central venous saturation, respectively, it is probably advantageous to offer a maximized pump flow. So far, high pump flows have been successfully offered only in patients with a total artificial heart, but this phenomenon has not been analyzed in proper studies (Copeland et al. 2003).

6.1.1.2 Pulsatility

The significance of pulsatility during extracorporeal circulation was a matter of research for many years. Frequently, there is an erroneous assumption that a roller pump generates only a

weak pressure profile. In fact, roller pumps create a high pulsatility with a hard pulse (d*p*/d*t*, pressure increase over time), which is dampened by the long tubing system as well as by the windpipe function of the aorta. For practical purposes, pulsatility can be most simply generated by varying the rotational speed of the pump, even with an a priori nonpulsatile centrifugal pump. However, most of the pressure pulse does not reach the aorta as the compliance of the oxygenator absorbs the pressure pulsation.

Important knowledge with regard to the physiological relevance of pulsatility has been gained with the introduction of axial and centrifugal flow pumps for long-term ventricular assist. Taken together, it seems that pulsatility is meaningless as long as the pump flow is normal or mildly elevated (>100 mL/kg/min). The same is true for an inadequate low flow (<40 mL/kg/min) with inadequate oxygen supply, anaerobic metabolism, and acidosis. Only in a borderline low but not critical range pulsatile perfusion may offer an advantage (Bartlett 2005). The reason for this is a stronger stimulation of aortic and carotid sinus pressure receptors by the nonpulsatile flow, which ensues a worse microcirculation following an increased endogenous catecholamine release. As the extracorporeal circulation always provides sufficient oxygen, this mechanism does not play a role in daily practice, i.e., nonpulsatile flow per se is not harmful.

6.1.1.3 Oxygen Consumption

The oxygen consumption (VO_2) is a global instrument to measure cardiopulmonary function and oxygen transport. In adults, oxygen consumption is 3–5 mL/kg/min and depends mainly on the tissue metabolism. At rest, oxygen consumption equals the basal metabolism and increases with physical activity accordingly (up to tenfold). With fever or following catecholamine application, it only rises about 50–60 %. In healthy people, there is also a linear relationship between oxygen consumption and heart rate. Oxygen is taken up by the lung as necessary, independent of lung function. Therefore, oxygen consumption can be measured with respiratory parameters. As the arterial oxygen content is independent of age and body size and oxygen requirement is regulated by cardiac output, the oxygen consumption (VO_2) can be calculated as product of the difference between arterial (C_aO_2) and venous (C_vO_2) oxygen content and the cardiac output according to Fick:

$$VO_2 = \left(C_aO_2 - C_vO_2\right) \times \text{Cardiac output} \times 10 \quad [\text{normal}: 200 - 250 \text{ mL/min}]$$

The arterial oxygen content (C_aO_2) defines the amount of oxygen, which is bound to hemoglobin and dissolved in plasma, and can be calculated with the following formula (arterial oxygen saturation S_aO_2)[1]:

$$C_aO_2 = \left(\text{Hb} \times 1.39 \times S_aO_2\right) + \left(P_aO_2 \times 0.003\right) \quad [\text{normal}: 20.4 \text{ mL } O_2/100 \text{ mL blood}]$$

The central venous oxygen content (C_vO_2) can be calculated in a similar way (venous oxygen saturation S_vO_2):

$$C_vO_2 = \left(\text{Hb} \times 1.39 \times S_vO_2\right) + \left(P_vO_2 \times 0.003\right) \quad [\text{normal}: 15.7 \text{ mL } O_2/100 \text{ mL blood}]$$

The arteriovenous oxygen difference ($AVDO_2$), which is normally 4–6 mL O_2/100 mL blood, is a parameter of tissue perfusion. A high difference (>6 vol.%) is seen with physical activity and cardiovascular decompensation and a low difference during hypothermia and sepsis.

The systemic oxygen delivery (DO_2) is fourfold higher as the oxygen consumption (VO_2) and can be calculated from the arterial oxygen content and the cardiac output and therefore depends on the amount of hemoglobin, its saturation, as well as the arterial partial oxygen tension. Accordingly, oxygen extraction describes the quantity of oxygen which actually participates at the gas exchange. The normal level is 26 ± 2 %. Calculation is as follows:

$$O_2ER = \frac{VO_2}{DO_2} \times 100$$

DO_2 is independent of the patient's size:

$$DO_2 = C_aO_2 \times CO \times 10 \quad [\text{normal}: 800 - 1000 \text{ mL/min}]$$

If the oxygen delivery declines, oxygen consumption first remains normal, i.e., more oxygen is retrieved in the periphery and the central venous

1 S_aO_2 = arterial oxygen saturation, 1.39 = Hüfner's constant (1 g hemoglobin can bind 1.39 mL of oxygen theoretically), P_aO_2 = arterial partial oxygen tension, and 0.0003 = Bunsen solubility coefficient

oxygen saturation drops. Only when DO_2 is no more but twice of the oxygen demand, an oxygen debt and anaerobic metabolism develop. A 1:1 use of delivered oxygen is impossible since a few tissues with a low oxygen need (skin, tendons, body fat) are relatively oversupplied.

In the daily routine of cardiac surgery, oxygen delivery is hardly ever determined, as oxygenation can be analyzed quite reliably with pO_2 and oxygen saturation. In critically ill patients, this can be problematic since more oxygen can be available with normal hemoglobin and a pO_2 of 40 mmHg as in an anemic patient with a pO_2 of 100 mmHg. Interestingly, the human organism has physiologic regulatory mechanisms which always aim at a normalization of DO_2. In this regard, cardiac output increases in case of anemia or hypoxia until normal levels are regained. In chronic hypoxia, the number of red blood cells increases, additionally. Artificially ventilated, hypoxic, anemic, and hypermetabolizing patients should therefore be generously treated with red blood cell transfusion, and not only the FiO_2 (fraction of inspired oxygen) of the ventilator increased.

Carbon dioxide elimination (VCO_2) corresponds closely to the oxygen consumption. However, the carbon dioxide does not have a linear relationship with increasing exercise. At about 70 % of maximal oxygen consumption, carbon dioxide elimination rises exponentially, and a non-compensated metabolic acidosis occurs. The relationship between carbon dioxide production and oxygen consumption is termed respiratory quotient ($RQ = VCO_2/VO_2$), which is also dependent on nutrition. In Europe the respiratory quotient is about 0.82.

The pCO_2 in arterial blood is 40 mmHg and is kept constant by autoregulation. A metabolic increase in carbon dioxide production is followed by an increased respiratory elimination. Accordingly, carbon dioxide elimination is not only dependent on hemoglobin and cardiac output but also on respiration. As the carbon dioxide elimination via the lung is much more effective than oxygenation, it remains intact for a long time in case of severe pulmonary dysfunction.

6.1.1.4 Gas Exchange During Extracorporeal Circulation

During extracorporeal circulation as long as the heart is ejecting, gas exchange occurs by both the lung and the oxygenator. Once the aorta is cross-clamped, the lung cannot contribute to gas exchange. For oxygen transfer through the oxygenator, especially during aortic cross-clamp, the pump volume plays an important role as the oxygen transfer increases almost linearly with the pumped volume. Further influencing variables are related to the properties of the oxygenator. All available oxygenators have a different internal resistance and oxygenation performance. The so-called rated flow of an oxygenator determines its capacity, i.e., the flow at which venous blood ($S_vO_2 = 75\,\%$) with a hemoglobin of 12 mg/dL can be still fully oxygenated. For most oxygenators, maximal rated flows are about 7 L/min. As long as the pump flow is below this limit, all blood is fully saturated, and the oxygen content is determined by the blood flow and the arterial oxygen content. The *sweep gas* is the ventilating gas blown into the oxygenator, which is either a mixture of oxygen and carbon dioxide (heart-lung machine) or pure oxygen (ECMO). In exclusive carbon dioxide elimination, the gas flow can be raised up ten times (gas: blood = 10:1).

If blood is fully saturated, the maximum oxygen uptake capacity corresponds to the arteriovenous oxygen difference ($AVDO_2$). With low hemoglobin and a high central venous saturation, the maximum oxygen uptake capacity is diminished. It can be counteracted by an augmentation of the pump flow. In low flow situations, more oxygen can be provided only by an increase of the oxygen uptake capacity.

With a *venoarterial perfusion*, the arterial blood reinfused is saturated to 100 %, and the pO_2 can be increased up to 500 mmHg (commonly, only 150–200 mmHg are used!). If pulmonary function would be totally lost, the left ventricular blood would be identical with the right atrial blood, which would ensue a saturation of about 75 % and pO_2 of 35 mmHg. In the body, the well-oxygenated perfusate would mix with the badly/non-oxygenated blood from the lung. With the assumption of a 50 % perfusion by the extracorporeal circulation, an oxygen content of c. 18 mL/100 mL blood with a saturation of 90 % and a pO_2 of 55 mmHg would be achieved (Bartlett 2005).

In case of *venovenous perfusion*, which is performed only as an ECMO treatment, the P_aO_2 and the arterial saturation in a hypothetically complete lung failure would be identical to the post perfusion central venous saturation. In a venovenous

ECMO, the arterial saturation would not raise higher than 95 % and would be typically even lower, P_aO_2 would be only around 40 mmHg, and the patients would be cyanotic and hypoxic (Bartlett 2005). However, normally, cardiac output in these patients is compensatorily increased and the systemic oxygen supply sufficient. An improvement of lung function increases arterial oxygenation, so that recovery of native pulmonary function can be monitored by the difference of arterial and venous saturation.

As in the native lung, carbon dioxide elimination in the oxygenator is much more efficient than oxygen uptake. Carbon dioxide elimination during extracorporeal circulation is (as in the native lung) mainly determined by the properties of the oxygenator and hardly by the pump flow. An increase of the membrane surface or the gas flow improves carbon dioxide elimination, but not the oxygen uptake.

In both venoarterial and venovenous ECMO, carbon dioxide (but not oxygen) levels can be adjusted to any desired level by choosing the respective membrane surface and the appropriate gas flow. In clinical practice, the oxygenator is usually oversized, and increased carbon dioxide elimination with a respiratory alkalosis can develop if the gas flow is not reduced. This overdimension can be useful for long-term use when the gas exchange surface gradually declines.

6.1.1.5 pH Management: α[Alpha] Stat and pH Stat

The gas exchange by the oxygenator does not only allow sufficient oxygenation and elimination of carbon dioxide, it also has a profound impact on the acid-base balance and the blood pH. As changes in the acid-base balance and blood pH have significant consequences in the physiology of the circulation, close monitoring and an adequate management are crucial.

There are two possibilities for the pH and pCO_2 management. With lower body temperatures, pCO_2 drops and the pH increases with 0.017 °C, i.e., at 25 °C the pH is 7.6. Employing the *α-stat* management, the pH changes are not counterbalanced; a relative alkalosis is the consequence. With the *pH-stat* approach, the temperature related pH changes are counterbalanced with an increased carbon dioxide application to maintain pH as in respiratory acidosis. In case of the α-stat management, the cerebral blood flow correlates with cerebral oxygen consumption during hypothermia as the cerebral auto regulation remains intact. It is the temperature regulation type in poikilothermic animals, where the degree of ionization of several important enzymes remains intact. Accordingly, the α-stat management seems to be more physiologic and is mostly preferred in adult perfusion. The advantage of the pH-stat approach, which is found in hibernating animals, is the better cerebral perfusion due to the carbon dioxide-related vasodilatation. This technique is partially favored in pediatric surgery (see also ► Chapter «Advances in Cardiopulmonary Bypass for the Neonate and Infant», Sect. 7.3.2.2).

6.1.2 Anticoagulation During Extracorporeal Circulation

Intact vessel endothelium has active and passive antithrombogenic properties such as the release of prostacyclin and endothelium relaxation factor, which inhibit platelet aggregation. It also activates the physiologic anticoagulant protein C and inactivates thrombin.

The artificial surfaces inside the oxygenator, the reservoir, the pump, and tubing (PVC, polyurethane, silicone) have no endothelial coverage and are thrombogenic. There is immediate platelet adhesion and consecutive thrombus formation. An activation of the coagulation cascade, the kinin-kallikrein system, the fibrinolytic system, and the complement system follows. The intrinsic coagulation pathway is initiated by the factor XII high-molecular-weight kininogen-prekallikrein complex, whereas the extrinsic cascade is activated with the release of tissue phospholipids. The median sternotomy also releases tissue thromboplastin, which activates platelets as well. The hemodilution during extracorporeal circulation further reduces the concentration of anticoagulation factors, platelets, and physiologic anticoagulants protein C, protein S, and antithrombin III.

Due to the activation of the coagulation systems by the surgical procedure and the use of the heart-lung machine, a strict anticoagulation is necessary. This is generally accomplished with heparin at a dose of 300–400 IE/kg. This dose is termed «full heparinization.» During surgery, anticoagulation is monitored with the activated clotting time (ACT). An ACT of 350–450 s is considered ade-

quate. In case of heparinized minimized extracorporeal systems, an ACT of >250 s seems sufficient. After termination of cardiopulmonary bypass, a 1:1 antagonization of heparin with protamine normalizes the ACT to a level of about 120 s.

6.1.2.1 Heparin

Heparin was discovered at the Johns-Hopkins University in Baltimore in 1916 and was introduced into clinical practice in the 1930s (McLean 1916). In 1939, it became evident that a plasmatic factor is necessary for the anticoagulant action of heparin. The identification of this factor, termed antithrombin III, succeeded not before the 1970s (Brinkhous et al. 1939).

Standard heparin (unfractionated heparin, UFH, chain length ≥18 saccharides) is a mixture of polysaccharides (negative loaded sulfated glycosaminoglycans) and is mainly obtained from porcine small bowel and bovine lungs. Fractionated low-molecular-weight heparin (LMWH, chain length 5–17 saccharides) has a shorter chain length and differs with regard to the various coagulation factors.

Both types of heparin bind antithrombins (AT), predominantly AT III, by which a complex is formed, which accelerates the activity of AT III a thousand times. UFH acts faster as LMWH, since it inactivates not only the prothrombinase complex (consisting of the activated factor X, activated factor V, calcium ions, and phospholipids) as does LMWH but also thrombin. Further mechanisms of action include the inactivation of the factors IX, XI, XII and kallikrein, and the binding of calcium ions, which augments the anticoagulant properties. Because of the different effectiveness, the heparin dosage is standardized in international units (IU) and not in milligram (mg). One unit of heparin prevents coagulation of 1 mL citrate plasma after addition of calcium chloride at 37 °C for an hour. AT III is substituted at levels <50 % of normal because of its importance.

It is noteworthy to recognize, that thrombin is not totally inactivated during extracorporeal circulation despite high dosages of heparin. As a consequence, thrombus formation may occur in the clinical setting despite full heparinization.

Apart from the anticoagulation properties, heparin exhibits various other traits. It increases fibrinolysis by release of tissue plasminogen activator (tPA) and has an anti-inflammatory effect by hindering granulocyte migration into the tissue.

6.1.2.2 Heparin-Induced Thrombocytopenia (HIT) and Heparin Analogues

During treatment with heparin, thrombocytopenia can develop, where two different types can be distinguished:

- Heparin-induced thrombocytopenia type 1 (HIT 1): 2–4 days after the start of heparin treatment, the count of platelets mildly decreases due to direct activation. Within a few days, the number of platelets spontaneously normalizes without therapeutic means. The exact incidence is unknown. In the literature, reported incidences vary from 1 to 25 % with unfractionated heparin, while LMWH heparins are told to have a lower risk.
- Heparin-induced thrombocytopenia type 2 (HIT 2): The HIT 2 occurs less often and manifests after 4–14 days with a much more dramatic drop of platelet numbers. The underlying pathophysiology bases on an antibody formation against heparin bound to antithrombin III. In about 75 % of cases, the heparin-platelet factor 4 (H-PF 4) complex is the causative antigen. The antibody, mostly IgG, recognizes H-PF 4 and activates platelets via the Fc receptor leading to platelet aggregation. Despite the thrombocytopenia, bleeding complications are infrequent, whereas thromboses with so-called white clots are reported to form in arterial and venous vessels in 50–70 % of cases (Greinacher et al. 2003). HIT 2 is a life-threatening complication with a mortality rate of more than 20 %.

Patients with a HIT 2 syndrome must not be treated with heparin, i.e., heparin therapy has to be stopped immediately. Anticoagulation can only be performed with *alternative drugs*, of which a few are available (Magnani 1993; Warkentin and Greinacher 2003) (■ Table 6.2):

- *Argatroban* (Argatra™): Argatroban is a synthetic direct thrombin inhibitor (arginine analogue), which is only used in patients with HIT 2. The dosage is adjusted with the aPTT, which is 1.5–3 times augmented. The metabolism is mostly hepatic and elimination over the feces. Therefore, renal failure is not problematic. As half-life is only 50 min, argatroban is the mostly used alternative drug to replace heparin, also in ECMO therapy.

Table 6.2 Heparin and alternative anticoagulants for extracorporeal circulation

Anticoagulant drug	Mechanism of action	Neutralization	Administration and dosage	Control parameter and therapeutic range	Elimination and half-life (HL)
Heparin, UFH	Inhibitor of thrombin and prothrombinase complex	Protamine 1:1	I.v. bolus: 300–400 U/kg	ACT >400 s	(40 %) Binds to endothelium, macrophages, and plasma proteins –5–15 min, thereafter renal elimination
					HL: 60–90 min
Argatroban (Argatra)	Synthetic direct thrombin inhibitor (arginine analogue)	Not possible	I.v. bolus: 0.3–1 mg/kg	ACT >400 s	Liver, HL: 52 min
			Infusion: 2–40 µg/kg/min		
Bivalirudin (Angiomax)	Synthetic direct thrombin inhibitor (arginine analogue)	Not possible	I.v. bolus: 1 mg/kg	Kaolin-ACT >400 s, ecarin clotting time (ECT): 400–500 s	Proteolysis, kidney c. 20 %
			Infusion: 2.5 mg/kg/h		HL: 25–34 min
Danaparoid (Orgaran)	Anti-factor Xa	Not possible		Factor Xa: 1.5 ± 0.3 U/mL	Kidney: 40–50 %
					HL (anti-Xa): 19–24 h
Lepirudin (Refludan)	Direct thrombin inhibitor	Not possible	I.v. bolus: 0.25 mg/kg	Ecarin clotting time (ECT)	Catabolic hydrolysis kidney c.50–60 %
			Infusion: 0.5 mg/min	Plasma levels: 3.5–4.5 µg/mL	HL: 1.3 h

- *Bivalirudin* (Angiomax™): Bivalirudin is a synthetic bivalent reversible thrombin inhibitor (polypeptide containing 20 amino acids), which has been occasionally used for extracorporeal circulation in HIT 2 patients. A rather short half time of only 25–34 min due to a proteolytic degradation independent of liver and kidney function is advantageous (renal elimination 20 %). Moreover, bivalirudin can be cleared via dialysis (Almond et al. 2006). The dosage is monitored with the ecarin clotting time, which is a meizothrombin generation test that can be used to measure the activity of the direct thrombin inhibitors. It should be increased to 400–500 s. A longer-term use of bivalirudin has been reported in ECMO therapy, where the ecarin clotting time was kept at 300–350 s (Koster et al. 2007).
- *Danaparoid* (Orgaran™): Danaparoid sodium is extracted from porcine intestinal mucosa and is a mixture of low-molecular-sulfated glycosaminoglycans (heparan sulfate 84 %, dermatan sulfate 12 %, chondroitin sulfate 4 %) with only low activity against antithrombin but strong AT III-mediated anti-factor Xa activity. The cross-reactivity with HIT 2 antibodies is low. The monitoring of anticoagulation is only possible by analyzing factor Xa levels as no antidote exists. Accordingly, overdosing may lead to bleeding complications. The biocompatibility is close to 100 %; the half-life is 19–24 h, being hardly affected by renal insufficiency (Wilde and Markham 1997).
- *Lepirudin* (Refludan™): Lepirudin is a recombinant hirudin (single-stranded polypeptide), which is produced with genetically engineered yeast cells ([Leu1, Thr2]-63-desulfohirudin). It binds noncovalent without the aid of cofactors to thrombin and inhibits its prothrombotic activity. Thus, lepirudin is a selective and irreversible thrombin inhibitor. The dosage is guided by the activated partial thromboplastin time (aPTT). With high dosages at an aPTT >70 s as it is necessary for extracorporeal circulation, the validity of aPTT is limited, and the measurement of the ecarin clotting time (measurement of anti-IIa activity) is superior (Greinacher et al. 2003). Lepirudin undergoes only minimal metabolism in the liver, and up to two thirds are eliminated unaltered via the kidney. Half-life is about 1.3 h and considerably prolonged in case of renal failure.

If patients just have a HIT 2 history without detectable antibodies, surgery can be performed with heparin, and the bleeding risk will be lower than with intraoperative alternative anticoagulation. As new antibodies may be generated with the repeated heparin use, immediately after this second surgery, anticoagulation has to be changed to alternative drugs in all cases with history of HIT 2. Due to the significant bleeding risks with alternative anticoagulation, there is a new discussion about considering heparin use during extracorporeal circulation even in the presence of HIT antibodies.

Heparinized systems do not require full heparinization. However, these systems renounce the sucker as the collected blood would coagulate in the reservoir despite heparinization. Heparin is covalently bound on the inner surface (e.g., with the Carmeda technique) of all blood-contacting elements including cannulas, tubing, oxygenator, and filter and can remain efficacious over months without provoking systemic coagulation. A development of HIT 2 has not been reported so far. A routine use of the heparinized system is hindered by the increased costs.

6.1.2.3 Platelet Aggregation Inhibitors

Platelet aggregation inhibitors (◘ Table 6.3) are an integral part of modern interventional cardiology of coronary artery disease. Especially the long-term success of percutaneous interventional stent placement is significantly related to the combined treatment with acetylsalicylic acid (aspirin) and thienopyridine derivates (clopidogrel). These platelet inhibitors as well as a medication with GP IIb/IIIa inhibitors (Aggrastat) increase the risk for bleeding complications in a surgical procedure. Even if a high bleeding tendency does not manifest in all patients, it seems advantageous to wait prior to surgery until the drugs' platelet-inhibiting properties ceased, if possible. For acetylsalicylic acid medication, halting the medication for 5–7 days is usually sufficient; the best control parameter is the normalization of the bleeding time. In emergency situations, such as unstable angina, acute myocardial infarction, or PTCA complication, a delay of surgery is not possible, but the surgical procedures can still be performed with an acceptable risk, which in general is limited to an increased use of blood and blood products.

The significance of excessive thrombocytosis is not well known, but successful open-heart

Table 6.3 Platelet aggregation inhibitors used in cardiac surgery

Drug	Mechanism of platelet inhibition	Reversibility	Administration	Elimination half-life	Recovery of platelet function
Aspirin	COX-1 inhibitor	Irreversible	Oral (1× daily)		Production of new platelets
Thienopyridine	ADP P2Y12 receptor antagonist	Irreversible	Oral (1× daily)		Production of new platelets
Ticlopidine					
Clopidogrel					
Prasugrel					
Ticagrelor	ADP P2Y12 receptor antagonist	Reversible noncompetitive	Oral (2× daily)	7 h	80 % recovery by 72 h
Abciximab	Fibrinogen receptor antagonist (GP IIb/IIIa)	Monoclonal antibody	Intravenous		≥50 % recovery by 48 h
Eptifibatide	Fibrinogen receptor antagonist (GP IIb/IIIa)	Reversible	Intravenous	2,5 h	50 % recovery by 4 h
Tirofiban	Fibrinogen receptor antagonist (GP IIb/IIIa)	Reversible	Intravenous	2 h	4–8 h
Cilostazol	PDE inhibitor	Reversible	Oral (2× daily)	11–13 h	
Dipyridamole	PDE inhibitor and other mechanisms		Oral	14 h	

From Ferraris et al. (2012); used with permission

Table 6.4 Surface-coating techniques

Trade name	Type of surface coating	Manufacturer
Bioline	Covalent heparin binding	Maquet
Carmeda	Covalent heparin binding	Medtronic
Physio	Synthetic phosphorylcholine coating (heparin-free)	Dideco-Sorin
Softline	Synthetic polymer coating (heparin-free)	Maquet
Trillium	Covalent heparin coating	Medtronic
X-coating	Synthetic polymer coating (poly-2-methoxyethylacrylat, heparin-free)	Terumo

surgical procedures with a heart-lung machine have been described.

6.1.2.4 Surface Coating

The aim of surface coating (Table 6.4) is to augment biocompatibility of foreign material, i.e., to lower the risk of thrombus formation. Since many years, several different techniques of surface coating, mainly various types of heparin coating, are tested experimentally and in clinical practice. Distinct advantages and disadvantages of the coating techniques are not evident, so far. However, it seems important to achieve complete coverage of the whole extracorporeal circuit from «tip to tip» as only that allows abdication of full heparinization. As many adverse events manifest only after longer-term extracorporeal circulation, the value of surface coating in the daily routine of extracorporeal circulation is controversially discussed.

For heparin coating, heparin is covalently bound to the artificial surface in order to mimic the antithrombogenic properties of heparan sulfate on the natural endothelium. The exact mechanism of action of the bound heparin is still unclear, but a diminished activation of complement, of proinflammatory cytokines, and of platelets has been widely demonstrated.

Polypeptides are attached to the artificial surface with electrostatic forces and van der Waals forces. As a consequence, the surface is hydrophilized and more rapidly moistened, which hinders the adhesion of plasma proteins.

The polymer coverage X-coating (PMEA = poly(2-methoxyethylacrylate)) consists of two layers. A hydrophobic layer binds to the foreign surface; the hydrophilic layer is at the luminal side and in contact to the blood. The hydrophilic layer forms a barrier by an uptake of water, allowing the blood proteins to move along without adherence and denaturation. Platelet adhesion is inhibited too.

6.1.3 Myocardial Protection

The aim of myocardial protection is to create conditions which allow a surgical procedure on the heart while myocardial integrity and function are preserved. The optimal conditions are not the same for all operations but depend on the pathology of the heart and the surgical requirements to repair it. Finally, there is always an individual compromise between optimal surgical conditions and ideal myocardial protection (Guyton 1995).

6.1.3.1 Concepts of Myocardial Protection

Several concepts have been devised for myocardial protection, which can all be employed consecutively (Guyton 1995):

- **Myocardial Protection Prior to Cardiac Arrest**

The induction of anesthesia in patients with impaired left-ventricular pump function or coronary heart disease is more dangerous than in healthy patients. Several reports have shown that an injury of myocytes starts already before initiation of extracorporeal circulation in 18 % of patients (Delva et al. 1978). As many patients reach the operation room in a suboptimal status (agitation, tachycardia, hypoglycemia, hypovolemia) and are thus opposed to an increased risk, a careful hemodynamic and pharmacological optimization should be performed prior to surgery in elective cases.

The decline of mean arterial pressure during extracorporeal circulation below 60 mmHg can lead to subendocardial ischemia even in healthy patients. Accordingly, special care has to be taken to maintain sufficient perfusion pressure in patients with coronary artery disease. If necessary, perfusion pressure should be augmented with α-adrenergic drugs like norepinephrine, despite the risk of significant side effects. Furthermore, the heart-lung machine implies hemodilution, which also may lower subendothelial perfusion (Kleinman et al. 1978). Hypothermia can impair autoregulation of local blood flow and translate into local hypoperfusion. In hypertrophied hearts and those with coronary artery stenosis, ventricular fibrillation can also favor subendothelial ischemia. The same is true for overdistension of the ventricle. Therefore, an immediate vent placement should follow if a distended ventricle cannot be rapidly arrested by clamping the aorta.

■■ Lowering the metabolic rate during cardiac arrest

After optimal preparation for the ischemic arrest, the latter should be withstood in the best way possible. For the myocardium, rapid surgery with brief ischemia is best—this, however, is rarely possible. Therefore, the heart is protected with hypothermia and cardioplegia.

It is long known that the heart can be protected with hypothermia. In the nineteenth century, Van't Hoff demonstrated a decline of myocardial metabolism of 50 % for every 10 °C drop in cardiac temperature. Thus, the use of hypothermia during cardiac surgery was suggested early and initially applied to the whole body. Later, surface cooling with irrigation of cold saline was introduced.

Simple cardiac surgical cases are operated upon with adequate cardioplegia in normothermia. In more difficult cases with extended ischemic times exceeding 1.5–2 h, hypothermia around 30 °C is mostly favored. Only if a long ischemic time beyond 2 h is anticipated, hypothermia below 28 °C is recommended. Nowadays, even rather complex operations with ischemic times of 3 h can be performed safely if myocardial protection is adequate.

Many earlier publications emphasized a cooling rate not to exceed 1 °C/min for the patient. This is no longer true as an improved gas exchange management at the membrane oxygenator allows faster cooling, as it is our practice for years. Yet, the temperature difference between heat exchanger and blood in the oxygenator should not exceed 10 °C, even if scientific evidence is lacking. If deep hypothermia below 20 °C is aimed at, e.g., for aortic arch surgery, administration of an α-blocker can be helpful as it enables a more evenly and faster temperature decline. During deep hypothermia, a circulatory arrest is relatively well tolerated for up to 45 min.

Historically, rewarming was even more carefully performed than cooling, since the high pO_2 in bubble oxygenators could lead to gas embolism. Since introduction of membrane oxygenators and a precise pO_2 management to achieve 150 mmHg at the outlet, the formation of microbubbles is much less, and therefore a faster rewarming is possible. Nevertheless, blood temperature in the oxygenator should not exceed 38 °C.

The underlying pathophysiology during hypothermia and rewarming are only partially known. With cooling, the metabolism responds rather inconsistent, which also leads to a significant alteration of myocardial homeostasis. This means that the supply of the hypothermic heart with oxygen and substrates does not maintain normal cellular function (Cameron and Gardner 1988). A further disadvantage, especially for deep hypothermia, is a significant postoperative coagulopathy and cardiac edema formation.

Cardioplegia is more effective in protecting the heart than hypothermia alone. The oxygen consumption of an arrested heat is only about one fifth of a normal beating heart at 37 °C. The combination of hypothermia and cardioplegia potentiates cardiac protection. Studies have shown that even rather cold solutions (2 °C) do not harm the myocardium, but the cooling of heart with infusion of cold solutions is quite heterogeneous, especially in patients with coronary artery disease. A topical cooling may help to create a more uniform hypothermia. The optimal myocardial temperature is still discussed controversially. While crystalloid cardioplegic solutions are applied with 4 °C, the assumed temperature optimum for blood cardioplegia is higher (15–20 °C). Even normothermic blood cardioplegia protocols have been established in some institutions (Abah et al. 2012). Due to the higher temperature range, blood cardioplegia requires reinfusion about every 20 min.

A Favorable Metabolic Milieu Increases Safety During Cardiac Arrest

During cardioplegic arrest, cardiac metabolism is altered. Accordingly, it is important to maintain an adequate metabolic milieu during cardioplegic arrest. This task is in part accomplished with cardioplegia in various ways:

1. By minimizing interstitial and intracellular edema formation
2. By hindering loss of cellular metabolites
3. By supplying sufficient substrates for the metabolism
4. By preserving an equated acid-base balance

Frequently, the metabolism is not properly kept up, as coronary artery stenosis and myocardial hypertrophy lead to regional underperfusion and hyperperfusion. Moreover, cardioplegia can be washed out in part by collateral flow. In this regard, blood cardioplegia seems advantageous as blood is the natural perfusion media with all nutritive elements and excellent buffering properties. In the same way, reconvalescence of ischemic myocardium with blood cardioplegia is probably superior (see below).

Controlled Reperfusion Lowers Structural and Functional Myocardial Damage

The problem of reperfusion injury caused by oxygen free radicals and a massive increase of endothelial permeability with cellular edema formation is well known. The increasing tissue pressure hinders reperfusion, and the tissue edema leads to an increased diffusion distance through the tissue. Both worsens metabolism. Several concepts for controlled reperfusion with warm and cold, low calcium, and substrate-enriched solution have been designed and present advantages in experimental and clinical studies. However, there is still no defined optimum and no concept for daily routine established for controlled reperfusion after cardiac ischemia (Mohan Rao and Simha 2011).

6.1.3.2 Cardioplegia Strategies

Over the years, a wide spectrum of cardioprotective (protecting the myocardium) strategies has evolved. Multidose crystalloid cardioplegia was introduced in 1976. Cold blood cardioplegia followed in 1978 with the idea to add myocardial nourishment to the substrate-depleted heart (Buckberg 1995). The idea of warm cardioplegic reperfusion («hot shot») was to limit reperfusion damage (1977). The rationale for this cardioprotective action is that amino acids like glutamate and aspartate play an important role in myocardial intermediary metabolism and their relative importance is further enhanced during and after ischemia (Caputo et al. 1998). Before the release of the aortic cross-clamp, a normothermic substrate-enriched blood cardioplegia is applied, mostly via the coronary sinus to actively resuscitate the ischemically damaged, substrate-depleted myocardium by maximizing the kinetics of repair. Thereafter, reperfusion with normothermic blood follows until cardiac activity resumes (Ascione et al. 2008). Considering the induction of cardioplegia as first phase of reperfusion, warm cardioplegic induction was extensively studied in 1983 to prove the «active resuscitation» of the heart (Buckberg 1995) (◘ Table 6.5).

The techniques of delivery include single and multidose, continuous, antegrade, and retrograde (either, both alternatively or simultaneously). For single-dose cardioplegia application, low- and high-volume concepts exist, which means that some centers administer less than 1000 mL and others more than 2000 mL. The rationale for multidose cardioplegia derives from the occurrence of noncoronary collateral flow, which replaces the carefully formulated cardioplegic solution with systemic blood at the temperatures prevailing in the surrounding systemic arteries. Additional benefits of multidose cardioplegia are formulations that include buffering and hypocalcemia which may limit reperfusion damage during subsequent doses (Buckberg 1995).

Microplegia is a more recent concept. It is marketed as a cost-effective strategy utilizing undiluted blood with targeted amounts of cardioprotective additives, adjustable to meet the changing requirements of each patient during cardioplegia procedures (Menasché 1996, 1997). As it delivers blood from the circuit and additives for cardioplegia with minimal crystalloid, it is sometimes called blood cardioplegia without the crystalloid. Standard blood cardioplegia contains crystalloid in a 4:1 or 8:1 dilution. The constituents of microplegia total 1.5 mL of crystalloid for each 100 mL of circuit blood, equalling a ratio of 66.6:1.

Regardless the delivery technique, no superiority of either could be proven. As a consequence, cardioplegia administration is far from being

Table 6.5 Crystalloid preservation solutions

Bretschneider's solution	Histidine	180.0 mmol/L
	Mannitol	30.0 mmol/L
	Histidine × HCl (H_2O)	18.0 mmol/L
	Sodium chloride	15.0 mmol/L
	Potassium chloride	9.0 mmol/L
	Magnesium chloride (6 H_2O)	4.0 mmol/L
	Potassium hydrogen-2-oxoglutarat	1.0 mmol/L
	Tryptophan	2.0 mmol/L
St. Thomas solution	Sodium chloride	110.0 mmol/L
	Potassium chloride	16.0 mmol/L
	Magnesium chloride	16.0 mmol/L
	Sodium hydrogencarbonate	10.0 mmol/L
	Calcium chloride	1.2 mmol/L
University of Wisconsin solution	Potassium lactobionate	100.0 mmol/L
	Raffinose	30.0 mmol/L
	Potassium phosphate	25.0 mmol/L
	Magnesium sulfate	5.0 mmol/L
	Adenosine	5.0 mmol/L
	Glutathione	3.0 mmol/L
	Allopurinol	1.0 mmol/L
	HAES (polyhydroxyethyl starch)	5.0 %
	Heparin	1000 U/L
Celsior solution	Sodium hydroxide	100.0 mmol/L
	Lactobionate	80.0 mmol/L
	Mannitol	60.0 mmol/L
	Histidine	30.0 mmol/L
	Glutamate	20.0 mmol/L
	Sodium chloride	15.0 mmol/L
	Magnesium chloride (6 H_2O)	13.0 mmol/L
	Glutathione	3.0 mmol/L
	Calcium chloride (2 H_2O)	0.25 mmol/L

From Schmid (2014); used with permission

standardized, and every surgeon chooses the most convenient and in his eyes superior technique to deliver cardioplegia.

6.1.4 Side Effects of Extracorporeal Circulation

6.1.4.1 Respiratory System

Open-heart surgery employing cardiopulmonary bypass can compromise the whole respiratory system including the lung, bronchial system, chest wall, and diaphragm, especially if there is extensive preexisting disease. The most frequent comorbidities are nicotine abuse and pulmonary emphysema, but chronic bronchitis, subclinical pneumonia, preoperative lung edema, and muscular weakness are also important. During extracorporeal circulation with the heart arrested, the lung is only perfused by the bronchial arteries since the pulmonary blood flow is interrupted or virtually absent. It is unclear whether the alveolar cells suffer ischemia/reperfusion injury during surgery. Various other factors including hemodilution, lowered oncotic pressure, microembolism, and release of vasoactive and inflammatory substances increase vascular permeability, perivascular edema, and bronchial secretion. The combination of the aforementioned factors leads to a decline of pulmonary compliance and functional residual capacity, as well as to an increase of breathing work. Moreover, a sternotomy or thoracotomy has an immense influence on the compliance of lung and chest wall (Peters et al. 1969). Three days after surgery, a maximal loss of compliance of about 30 % is present, and after 6 days, a significant decrease of compliance is still evident (Vargas et al. 1992). Lung volume and pulmonary flow rates drop immediately after surgery and can persist for 6 weeks (Berrizbeitia et al. 1989). Disconnection of the ventilator, the complete withdrawal of the positive end-expiratory pressure (PEEP), and single-lung ventilation frequently have the consequence of a relevant gas exchange disorder during weaning off cardiopulmonary bypass and thereafter. Immediately after extubation, functional residual capacity is decreased by 40–50 % and hardly recovers during the first 72 h (Stock et al. 1986). The entry into the pleural space and the preparation of the ITA vessels have no isolated impact.

The problem of postperfusion syndrome, also known as «pump lung,» is rather historical. In the early days of extracorporeal circulation, 15–25 % of patients suffered fatal postoperative lung failure. During autopsy, atelectasis, abnormal elastic fibers, but no edema or cellular infiltrates were seen (Baer and Osborn 1960). Due to comparable findings in postmortem examination, it is assumed that the postperfusion syndrome is a special type of adult respiratory distress syndrome (ARDS). Nowadays, ARDS is a rare finding after extracorporeal circulation and mostly a consequence of intrabronchial bleeding due to a traumatic lesion following intubation or right heart catheterization. The impact of blood product transfusion is still unclear.

6.1.4.2 Renal System

The influence of extracorporeal circulation on kidney function has been already studied 40 years ago. At that time, a decline of renal blood flow and glomerular filtration during extracorporeal circulation of 25–75 % was reported (Lundberg 1967; Porter et al. 1966). These alterations were only partially reversible within the early postoperative days. Likely underlying causes were hypothermia, renal vasoconstriction, and the loss of pulsatile perfusion. In summary, the best results with nonpulsatile perfusion could be achieved with a mean systemic blood pressure >65 mmHg and a pump flow of 30–50 mL/kg (Hilberman et al. 1979; Yeboah et al. 1972).

It has been shown that the preoperative organ function of the kidney and all other organs is decisive for its behavior during extracorporeal circulation. The most important negative impact factors are age >70 years, diabetes mellitus, heart failure, and a prolonged duration of surgery and/or cardiopulmonary bypass, respectively (Bhat et al. 1976; Stafford-Smith et al. 2008).

During surgery with extracorporeal circulation, a certain degree of kidney injury seems to be unavoidable. Renal flow, creatinine clearance, water elimination, and urine volume decrease. A mild proteinuria is common. Hemodilution ameliorates these side effects by improving renal blood flow, glomerular filtration rate, creatinine and water clearance, and urine excretion.

After surgery, hypotensive periods are the main reason for acute renal failure. A diminished renal perfusion augments production and release of renin and angiotensin II, which further impair renal perfusion. Kidneys with preexisting

dysfunction and those with ischemic damage are very susceptible to additional injury. Overall, a postoperative oliguric renal failure increases the mortality and morbidity risk eightfold.

6.1.4.3 Gastrointestinal System

The incidence of severe gastrointestinal complications is estimated to be about 1 %, i.e., gastrointestinal complications during and after extracorporeal circulation are rare (Filsoufi et al. 2007). Until now, there are only few data on this topic available. In contrast to the lung, there seem to be no typical gastrointestinal consequences or lesions during extracorporeal circulation. In a clinical inconspicuous setting, blood chemistry may present elevated liver enzymes, an increase of serum amylase, and in animal studies also mild edema formation in intestines and pancreas. The main cause of gastrointestinal complications is probably hypotension, however, still an unproven assumption. Arterial hypotension seems to promote gastric acidosis, where a relationship between gastric pH level and duration of extracorporeal circulation has been found. In the intestines, an increased endotoxin release suggests a disturbance of the intestinal barrier (Andersen et al. 1993).

The role of extracorporeal circulation in the development of nonocclusive mesenteric ischemia (NOMI) is unclear. Nevertheless, NOMI is a serious complication in open-heart surgery and associated with a significant mortality (Klotz et al. 2001). Initially, NOMI leads to intestinal distension and paralytic ileus, which is followed by intestinal necrosis.

Human and animal studies on liver and pancreas during nonpulsatile extracorporeal circulation demonstrate a considerable decline of organ perfusion. Complications are less when pulsatile flow is established (Ranmsey 1995).

6.1.4.4 Endocrine System

Through many physiological interactions, extracorporeal circulation affects the endocrine system in multiple ways. A distinct analysis of the hormonal changes is difficult as further parameters including age, comorbid conditions, and anesthetics also have impact on the endocrine system.

▪▪ Glucose/Insulin

Alterations of glucose and insulin levels are primarily influenced by infusions and priming liquids of the heart-lung machine. The consecutive impact of the extracorporeal circulation on pancreatic function and glucose metabolism is different in diabetic and nondiabetic patients:

- In nondiabetic patients, glucose levels during extracorporeal circulation are elevated and normalize thereafter within 1–2 days. When employing hypothermia, the increase in glucose levels is less pronounced and starts immediately with rewarming of the patient (Kuntschen et al. 1985). High postoperative glucose levels have been associated with a poor neurological recovery after cerebral events (Longstreth and Inui 1984). The insulin level declines with induction of anesthesia, remains low during extracorporeal circulation, and rises again with rewarming.
- Diabetic patients suffer insulin deficiency during extracorporeal circulation, which is far smaller under hypothermic conditions. During rewarming of the patients, insulin levels can increase up to sixfold and then normalize within 3 days (Crock et al. 1988).

▪▪ Thyroxine

With the initiation of extracorporeal circulation, triiodothyronine (T3) levels drop and consecutively recover to about 60 % of normal. Thyroxine (T4) and thyrotropin (TSH) decline insignificantly, although heparin augments free T3 and T4 levels. The combination of a low T3, low normal T4, and normal TSH is also seen in numerous other diseases and also in trauma patients and is called euthyroid sick syndrome or low T3 syndrome (Holland et al. 1991).

▪▪ Parathyroid Hormone (PTH) or Parathormone

With going on cardiopulmonary bypass, PTH levels decrease and normalize again 90 min after termination of extracorporeal circulation. The impact of hypothermia is unclear and controversially discussed (Bannister and Finalyson 1995).

▪▪ Antidiuretic Hormone (ADH), Also Known as Vasopressin or Arginine Vasopressin (AVP)

Trauma and surgical stress promote ADH release, which can be counteracted by an appropriate narcosis (with opioids). Despite anesthesia, cardiopulmonary bypass increases ADH, which returns to normal the following day (Kuitunen et al. 1993).

6.2 Components of Extracorporeal Circulation Systems

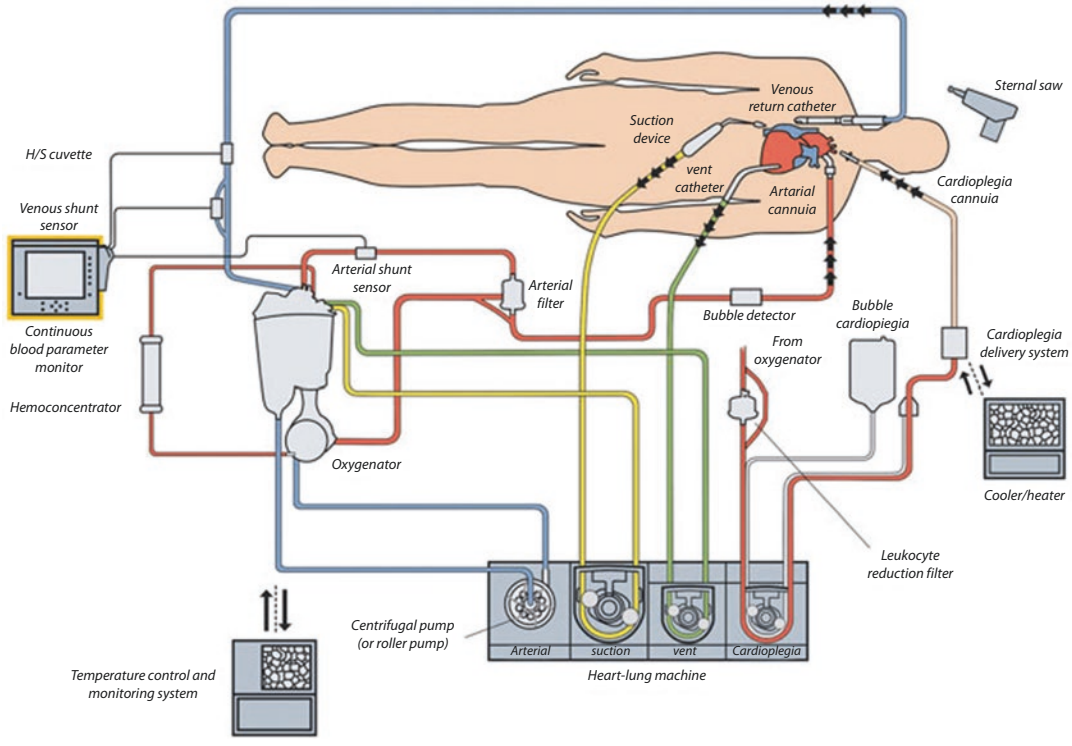
The standard heart-lung machine is the central part of the most frequently utilized type of extracorporeal circulation (ECC). It is the workplace of the perfusionist, who monitors and pilots the extracorporeal circulation during the surgical procedure. All steerable parts of the device are mounted on a console and aligned to each other in order to be easy to read and to reach and to keep the workplace ergonomically optimized.

6.2.1 Standard Heart-Lung Machine

The heart-lung machine (◘ Fig. 6.1) enables surgical procedures on the arrested heart by maintaining systemic perfusion and replacing pulmonary function, also. Moreover, operations can be executed with the heart beating. Surgery on neighboring structures, which would not be tolerated hemodynamically without extracorporeal support, is also facilitated avoiding considerable blood loss in these cases, too.

With a standard heart-lung machine circuit, blood is drained from the right atrium or the caval veins with cannulas. With the aid of a pump, it is transported through an oxygenator back into the aorto-arterial tree. An arterial filter lowers the load of systemic emboli (microparticles and air bubbles). One or more suckers or vent lines collect blood from the operative field and take it back to the reservoir after passing a venous filter with an integrated bubble trap. Usually, there is also a separate system for cardioplegia application. Multiple sensors with an online display for line pressures, temperatures, electrolyte concentrations, and blood gases guarantee monitoring of the physiologic milieu and enhance the security of the extracorporeal circulation system.

A hypo-/hyperthermia system can be optionally used to cool and to rewarm a patient during the surgical procedure. The hypo-/hyperthermia system cools down and heats a water circulation, which is connected to the oxygenator and thus alters blood temperature.



◘ **Fig. 6.1** Configuration and setup of a standard heart-lung machine (Courtesy of Terumo)

6.2.1.1 Pumps

The arterial pump and the oxygenator are the most important components of the extracorporeal circulation. The main task of a pump is to sustain sufficient blood flow for systemic circulation and to assure adequate end-organ perfusion during cardiac arrest. The pumps further allow unloading and venting of the heart, suction with various types of suckers, and also application of cardioplegic solution.

▪▪ Roller Pump

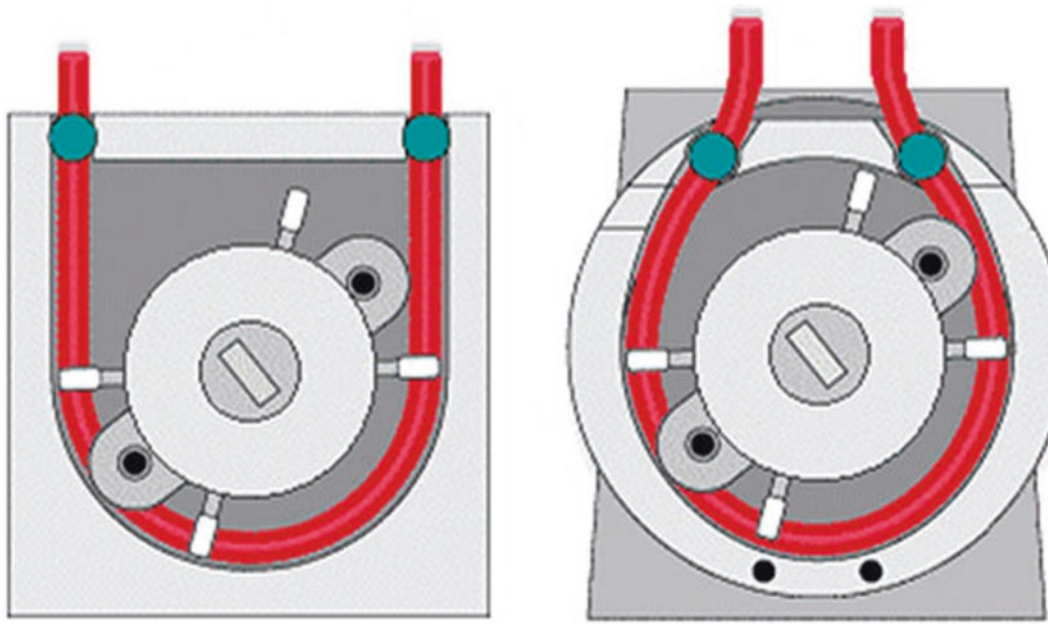
The traditionally used pump is the peristaltic roller pump (◘ Fig. 6.2). A peristaltic pump works by an alternating pattern of squeezing and releasing flexible tubing to move fluid through the pump. The roller pump consists of a stator and a rotor, connected to a drive unit. The stator is a pump bed holding an elastic silicon tube which is arranged around the rotor. Small amounts of blood are trapped in the silicon tube and massaged forward along the tube by rotating cylindrical rollers. Valves are not necessary for unidirectional flow. Several types can be discriminated with regard to number of rollers, with double roller pumps being the mostly used.

Pump flow primarily depends on the rotational speed and the diameter of the tube. It is important for the rollers to be occlusive, i.e., the wipers are totally compressing the lumen of the tube, as backflow would considerably increase the degree of hemolysis.

The design of the roller pumps is variable and has undergone certain modifications with time. The pure U form has merged into an omega style, which is hemodynamically beneficial. A lower-pressure increase (dp/dt) reduces the stress of blood components. There are large and small pumps and double-headed pump consoles available. All are driven by electric motors adjustable from 1 to 250 rpm.

▪▪ Centrifugal Pump

Centrifugal pumps (◘ Fig. 6.3) are hemodynamically equally effective as roller pumps, but much less traumatic to blood elements (cells and proteins), and hence advantageous. The inlet in the central axis takes up the blood which is then expelled at the peripheral outlet by rotation of the pump head. As there is no valve, blood can pour through the pump in both directions (depending on the pressure gradient), if the pump head halts. Accordingly, the arterial line has to be immediately clamped in case of a pump stop. The pump flow is continuous and pulseless and increases with the rotational speed. However, in contrast to the roller pump, the pump flow of a centrifugal pump is dependent on preload and afterload. It rises with an augmented preload and a reduced afterload. A deleterious increase of the line pressure, e.g., with a kinking tubing, therefore does not occur. But due

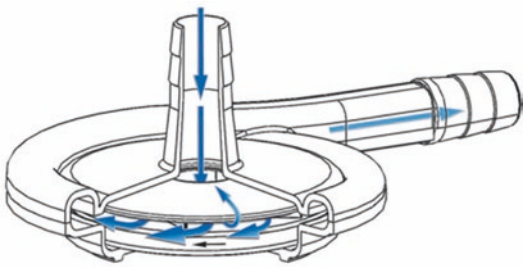


◘ **Fig. 6.2** Roller pumps from Stöckert/Sorin (Courtesy of Sorin)

to the preload and afterload sensitivity, surveillance of the line pressure is not sufficient. A flow measurement is mandatory and can be achieved with electromagnetic or Doppler sonography devices. Centrifugal pumps can generate forward pressures up to 900 mmHg; maximal suction is about 400–500 mmHg. As a consequence, cavitation phenomena as well as gaseous and microparticle embolism are reduced (◘ Table 6.6).

6.2.1.2 Oxygenators

The purpose of an oxygenator (◘ Fig. 6.4) is to replace the gas exchange function of the lung during extracorporeal circulation. An oxygenator not only enriches venous blood with oxygen but also eliminates carbon dioxide. By doing this, blood elements should not be traumatized, and the priming volume to fill the oxygenator should be as low as possible. Basically, there are different possibilities for a blood and gas interaction: blood can be fed to a gaseous phase (film oxygenator—obsolete in clinical practice), gas can be added to blood (bubble oxygenator—rarely used anymore), or blood and gas can be separated by a membrane (today's membrane oxygenator).



◘ **Fig. 6.3** Schematic drawing of a centrifugal pump (Courtesy of Maquet)

The 300 million alveoli of the human lung generate a gas exchange area of 160 m^2. Within the alveoli, the red blood cells come as close as 0.7 µm to air, which allows sufficient diffusion of oxygen and carbon dioxide in either way. In the oxygenators, the blood capillaries are much larger, and the gas exchange area is considerably smaller as compared to the human lung.

▪▪ Bubble Oxygenator

Bubble oxygenators consist of three components including the oxygenation chamber, the defoamer, und an arterial filter. These components can be aligned in series or in a concentric manner from inside to outside. First, oxygen is passed through a dispersion plate into the venous blood. Bubbles are generated, with their size depending on the outlet size of the dispersion plate, gas flow, blood viscosity, and surface tension of the blood. Gas exchange takes place at the surface of the bubbles. Smaller bubbles offer a larger gas exchange area but are more difficult to be removed afterward. Nitrogen cannot be added to the gas inflow as a significant risk for embolism would evolve due to its low solubility.

The elimination of the gaseous bubbles occurs in the defoaming chamber. The defoamer is mainly composed of polypropylene fibers and polyurethane foam, coated with antifoam silicone. The remaining air bubbles are destroyed or finally trapped by a filter (125–175 um). Important functional parameters are blood flow behavior and velocity, surface active substances, and absorption mechanisms. As nitrogen cannot be supplemented as part of the gas flow, considerable nitrogen losses can occur. Finally, the blood is collected in a reservoir. The maximal operating time of a bubble oxygenator is limited to 6–8 h.

◘ **Table 6.6** Clinically available centrifugal pumps

	ROM (1/min)	Flow (L/min)	Pressure (mmHg)	Bearing	Heparin coating
Biomedicus 540 and 550®	0–4500	0–9.9	–300–999	Mechanic	Carmeda
Delphin® (Sarns)	0–3600	0.3–9.9	0–700	Mechanic	X-coating
Capiox® (Terumo)	0–3000	0–8.0	0–800	Mechanic	X-coating
Rotaflow® (Maquet)	0–5000	0–9.9	0–750	Magnetic	Bioline
Centrimag® (Levitronix)	1500–5500	0–9.9	0–600	Magnetic	–

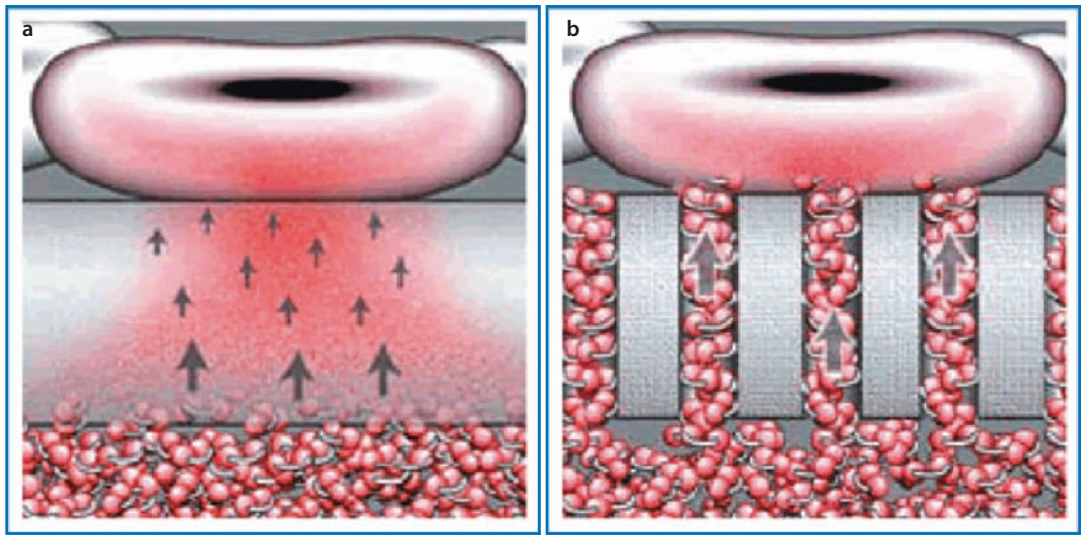


Fig. 6.4 Oxygenator with semi-permeable silicone membrane **a** and microporous membrane **b** (Courtesy of Maquet, Sorin and Medtronic)

Membrane Oxygenator

The membrane oxygenator mimics the human lung better as blood and gas are separated by a gas permeable membrane. The blood is pressed in between numerous small capillaries. The membrane was formerly manufactured of cellulose, polytetrafluorethylene, and polyethylene; now there are only two types left: diffusion membrane (silicone) and microporous membrane oxygenators.

Microporous Membrane Oxygenators

Nowadays, the majority of oxygenators are made of capillaries with a micro porous surface structure. The membrane of these microporous capillary membrane oxygenators consists of polypropylene, a hydrophobic material containing pores with a size 0.03–0.07 μm in half of the surface. Gas exchange is by free diffusion through the pores, i.e., blood is in direct contact to the gas. Since the membrane surface is hydrophobic and the pores are small, no ultrafiltration of water occurs and gas and serum remain separated. If the gaseous pressure in the capillaries exceeds that of blood, gas can pass the micropores. So membrane oxygenators have a lower diffusion resistance and an excellent carbon dioxide transfer without the need of enlarging the membrane surface. Longer use may lead to adsorption of plasma proteins to the wall of the pores, which renders them hydrophilic and decreases surface tension. Eventually, plasma leakage can develop necessitating an oxygenator replacement.

Diffusion Capillary Membrane Oxygenators

In this type of oxygenator, the capillaries are additionally covered with a thin (<1 μm) skin as a barrier to prevent plasma leakage. This barrier is frequently composed of silicon rubber, a homogeneous nonporous material. The gas exchange occurs (as before) in the microporous part by diffusion. The driving force is the diffusion pressure or the difference of partial pressures of the gases, respectively. Within the barrier, transportation is based on a solution process, i.e., the gases dissolve in the polymer matrix, penetrate the barrier, and pass out again. The diffusion rate is related to the pressure drop and to the permeability of the membrane but independent of the gaseous substances. As the pressure difference is high for oxygen (up to 720 mmHg) and low for carbon dioxide (45 mmHg), oxygen transfer is sufficient, and carbon dioxide elimination is more difficult. The diffusion of anesthesiology gases is limited due to their large molecule size.

The Newest Developments

are oxygenators with a polymethylpentene coating. A better gas transfer coefficient enables an unrestricted gas exchange, and plasma leaking during long-term use does not occur. Priming volume and pressure gradients are comparable to the microporous design.

Membrane oxygenators are considerably safer than bubble oxygenators since only few solid and gaseous emboli are generated and the regulation

of the gas exchange is simplified. In all membrane oxygenators, oxygen diffuses along a concentration gradient through a membrane according to Fick's principle, depending on the oxygen pressure gradient and the permeability of the membrane. Since gas and blood are physically separated, other gases like nitrogen or air can be added to alter the oxygen concentration (FiO_2) or transfer. The carbon dioxide elimination works similarly, as it diffuses along a concentration gradient from the venous blood to the gaseous phase. The exchange rate is related to the surface, the carbon dioxide gradient, and the permeability. A loss of nitrogen can be counteracted by a high nitrogen supplementation at the inflow gas (which is not possible in the bubble oxygenator).

The effective gas exchange area for adults in the current oxygenators is ranging from 1.3 to 2.5 m^2; the respective heat exchange area is 0.14–0.6 m^2. Transfer rates for oxygen and carbon dioxide may be as high as 450 mL/min. During long-term use (as in ECMO), aqueous vapor can condensate in the capillaries and compromise gas exchange. Nevertheless, membrane oxygenators have much longer run times than bubble oxygenator, they may run up to several weeks, and the impairment of the blood components is less.

6.2.1.3 Venous Reservoir

The venous reservoir (◘ Fig. 6.5) receives the venous return and the spilled blood from the operative field is collected by the suckers in a large container or bag. Drainage of the venous system and/or the heart is usually passive by gravity with the reservoir being mounted 40–70 cm below the level of the heart. Apart from the position of the reservoir, central venous pressure, cannula size, and tubing affect drainage. Cardiopulmonary bypass can run on rather low central venous pressures by partially exsanguinating the patient (minus 1–3 L), namely, shifting part of the combined patient/ECC circuit into the venous reservoir.

◘ **Fig. 6.5** Venous reservoir: hard shell (*left*) and soft bag (*right*) (Courtesy of Maquet)

Most reservoirs have an integrated blood filter. It is composed of Dacron wool or polyurethane foam and catches particles from 20 to 100 um, depending on the filter size. An incorporated bubble trap allows elimination of air bubbles. Furthermore, the venous reservoir offers access for drug application and blood sample withdrawal.

Technically, reservoirs can be constructed as a rigid container or a soft bag. The rigid systems are advantageous as they are larger, and volume estimation and air elimination are simpler. Likewise, priming and vacuum-assisted drainage are easier.

6.2.1.4 Bubble Trap and Arterial Filter

Bubble traps are incorporated as first element into the venous line, i.e., prior to the pump and oxygenator. Blood and air bubbles are split up by gravity and centrifugal forces, and the blood additionally passes a membranous sieve with a porosity of 40–200 um. The priming volume is about 150 cm^3, which is not problematic in a normal heart-lung machine but is of significance in a mini-ECC setting. Special air removal devices consist of combined bubble detection and bubble elimination, which functions as an automatic process in a rather effective manner.

Arterial filters are integrated into the arterial line prior to the blood returning into the patient. They also have a sieve with a pore size of 20–40 um, trapping air bubbles and small solid particles. A peculiar variant is the so-called dynamic bubble trap, which accumulates the bubbles in the midline stream and eliminates them from there.

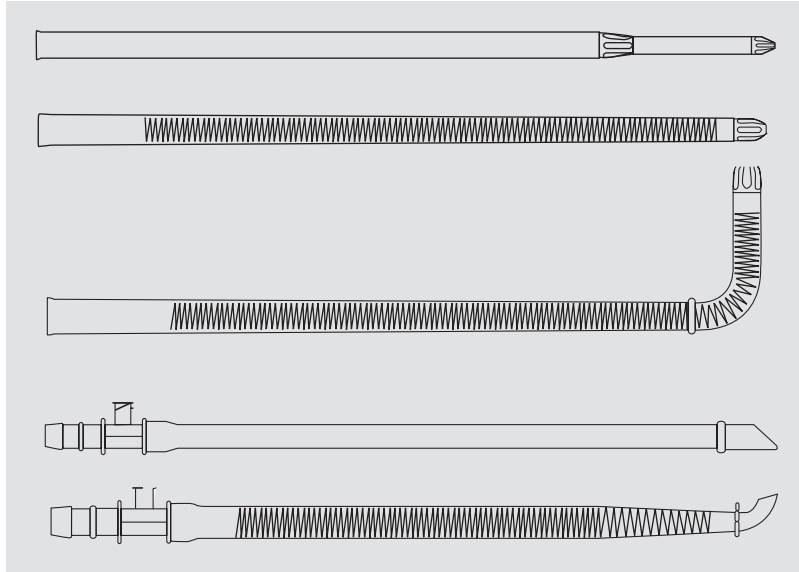
Bubble traps and arterial filters are available as single components as well as an integrated part of a complete system, e.g., cardioplegia sets. The sizes have to be adapted because of priming volumes and flow limitations in very small patients only. The efficacy of bubble traps and arterial filters is judged rather inconsistently. However, most studies demonstrate a reduction of air bubbles and microembolism in transcranial Doppler sonography measurements.

6.2.1.5 Gas Blender

With only few exceptions, oxygen and carbon dioxide transfer is determined by a gas blender. Gas flow can be altered from 0 to 16 L/min, and air can be supplemented so that an oxygen tension of 21–100 % can be offered to the patient. A high oxygen concentration leads to a higher pO_2 and consecutive enhanced oxygen transfer. In contrast, carbon dioxide transfer is governed by the gas flow. A higher gas flow accelerates carbon dioxide washout by better maintaining the pCO_2 pressure difference. Another way to regulate carbon dioxide exchange is to admix it to the sweep gas.

6.2.1.6 Cannulas and Tubing

Various cannulas (◘ Fig. 6.6) are available to connect an extracorporeal circuit to a patient. Standard cannulas are manufactured by a translucent flexible synthetic material. The cannula



◘ **Fig. 6.6** Curved and straight arterial cannulas, curved and straight venous wire-enforced cannulas, two-stage venous cannula (Courtesy of F. Merkle)

tips are composed of a rigid material, either of synthetic material or of metal. The cannula tips are also the narrowest part of the cannula and therefore responsible for pressure drops, jets, turbulences, and cavitation phenomena (vein collapse around the cannula due to excessive drainage). Cannulas can become either directly or indirectly (jets) most dangerous as they can lacerate the arterial wall (dissection!), loosen atherosclerotic plaques, and cause hemolysis. Hemolysis and protein disintegration may also occur with pressure gradients >100 mmHg. Kinking is prevented in all cannulas. Arterial cannulas are most often have a stiffened wall of various kinds, while venous cannulas have a metallic spiral reinforcement inside the cannula wall. Numerous cannula heads have been designed to accommodate the clinical needs. Angled cannula heads are advantageous for bicaval cannulation; single cannulas for the right atrium can be straight or angled. As drainage can be impaired with single (one-stage) right atrial cannulation, a so-called two-stage cannula was designed, which drains the superior caval vein indirectly via the right atrium and the inferior caval vein directly.

Central cannulation of the heart and/or the adjacent large vessels offers the best drainage and consequently provides the best cardiopulmonary support/temporary cardiopulmonary replacement. According to the planned procedure, the arterial cannula can be either inserted into the ascending aorta, the aortic arch, or brachiocephalic trunk. A more distal cannulation, especially in the aortic arch, reduces the risk for cerebral embolism. Extrathoracic but still central cannulation can be accomplished via the axillary, subclavian, or carotid artery. All aortic cannulas are introduced after a 5 mm stab incision and during a mean arterial pressure of 60–80 mmHg. They are fixed with purse-string sutures in the adventitial layer, which can be reinforced by pledgets. Thus, the aortic insertion can be sealed and the cannula fixed. Transmural stitches are avoided as they would increase the risk of subadventitial hematomas and continuous bleeding. During cannula placement, it is important to verify that the tip is readily inserted into the aortic lumen and directed toward the aortic arch. Extrathoracic cannulas are inserted in the same manner as any other peripheral cannula. Possible complications include vessel wall tearing and dissection (aortic dissection <1 %), dislodgement of atheromas, and thrombi (stroke !). A screening for endovascular atheromas can be performed by palpation, echocardiography, or with epiaortic ultrasound (Bolotin et al. 2005). The latter has been recommended in patients with a history of transitory ischemic attack or stroke, severe peripheral arterial occlusive disease, and palpable or visible aortic wall calcifications and even in any patient beyond an age of 50–60 years! The practicality of these measures has to be accessed on an individual basis. An extraordinary risk for thromboembolism and stroke is present in patients with a porcelain aorta, which is evident in 1.2–4.3 % of cases. A special protection system positioning a sieve as a filter (pore size 120 um) just before the aortic cannula did not gain widespread acceptance, even if clinical studies demonstrated collection of embolic dfebris in 97 % of patients (Banbury et al. 2003) (◘ Fig. 6.7).

The purse strings for the venous cannulas either into the right atrium or into the caval veins are best performed with transmural sutures. If the right atrium has not to be entered during the procedure, e.g., none or only left-sided structures are opened, a two-stage cannula placed into the right atrial appendage will sufficiently drain both caval veins. A surgical procedure involving entry into the right atrium or the presence of an intracardiac shunt mandates separate bicaval cannulation employing tourniquets around both caval veins also. Right-angled cannulas for individual caval cannulation may be least disturbing. The cannulation of the superior caval vein can be achieved at the base of the right atrial appendage, i.e., via the right atrium, with a long tip cannula, or by direct access to the vein with a short tip cannula. It is important not to injure the sinus node and to avoid vessel narrowing after removal of the cannula. The inferior caval vein is best entered 1 cm above the diaphragm, more laterally than anterior. Both a straight or angled cannula serve the purpose well (◘ Figs. 6.8 and 6.9).

A persisting left superior vena cava (LSVC), which is present in 0.3–0.5 % of patients (Wood 1956), is usually connected to the coronary sinus and therefore drains into the right atrium. In 10 % of these cases (unroofed coronary sinus), however, it drains directly into the left atrium. These very rare cases should be picked up clinically due to oxygen saturations only around 90 %, unless they are masked by a large ASD with a supervening left to right shunt.

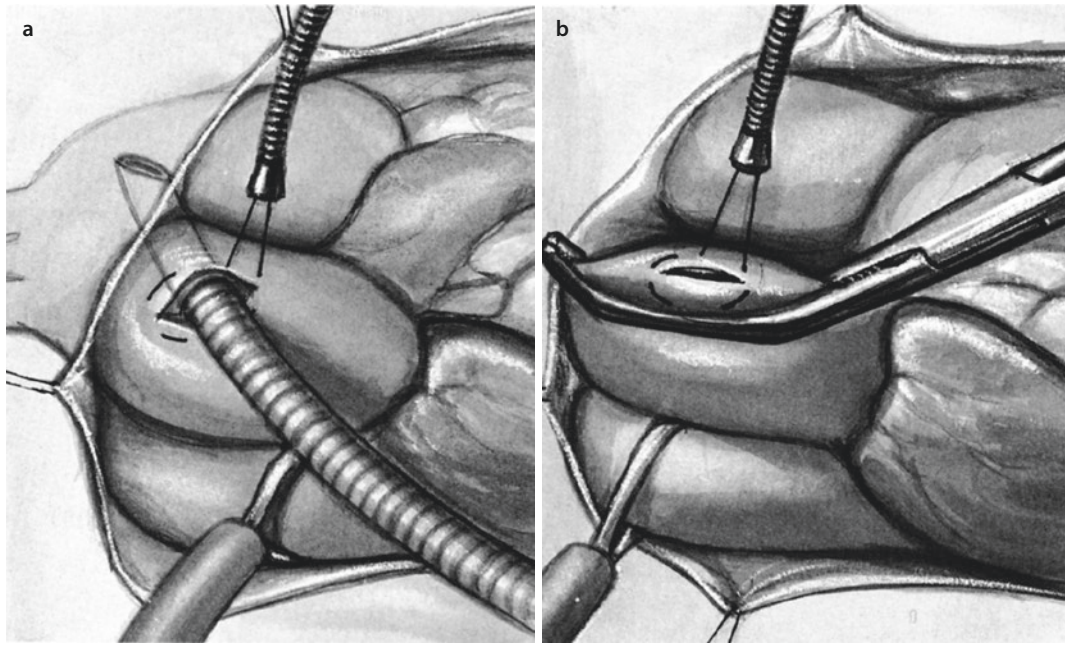


Fig. 6.7 Cannulation of ascending aorta. A purse-string suture is placed and the cannula inserted after a stab incision **a** or with the aid of a small Satinsky clamp in children **b**

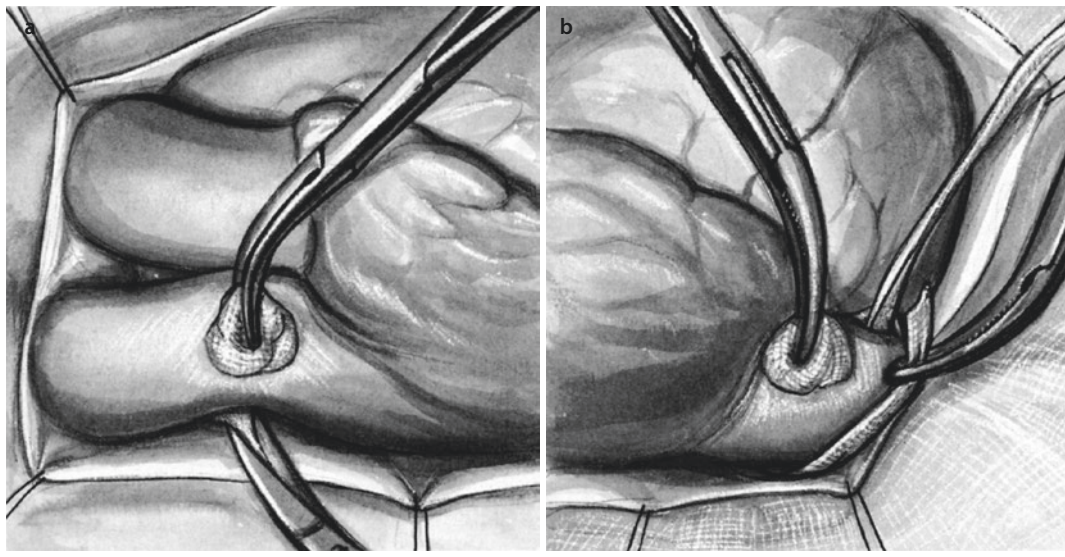


Fig. 6.8 Exposition of the superior caval vein **a**, the inferior caval vein is provided with a tourniquet **b**

Suspicion for any LSVC should arise when no or only a diminutive brachiocephalic vein or an unusually large/dilated coronary sinus is visible. In presence of a brachiocephalic vein, it may sufficiently drain the LSVC when temporarily or even definitely occluded. If probatory clamping of a LSVC without visible connection to the right side does not result in a left-sided caval pressure much higher than 15 mmHg, simple clamping may be allowed during ECC. Otherwise, clamping of the vessel could lead to venous stasis and finally to a cerebral impairment. In these cases, the left superior caval vein should be cannulated, either directly close to the left atrial appendage or via the coronary sinus. A retrograde cardioplegia has to be adapted to the anatomical findings.

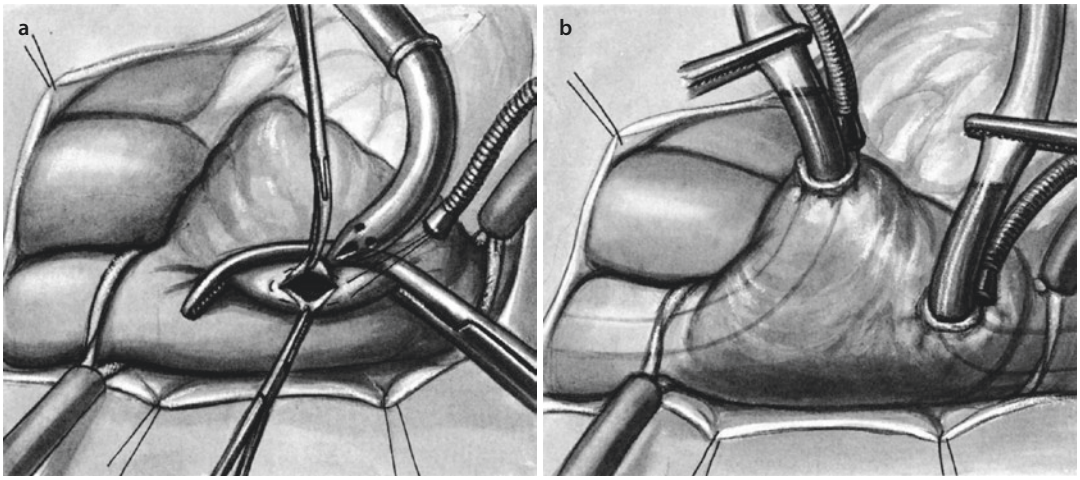


Fig. 6.9 Cannulation of the superior caval vein via the atrial appendage **a**; both caval veins are placed **b**

Absent or dilated coronary sinus may not allow for administration of retrograde cardioplegia.

The size of the aortic cannula is kept small to avoid extensive laceration of the aortic wall. However, the tip of the cannula is the narrowest part, where pressure drops and jets and turbulences develop which can injure the aortic wall from inside. Venous cannulas are chosen as large as possible to guarantee optimal drainage from the heart. According to Hagen-Poiseuille's law (at laminar flow), the resistance correlates with the 4 power of the radius of the cannula. Therefore, a short cannula with a large diameter allows for maximal pump flow.

At the arterial side, blood is propelled by the pump, i.e., flow resistance in cannula and tubing have to be overcome. The pressure in the arterial line rises in relation to the pump flow. Usually the flow is set, and the resultant pressure is measured. Line pressures up to 300 mmHg are tolerated. Systemic relationships of flow and pressure in cannulas and tubing are expressed with the help of the so-called M-figure. Small cannulas have a high shear stress which destroys blood cells. The critical limit of shear stress dependent hemolysis is unknown; in the literature, values from 80 to 400 N/m^2 have been reported. The limit for platelets is significantly lower with 10–35 N/m^2. The venous blood is mainly drained by gravity, where the central venous pressure and the hydrostatic pressure (difference in height between patient and reservoir) are the driving forces. With a known blood viscosity (c. 3 cP), the necessary minimal cannula size can be chosen.

Peripheral cannulation is an alternative to central cannulation. In standard surgical procedures with median sternotomy, it is no longer used, except for emergency situations including severe bleeding, cardiac arrest, acute aortic dissection, reoperation, and minimally invasive procedures. During recent years, the cannulation of the subclavian artery has proven very advantageous in patients with acute aortic dissection, since this vessel is only rarely involved in the disease, giving unrestricted flow access to the aortic arch. Mostly, the vessel is not directly cannulated. Instead, a Dacron graft (size 6–8 mm) is anastomosed to it in an end-to-side manner, and a straight aortic cannula is tied into it. Lacerations of the subclavian vein and the brachial plexus may occur but are infrequent. Apart from the subclavian vessels, iliac and femoral arteries as well as the jugular vein may serve as access for extracorporeal circulation. Arterial cannulas can be rather short; venous cannulas should be long enough to reach the right atrium in order to prevent collapse of the inferior caval vein resulting in poor drainage.

In contrast to intrathoracic cannulation, a peripheral access with a single venous cannula usually does not permit total bypass, i.e., complete mechanical support. Only 80 % of blood volume can be drained via peripheral cannulas, whereas 20 % of blood volume passes the lung. This means also that the maximal pump flow is lower as compared to central cannulation (3.5–4 L/min). With a femoral perfusion and a still ejecting heart, the arterial ECC blood hardly reaches the aortic arch.

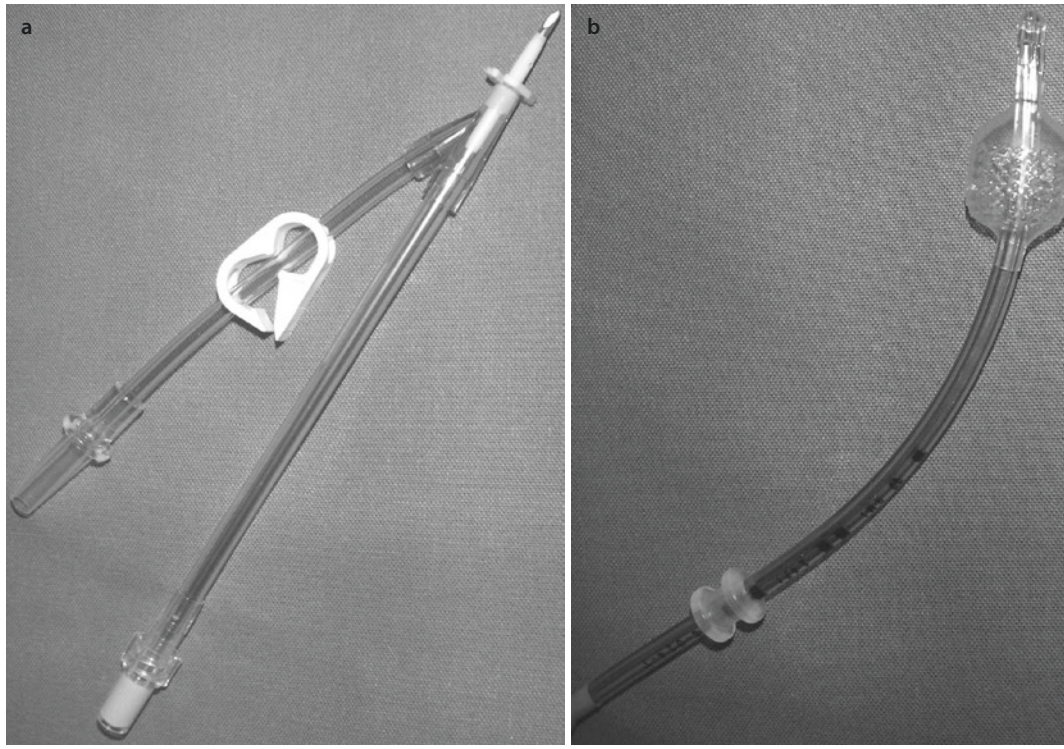


Fig. 6.10 Cardioplegia cannula with sidearm for venting **a**, coronary sinus catheter **b**

Venous drainage can be improved with suction by integrating a roller pump or centrifugal pump into the venous line or by connecting the hard shell reservoir to a vacuum. Venous suction for optimizing drainage has several advantages: (1) unloading of the right atrium and ventricle is improved; (2) the cannula size can be reduced by 25 %, which is very usefully in peripheral cannulation; (3) the extracorporeal circulation is less susceptible to an air block after lacerating of the right atrium; and (4) procedures at the pulmonary artery can be performed with a two-stage cannula.

The term «total bypass» is used when on full ECC flow, all systemic venous flow is forced into the venous cannulas by closing the tourniquets around the individual caval cannulas. This term may not be applicable for two-stage venous cannulation, although it may come close with excellent drainage.

6.2.1.7 Cardioplegia Administration

For the application of cardioplegia, a large bore sharp needle is sufficient. Alternatively, special catheters can be inserted and fixed with a suture. Most of the latter have a sidearm, which allows measurement of the aortic pressure during cardioplegia delivery. In case of retrograde cardioplegia administration, a balloon catheter is placed ventrally to the venous cannula with a purse-string suture and into the coronary sinus. There are self-inflating balloons and those to be manually inflated with the aid of a syringe. Catheter placement is simple and can be achieved even if only the right atrium and ventricle are prepared in redo procedures. Its highest value of retrograde catheters is in aortic root surgery as well as in coronary reoperations. Correct positioning can be judged best by digital palpation of the balloon just below the left atrial appendage. Failure of catheter placement is rare and then caused by a Chiari net (remnant of the embryologic large valve of the sinus venosus) or an extraordinary small coronary sinus. After initiation of extracorporeal circulation, a constant flow from the catheter must remain evident, despite proper venous drainage and low central venous pressure. If the heart is lifted up during retrograde cardioplegia, swollen veins including the posterior descending vein (V. cordis media) should be visible (Fig. 6.10).

6.2.1.8 Vent Placement

With institution of extracorporeal circulation, pulsatility decreases and with good drainage may finally cease on full flow and/or total cardiopulmonary bypass and an empty heart. However, as bronchial and Thebesian veins drain into the left atrium and ventricle even with total bypass, the left ventricle will fill and distend, or blood will spill into the operative field if the heart is entered and not vented after cross-clamping.

A vent catheter usually has a mandrel or a reinforced but flexible tip, which facilitates its placement. Main indication is a left-sided valve replacement or LV aneurysm resection. Thus, the operative field is kept bloodless, and de-airing the heart at the end of the procedure is easier. Standard approach is the right superior pulmonary vein. Cannulation through the interatrial groove just anterior to the pulmonary vein may prevent pulmonary vein obstruction in the rare event of tears in the vein requiring extensive sutures/repair. Alternatively, especially in emergency situations, vent placement can occur via the left ventricular apex after a stab incision. Insertion of the vent into the pulmonary artery trunk is also possible. For coronary artery bypass surgery, a vent is placed into the aortic root, often as a combined cannula for antegrade cardioplegia delivery.

6.2.1.9 Tubing

The tubing system connects the various components of the ECC with the patient. In many institutions, the ECC components are individually selected and preassembled in a custom pack, which eliminates the infectious risk almost completely. The length of the tubing must be appropriately sized to provide sufficient distance to the non-sterile heart-lung machine. In general, the diameter should be large enough to keep flow resistance and shear stress which impair blood components as low as possible. On the other hand, tubing should be shortest possible und small in diameter to allow minimal priming and low gradients along the tubing. Most commonly, for adult patients, the arterial line is 3/8″ in diameter and the venous lines 1/2″ in diameter.

Cannulas and tubing are transparent to facilitate the evaluation of the blood with regard to color, air bubbles, and clots. Most of the tubes are available with heparin coating, which is supposed to reduce the heparin need and thus lessens the risk of bleeding complications.

6.2.1.10 Open and Closed Systems

In open systems, the venous reservoir can be de-aired during operation. Mostly, the venous reservoir is built with a rigid housing and an integrated defoamer. The latter allows removal of air in a simple manner, but if the blood levels drop below a critical level, air embolism may occur. Therefore, a blood level sensor is necessary, which not only monitors the level and alarms in time but also stops the heart-lung machine automatically.

Closed venous reservoirs are flexible bags which can crumple. Air is trapped on top of it and can be removed via a valve. If the blood levels decrease, the walls of the bag collapse and prevent dislodgement of critical amounts of air to the patient.

Reliable data suggesting preference for one system over the other are not available; both systems are on the market with the rigid housing/open system taking the larger share.

6.2.2 Miniaturized Extracorporeal Systems

After more than 30 years of clinical success with standard ECC, about two decades ago the side effects of extracorporeal circulation became the focus of intensive discussion. Off-pump coronary artery bypass surgery (OPCAB) emerged, but the technical challenge of this new surgical technique could not be met by all surgeons. Even when OPCAB surgery could not convince the cardiosurgical community with clearly superior results, the desire for less traumatic tools and techniques remained and lead to the development of miniaturized extracorporeal systems. They combine an adequate safety standard with reduced side effects claimed (Remadi et al. 2004; Wiesenack et al. 2004).

A miniaturized heart-lung machine is not only a reduced size system but also a new concept of extracorporeal circulation. Its goal is a constant volume perfusion with minimal blood trauma, reduced hemodilution, less postoperative systemic inflammatory response syndrome (SIRS), lower transfusion requirements, and finally faster and better reconvalescence. The first mini-systems were slimmed standard heart-lung systems, i.e., suckers and the venous reservoir were left off and the tubing was shortened. The pump consisted (and still does) of a

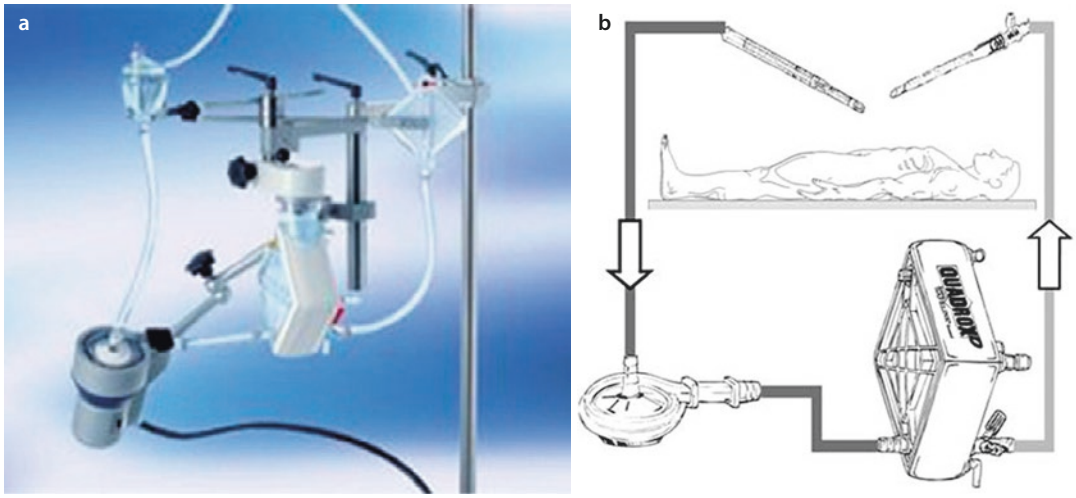


Fig. 6.11 MECC system. Set-up **a**, schema **b** (Maquet) (Courtesy of Maquet)

centrifugal pump and a low flow oxygenator with a small priming volume. Some systems are heparin coated including all tubing. A separate heating device is unnecessary as a heat exchanger is an obligate and integral part of each oxygenator. Bubble traps are optional. Cardioplegia is administered with low-volume techniques too. Most often, the Calafiore technique is employed, where arterial blood is deviated from the main line, enriched with potassium, and afterward reintegrated into the venous return (Calafiore et al. 1995). A systemic blood sucker does not exist as spilled blood is not immediately fed to the venous line to keep the circuit closed. Instead, it is collected and washed with a cell saver and returned to the patient thereafter.

All these individual procedures are not new, but their combination delineates a completely new principle of extracorporeal circulation. The main indication for miniaturized extracorporeal systems is coronary artery bypass (CABG) surgery where the cavities of the heart are not entered. An aortic valve replacement and a resection of a left ventricular aneurysm may also be achieved with a mini-system, but the surgical procedure is more complex and needs further refinements of the system, and the basic idea to prevent the blood air contact is partially undermined. It is self-evident that before starting valve surgery with a mini-bypass system, significant experience with coronary bypass surgery employing this system should have been obtained.

There are several mini-systems commercially available. Their components can be individually assembled, or the system can be purchased as a complete set. Due to the different technical features, the mode of operation of the systems varies. An optimum cannot be defined, yet.

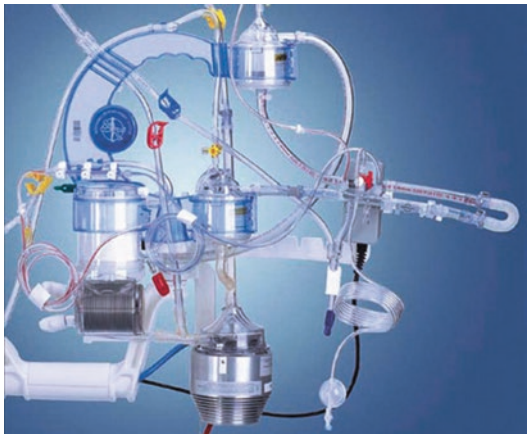
6.2.2.1 MECC System (Maquet®)

The MECC (*m*iniaturized *e*xtracorporeal *c*irculation) system (Fig. 6.11) was developed in the late 1990s and was the first mini-system which was commercially available. It is completely assembled from Maquet products (Maquet Cardiovascular, Rastatt, Germany; Wayne, NJ, USA):A Rotaflow® centrifugal pump, a Quadrox D® oxygenator with a diffusion membrane, and an optional venous bubble trap to eliminate circulating air bubbles. All components are heparin coated (Bioline®), allowing a short-term run of the device without full heparinization. This is truly advantageous for patients with a high bleeding risk. The arterial Quart® filter may be added as well but also increases the priming as does the bubble trap by 25 %. The preparation of the systems requires only about 1–2 min.

The Rotaflow® pump can propagate 4.0–4.5 L/min and has a priming volume of 32 mL. The Quadrox D® oxygenator offers a membrane surface of 2.4 m^2 and requires a priming volume of 250 mL. The great advantage of the MECC systems is that the bubble traps and the arterial filter can be easily left out which lowers the basic priming volume to 500 mL and hemodilution is minimal. No other system provides this opportunity.

6.2.2.2 Resting Heart System (Medtronic)

The Resting Heart® system (◘ Fig. 6.12) is a complete set based on Medtronic products (Medtronic, Minneapolis, MN, USA): the centrifugal Bio-Pump Plus® and their Affinity NT® membrane oxygenator. The whole system is heparin coated with the Carmeda® technology. The Bio-Pump Plus® can propel 1–6 L/min. The oxygenator has a membrane surface of 2.5 m^2 and a priming volume of 250 mL. An interesting feature is the Affinity Venous Air Removal Device (VARD®). With the help of two ultrasound detectors, air bubbles are recognized, an audiovisual signal is turned on, and the bubbles are automatically removed. A filter with a pore size of 38 um is integrated in the VARD®.



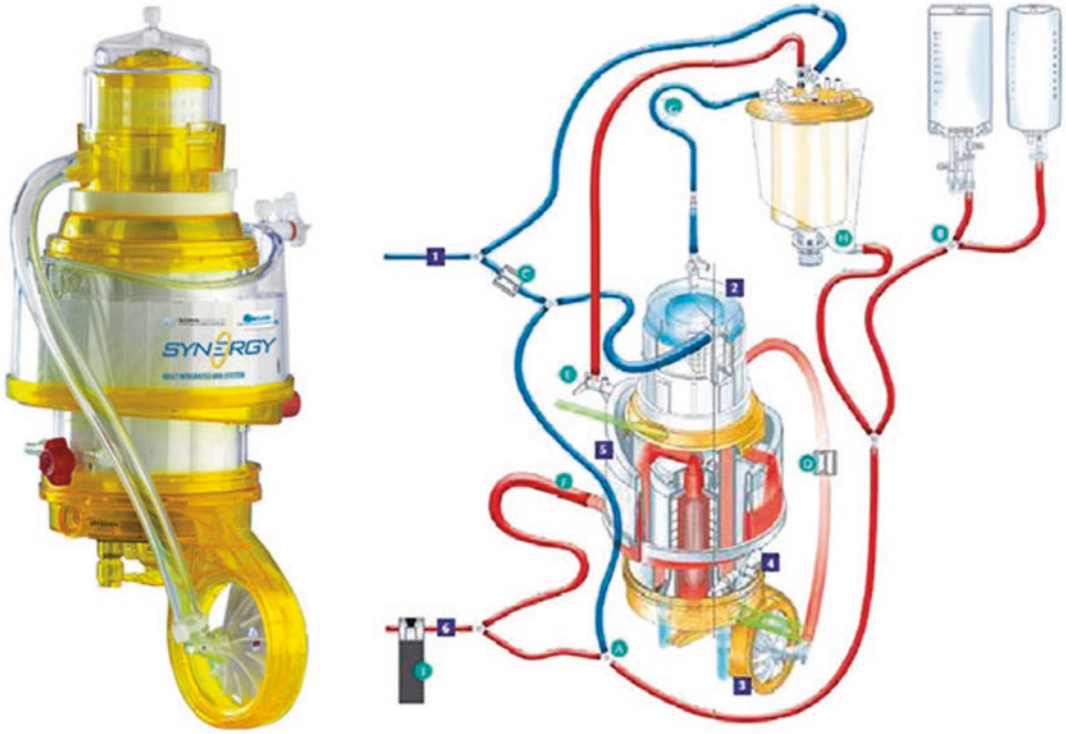
◘ **Fig. 6.12** Resting Heart system (Medtronic) (Courtesy of Medtronic)

The advantages of this system are its high safety level and the perfect bubble elimination. The large priming volume of 1400 mL is a disadvantage as it equals or even exceeds that of a normal heart-lung machine ECC circuit. Thus, hemodilution and inflammation are not substantially influenced.

Since April 2013, the complete ECC set is no longer available in the United States, but all components are still obtainable to assemble the system.

6.2.2.3 Synergy-Mini-Bypass System (Sorin®)

The Synergy® system (◘ Fig. 6.13) is a fully integrated complete system from Sorin (Sorin S.P.A, Milan, Italy) and includes a centrifugal pump, a microporous polypropylene oxygenator with a membrane surface of 2.0 m^2, an arterial filter, a venous bubble trap, and a heat exchanger within



◘ **Fig. 6.13** Synergy-Mini-Bypass system (Sorin) (Courtesy of Sorin)

one device body. The maximal pump flow is reported as 8 L/min. The compact construction renders the priming volume with 680 mL in an acceptable range, but the tubing system has to be added. An air purge system for automatized air bubble elimination can be well added to the system.

The Synergy system differs from its competitors by its compact construction. Another advantage is the possibility to convert the closed system in an open system with a reservoir with a few steps.

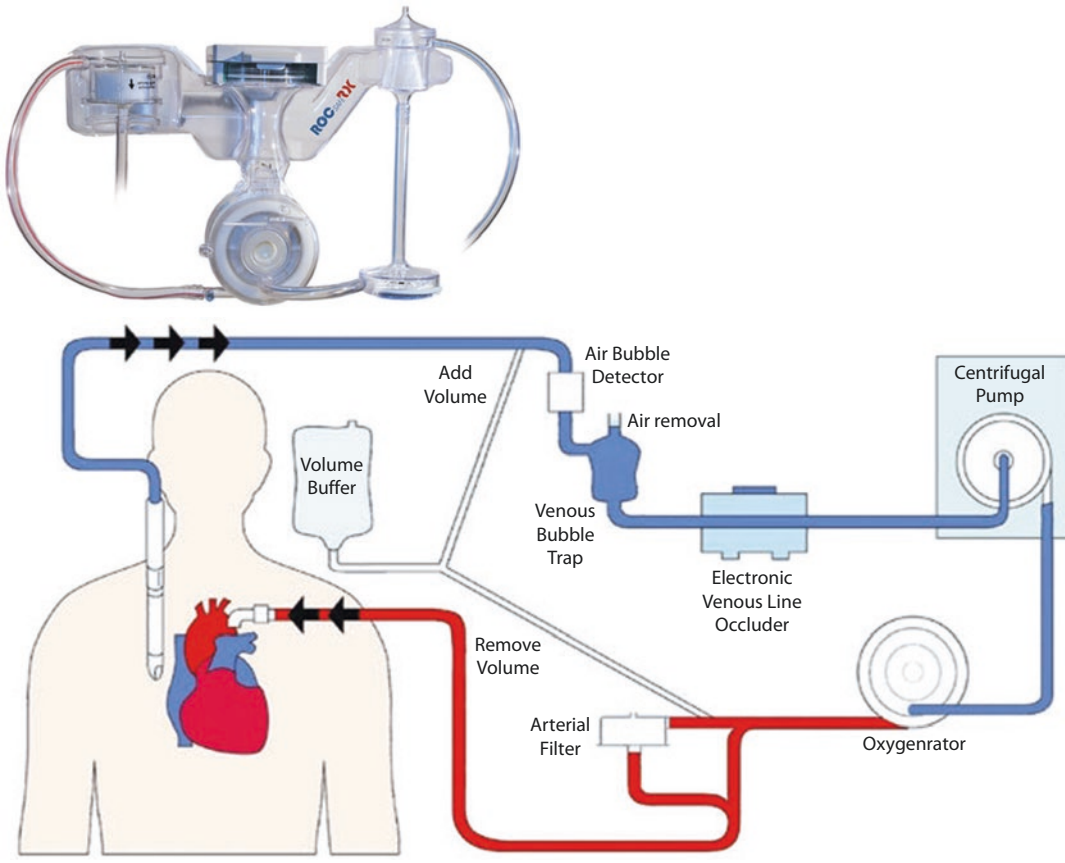
6.2.2.4 ROC-Safe System (Terumo®)

The ROC-Safe® system (Terumo Corp., Hatagaya, Japan), R, O, and C (◘ Fig. 6.14) being the initials of the perfusionist who invented the system, is a closed perfusion system, which was developed for coronary bypass surgery. With an additional module, other surgical procedures can be accomplished as well. Its centrifugal pump offers up to 6 L/min, whereas the polypropylene oxygenator has a surface of 1.8 m^2 and a heat exchanger integrated. A venous bubble trap removes larger bubbles; an arterial filter eliminates microbubbles. In case of air entering the circuit, an ultrasound detector reduces pump speed and finally blocks the venous line in an automated process. The inner surface of the whole system is equipped with the biocompatible X-coating.

The safety feature with the venous bubble trap and the arterial filter is opposed by a large priming volume which may lead to a considerable hemodilution. A retrograde autologous filling can lower the priming volume.

6.2.2.5 Modifications for Aortic Valve Surgery

Aortic valve replacement with mini-systems has been performed with several systems. Cannulation of the aorta and right atrium is as usual; blood cardioplegia is administered ante- or retrogradely. The main problem is to keep the aortic root dry. As a standard vent in the left atrium would aspirate large amounts of air and cause air blockade, it cannot be used when the aorta is opened. Instead,



◘ **Fig. 6.14** ROC-Safe system (Terumo) (Courtesy of Terumo)

a (second) vent catheter is inserted into the pulmonary artery, which drains the pulmonary vascular bed and the left atrium. All blood which is collected by the vent is immediately returned to the patient's venous line via a vacuum bag or cell saver system. Accordingly, the system has also be termed «semi-closed.» Despite the increased complexity, a small incision, minimal access aortic valve surgery is possible.

6.2.2.6 Functional Differences Between Mini and Standard Systems

The operation of both, the mini and standard systems, is comparable, but there are some differences due to the composition of the devices:

- The tubing of the mini-systems is usually shorter, so that the device has to be placed much closer to the surgeon. Heparin coating and the biocompatible surfaces which are hardly seen in standard heart-lung machines seem to be advantageous for the reduced need of anticoagulation, but there is hardly any evidence for that.
- Since mini-systems are closed systems, prior to initiation of extracorporeal circulation, all air bubbles have to be meticulously removed from both the arterial *and* venous line. Bubble traps, if present, are only useful for small amounts of trapped air.
- The principle of closed systems also includes that back bleeding during coronary artery bypass surgery cannot be arbitrarily removed by suction at the arterial vent, as air bubbles can enter the arterial line over the vent line with a high suction force. If back bleeding significantly interferes with the surgical efforts, a small probe or shunt or a lower flow may have to be chosen.
- The main risk with the use of a mini-system evolves once a severe surgical bleeding occurs. Hypovolemia can develop and jeopardize extracorporeal perfusion as an immediate retransfusion of large amounts of blood via the cell saver is impossible. The blood loss has to be replaced by transfusion of blood products as long as the patient's blood is prepared for retransfusion. That's why for open-heart surgery, the use of these mini-systems is not primarily recommended. In an emergency situation, only the Synergy system can be converted into an open circuit.

Though there are numerous differences in study parameters between standard and minimized heart-lung machine circuit, they translate hardly into advantages or disadvantages of either system, respectively. The large heterogeneity of mini-systems renders comparison difficult. A recent meta-analysis of randomized studies showed that mini-systems are associated with less hemodilution; less postoperative drainage and transfusion requirements; earlier extubation; reduced incidence of postcardiotomy heart failure; higher number of platelets; lower serum creatinine, C-reactive protein, troponin T, and creatinine kinase; lower interleukins (IL-8, IL-6, IL-10) and tumor necrosis factor alpha; and lower thromboxane B2, prothrombin fragment, neutrophil elastase, circulating endothelial cells, terminal complement complex, n-acetyl-glucosaminidase, intestinal fatty acids, and Clara cell 16 (Biancari and Rimpilainen 2009). The overall conclusion from thesis studies was that mini-systems are associated with a lower stroke risk, less blood loss, and lower mortality. These results still have to be critically interpreted.

6.2.3 Conduct of Cardiopulmonary Bypass

While there are rules to be obeyed during the conduct of cardiopulmonary bypass, within certain limits there is room for a rather wide variability. The reason for this is that most of the suggested parameters to be followed or aimed for have been empirically determined and the individual experience plays an important role on how to reach and maintain them.

6.2.3.1 Preparation of Extracorporeal Circulation

At the beginning, all sterile packed components of the heart-lung machine are assembled which takes about 15 min. Such a «dry» circuit can be stored as a stand-by tool for about 7 days. The so-called priming of the heart-lung machine, namely, filling with the perfusate chosen and de-airing the tube system, is not uniform. The basic perfusate consists of a balanced electrolyte solution. At several centers it is preferred to add colloidal solutions containing albumin, hydroxyethyl starch (HAES), or dextrane to obtain some osmotic pressure and thereby reduce extracellular fluid

retention. However, a clear advantage for the use of colloidal solutions has not been demonstrated, yet. The priming is recirculated sufficiently long to remove all air from the circuit. As the filling volume of the extracorporeal circuit equals about one third of the patient's blood volume, the hematocrit drops to about two thirds with the initiation of cardiopulmonary bypass. In case of hypothermic perfusion, the hematocrit is lowered even further. So far, an optimum for the hematocrit on extracorporeal circulation in adult patients has not been defined. After the priming, the heart-lung machine should be used within 8 h.

Prior to the start of extracorporeal circulation, the patient has to be sufficiently, so-called «fully» heparinized. For a standard heart-lung machine extracorporeal circuit in open-heart surgery, 300–400 IU/kg of heparin is considered a full heparinization. It is administered intravenously (see above). In (closed) heparinized (surface-coated) systems, one third to 50 % of this dose are usually sufficient for anticoagulation. Additionally, 2500–10,000 IU is added to the priming to make up for the additional volume and to prevent thrombotic complications within the circuit prior to go on bypass in case of blood priming. Two to 5 min after heparin administration and prior to the initiation of cardiopulmonary bypass, coagulation is controlled by the activated clotting time (ACT). Over the whole perfusion period, ACT should be kept between 350 and 400 and is therefore controlled regularly, i.e., at a 30 min interval.

6.2.3.2 Monitoring During Extracorporeal Circulation

During extracorporeal circulation, cardiovascular function, gas exchange, and acid-base balance have to be surveyed not only by the anesthesiologist but also by the certified clinical perfusionist. The perfusionist has to keep an eye on the monitor to read the electrocardiogram (ECG), the arterial blood pressure, the central venous pressure, the arterial saturation, and the body temperature(s). During complex surgical procedures, further parameters such as the left atrial pressure can be important too. Furthermore, an adequate urine production of 0.5–1 mg/kg/h should be present. If the latter is insufficient, augmentation of the pump flow should follow prior to the use of diuretics. During deep hypothermia, urine output decreases and may cease.

The perfusionist controls pump flow and line pressures as well as the filling of the venous reservoir at the steering console to maintain adequate cardiopulmonary support. Mean arterial pressure and pump flow depend on the degree of hypothermia; the latter and the amount of cardioplegia are related to the type of surgery planned. The important surveillance parameters are noted in the perfusion protocol. The interaction between perfusionist, anesthesiologist, and cardiac surgeon and the strict surveillance of the perfusion parameters allow the optimal conduct of cardiopulmonary bypass, as well as the prevention or early detection of complications.

6.2.3.3 Termination of Extracorporeal Circulation

After the surgical repair of the heart or great vessels has been completed, the patient can be weaned from cardiopulmonary bypass. At this point, the patient has to be rewarmed to at least 34 °C, and the intravascular compartment and the heart have to be refilled and de-aired by reducing the venous unloading. Myocardial contractility is judged visually be the cardiac surgeon and optionally by transesophageal echocardiography (TEE) also. If myocardial contractility is insufficient, it has to be augmented by appropriate drugs, mainly by catecholamines and phosphodiesterase inhibitors. Atrial fibrillation can be converted to sinus rhythm to improve cardiac performance; likewise, bradycardia can be counteracted by various pacemaker stimulation modes (A00, AAI, DVI, DDD, VVI, see ► Chapter «Device Therapy of Rhythm Disorders», Sect. 30.2.1, Table 30.2). In case of severely compromised cardiac pump function, biventricular stimulation and/or an intra-aortic balloon pump is favored, as is nitric oxide (NO) (up to 30 ppm) or prostaglandin (iloprost) inhalation in situations with right heart failure due to elevated pulmonary resistance/pulmonary hypertension.

When a normotensive pulsatile blood pressure is reached, the flow of the heart-lung machine is stepwise reduced and finally stopped. After termination of cardiopulmonary bypass, venous decannulation follows. When hemodynamics are stabilized, heparin is antagonized with protamine, mostly 1:1. ACT rapidly normalizes to a level <130 s. In contrast to heparin, protamine is not administered as a bolus but as a brief infusion over about 5 min or more. A rapid protamine application can cause a so-called protamine reaction, which is a life-threatening complication with pulmonary vasoconstriction and pulmonary edema. The blood, which has been collected in the

heart-lung machine, can be retransfused via the arterial cannula, with the help of vasodilative drugs, if necessary. The use of the pump suckers has to be stopped when 50 % of the protamine is given. If there is further bleeding, the blood is collected and retransfused by the anesthesiologist after being washed in a cell saver.

6.2.3.4 Anesthesia During Extracorporeal Circulation

During extracorporeal circulation, volatile anesthetic drugs can be administered at the heart-lung machine directly into the extracorporeal circuit, when the gas exchange membrane of the oxygenator is permeable for it (the diffusion membrane of polymethylpentene is not suitable!). Most of the volatile anesthetic drugs (sevoflurane, isoflurane, desflurane) act rapidly and allow for a reliable narcosis without hemodynamic compromise. They also cease their action fast. As the conductance of anesthesia is excellent and safe, volatile narcotics are used for many years in cardiac surgery. The use of a vaporizor mounted on a heart-lung machine, however, is somewhat problematic since this combination is not commercially available and self-assembled systems have to get approval by the respective authorities. In contrast to the legally optimal intravenous anesthesia, volatile anesthetics seem to increase end-organ tolerance against adverse influences. On the heart, they have a cardioprotective effect by an anesthesia induced preconditioning, and they lessen the reduction of the cerebral perfusion. A recent meta-analysis of the literature shows that volatile anesthetics increase cardiac performance and reduce the need of inotropic support and length of postoperative ventilation (Symons and Myles 2006).

6.2.3.5 Hemofiltration During Extracorporeal Circulation

The number of patients with impaired renal function or even with terminal renal failure who undergo open-heart surgery is steadily rising. Sufficient turnover and elimination of the fluids by the patient are not possible, neither during nor after the procedure. To prevent a fluid overload, a hemofiltration system can be integrated into the extracorporeal circuit. The hemofilter is connected between the arterial and venous line distal to the pump. It generates an ultrafiltrate over a highly permeable membrane as does a native glomerulus.

6.2.3.6 Problems and Complications During Extracorporeal Circulation

Problems and complications may arise from cannulas and tubing, from insufficient heparinization, and from unexpected cardiac findings.

■■ Aortic Cannulation

Aortic cannulation should be a technically simple procedure. As a consequence of malpositioning, the tip of the cannula can be within or close to the vessel wall. It also may be inadvertently directed toward the aortic valve. A thin vessel wall can tear, and in the worst case aortic dissection may occur. The latter can often be immediately recognized by a bluish coloration of the aortic wall and verified with transesophageal echocardiography. Then, an immediate aortic replacement with an interposition graft is necessary, but mortality is high. In case of atherosclerotic aortic vessel walls (high correlation with carotid stenosis and peripheral occlusive arterial disease), debris can loosen and embolize. Therefore, some institutions favor an intraoperative epiaortic ultrasound in patients with severe atherosclerotic disease. For coronary surgery, off-pump surgery may serve as alternative. Air embolism can be prevented with careful de-airing of the aortic cannula and arterial tubing.

■■ Venous Cannulation

The placement of the venous cannula(s) in patients with fragile atrial and/or caval walls may lead to considerable bleeding complications and also to air embolism. If a large amount of air is aspirated into the venous line, an air block will develop, i.e., the venous blood flow and finally also the heart-lung machine stop. A rapid de-airing procedure is necessary with head down positioning, compression of the liver, and initiation of venous suction. Sutures for repairing tissue tears as well as normal cannulation sutures can trap venous monitoring lines and catheters. They may also obstruct caval veins. Malpositioning of a venous cannula can render venous drainage inadequate and lead to venous congestion, which in case of temporary hepatic vein obstruction can lead to early postoperative (reversible) liver failure. Further causes of inadequate venous return are small or obturated cannulas and hypovolemia.

■■ Peripheral Cannulation

Peripheral cannulation, especially via femoral vessels, is prone to multiple complications including

leg ischemia, vessel wall laceration, vessel dissection, postoperative stenosis, thrombosis, lymphatic fistula, and infection. Most deleterious is leg ischemia during long-lasting surgery in patients with preexisting vascular disease. In these cases, it is advisable either to use a Dacron graft sutured to the vessel or a selective distal vascular perfusion over a sidearm of the arterial cannula.

■■ Aortic Valve Incompetence

(Over-)distension of the left ventricle after initiation of extracorporeal circulation with the heart arresting can be a sequela of aortic valve incompetence, or much less often due to an nondiagnosed patent ductus arteriosus. The first step is to decompress the heart manually; a brief halt of extracorporeal circulation is another option. If the heart continues to dilate, a rapid vent insertion, e.g., through the left ventricular apex, is recommended. Another option is to quickly clamp the aorta and to apply cardioplegia retrograde through the coronary sinus or directly into the coronary ostia.

■■ Low Perfusion Pressure

A drop of the systemic blood pressure during cardioplegia administration is normal. If the pressure remains low after termination of cardioplegia, vasopressors such as norepinephrine have to be applied.

■■ Myocardial Failure

If weaning from extracorporeal circulation mandates relatively high doses of catecholamines for sufficient myocardial contractility, a transesophageal echocardiography should be performed to analyze myocardial pump function and ventricular filling. Insertion of an intra-aortic balloon pump can be helpful to reduce the catecholamine demand and its related complications. Moreover, monitoring of the patient's left ventricular preload can be improved by placement of a left atrial catheter or a Swan-Ganz catheter. When catecholamine application leads to pulmonary hypertension, they can be administered over the left atrial catheter to avoid the pulmonary vascular complications. The right heart can be indirectly supported with inhalation of nitric oxide (NO) or prostaglandin administration, both lowering pulmonary artery resistance when elevated. A further option is the use of phosphodiesterase inhibitors, which also lower the pulmonary vascular resistance.

■■ Coagulation Disorder

A severe coagulopathy following termination of cardiopulmonary bypass is treated with transfusion of fresh frozen plasma (FFP), and platelets, as well as with packed red blood cells (PRBC) to replace the blood loss. Alternatively, the (important) various clotting factors can be measured and separately substituted—this philosophy has not yet gained widespread acceptance. Rather advantageous was the routine use of aprotinin, a fibrinolysis inhibitor which inhibits plasmin and kallikrein and also stabilizes the platelet membrane. However, due to a mildly elevated incidence of renal failure, the approval for aprotinin was withdrawn in some countries. It was substituted by tranexamic acid, which is less effective and also administered with various protocols. Platelet dysfunction is frequently treated with a vasopressin analogue (1-desamino-D-arginine vasopressin), but some studies question its advantageous properties as transfusion requirements were frequently unaltered (Mannucci 2000).

In case of large drainage losses, the blood should be collected in a reservoir and washed and retransfused with the CATS (Fresenius Continuous AutoTransfusion System, Terumo, Ann Arbor, MI) system. This is one of the few options which Jehova's witnesses mostly accept, among other additional measures like preoperative iron and EPO treatment. Jehova's witnesses further allow based on an individual patient decision the use of a cell saver, intraoperative autotransfusion without blood storage, and administration of coagulation factors (but not red and white blood cells, platelets, and fresh frozen plasma).

6.3 Extracorporeal Membrane Oxygenation

With the development of the heart-lung machine, mechanical support of the circulation by temporarily replacing heart and lung function allowed for open-heart/direct vision cardiac surgery since the mid-1950s. When the need for more prolonged support became evident, adequate long-lasting oxygenators had to be developed. With the availability of membrane oxygenators for this purpose, this prolonged type of extracorporeal circulation, in principle the same support as needed for open-heart surgery, was coined extracorporeal

membrane oxygenation (ECMO). Two types of ECMO have emerged as basic configurations: venoarterial and venovenous ECMO.

As in the standard ECC setup for on-pump cardiac surgery, the essential components of an ECMO circuit include a pump and an oxygenator. Oxygenator and pump are connected in a closed circuit to avoid blood-air contact. A venous reservoir is mostly absent. Some systems use a reservoir initially after setup to facilitate volume management. A bubble trap is optional. Integrated systems have bubble traps, sometimes working in an automated mode. In custom-made systems, they are often absent.

All components of the ECMO system are mounted on a steerable console, which can be placed aside the patient's bed. With special brackets, oxygenator and pump can also be fixed to the bed frame to alleviate patient care. The driving console has to be equipped with batteries, capable to maintain ECMO support for a minimum of 1 h. A heat exchanger can be implemented to cool or warm up patients as necessary. Meanwhile, there are also driving consoles available for use outside the cardiac surgery units. With these driving consoles, ECMO patients can undergo computed tomography or other diagnostic procedures, or ECMO can be available as a backup for high-risk interventional procedure in the cath lab.

The latest developments are ECMO systems allowing patient transport with an ambulance car or even a helicopter. The Emergency Life Support (ELS) system from Maquet® was the first device to get approval for air transportation from the European Aviation Safety Agency (EASA). These integrated devices are available as complete sets and are functionally well designed. Among the systems available, the Cardiohelp® (Maquet, Rastatt, Germany) is the most sophisticated and versatile device, currently FDA approved for the USA. This unique concept offers different versions for different tasks. With its tip-to-tip surface coating and approval for up to 14 days of support its short-term use, e.g., high-risk PTCA, as well as longer-term use including interhospital patient transport is possible (Philipp et al. 2011). For the other systems (Lifebridge®, Lifebridge, Ampfing, Germany; Life-Box®, Sorin, Milano, Italy), support is limited to 6 h and 5 days, respectively.

6.3.1 ECMO Parameters

The components of an ECMO circuit are selected in order to achieve a total support of the patients' cardiopulmonary function. Only in special cases, e.g., for carbon dioxide elimination when oxygenation may not be a problem, partial support with 25 % of normal cardiac output is sufficient.

According to the guidelines of the Extracorporeal Life Support Organization (ELSO), a blood flow up to 3 L/min/m^2 is necessary for sufficient support of heart and lung function. With regard to the age groups, this means pump flows of 100 mL/kg/min in newborns, 80 mL/kg/min in children, and 60 mL/kg/min in adults. The perfusion pressure in the arterial tubing should not exceed 400 mmHg; maximal suction at the venous line should be less than 300 mmHg. Adequate pump flow is present when continuous monitoring of the central venous oxygen saturation shows values >70 %. Most venoarterial and venovenous ECMO setups achieve about 3–4.5 L/min, depending on cannula size and pump characteristics and allow sufficient gas exchange and normal metabolism (O_2 supply in newborns 6 mL/kg/min, children 4–8 mL/kg/min, adults 3 mL/kg/min). Cardiopulmonary function can be well stabilized, allowing for recovery of heart and lung with strain taken off of them. With a complete loss of cardiopulmonary function, a less than optimal pump flow may still be sufficient to enable patient transport to another hospital for definite and potentially successful treatment.

6.3.2 Venoarterial ECMO

The primary indication for venoarterial ECMO (va-ECMO) is myocardial pump failure. Concomitant lung failure is thereby supported as well. For an emergency indication, cannulation should be simple and not require any or only limited surgical expertise. As a routine, peripheral cannula placement is generally favored. Percutaneous vessel cannulation, however, is much more demanding as it is more prone to complications when compared to a primary surgical cannula insertion. Peripheral venous drainage is performed through a femoral vein; arterial return can occur via a femoral or a subclavian artery. A complete unloading of the heart and support, respectively, is

not possible, mainly due to the limiting capacity of the peripheral venous drainage system. As a rule, about 80 % of blood is directed toward the ECMO, whereas 20 % still find its way into the pulmonary vascular bed and protect the latter.

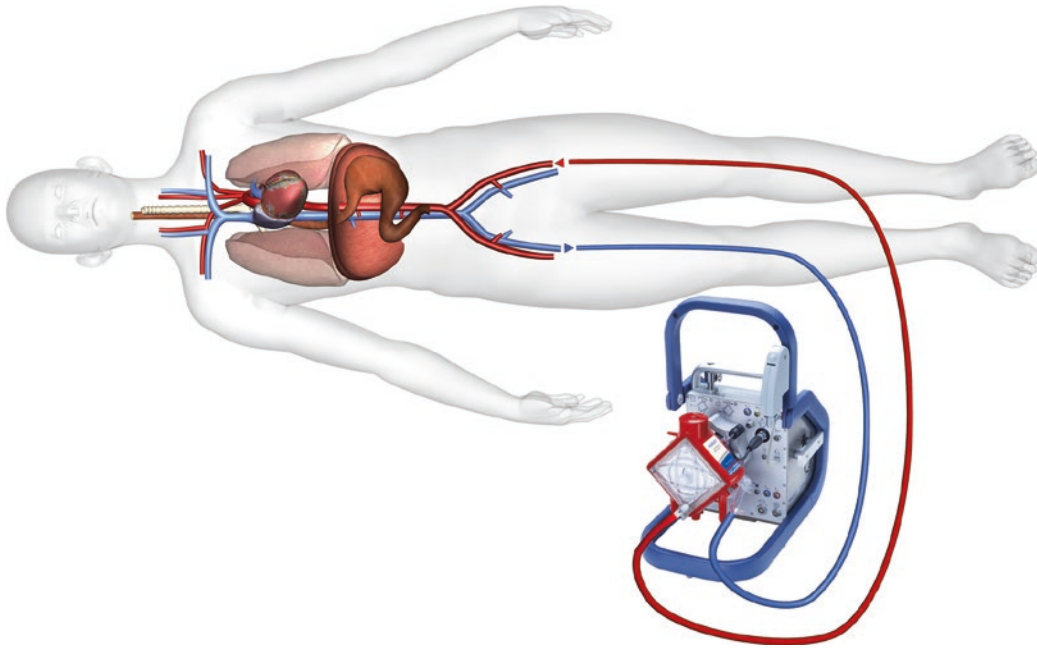
Patients with immediate postcardiotomy failure, who are still centrally cannulated at the ascending aorta and right atrial appendage, are usually connected to the ECMO system employing these cannulas in place. In this ECMO circuit, the blood is drained from the right atrium and reinfused into the ascending aorta, as with the routine intraoperative extracorporeal circulation (◘ Fig. 6.15).

6.3.3 Venovenous ECMO

The indication for venovenous ECMO (vv-ECMO) is respiratory failure without significant ventricular dysfunction. As in va-ECMO, peripheral cannulation is favored to lower bleeding complications. In the standard setup, venous blood is drained from the femoral vein and the arterialized blood returned into the (right) jugular vein. It is important to have the tips of both cannulas at a distance large enough to prevent a short circuit, i.e., pump recirculation. If a jugular access is impossible, a femorofemoral configuration is chosen, with a short drainage cannula and a long cannula for arterial reinfusion. As the drainage of a short cannula is worse and the inferior caval vein may collapse with increased suction, these techniques are less effective. Another alternative provide the double-lumen cannulas, which are inserted in the right jugular vein. As they drain mainly from the inferior caval vein and the outflow should be directed toward the tricuspid valve orifice, its placement is much more demanding. More effective than for oxygenation in adult applications is the use for venovenous CO_2 removal (see below: $ECCO_2R$) (◘ Fig. 6.16).

6.3.4 Indication for ECMO

There are no clear-cut indications for ECMO therapy. The large societies for cardiopulmonary medicine/surgery have not established respective guidelines. There are only guidelines from the Extracorporeal Life Support Organization (ELSO) which recommend ECMO placement when the risk to die without would be 50 %. Immediate ECMO is to be performed if the mortality risk approaches 80 %. In most institutions, the indication is determined by the institutional experience. A large experience with ECMO leads to a more liberal indication



◘ **Fig. 6.15** Peripheral (femorofemoral) venoarterial ECMO (Courtesy of Maquet)

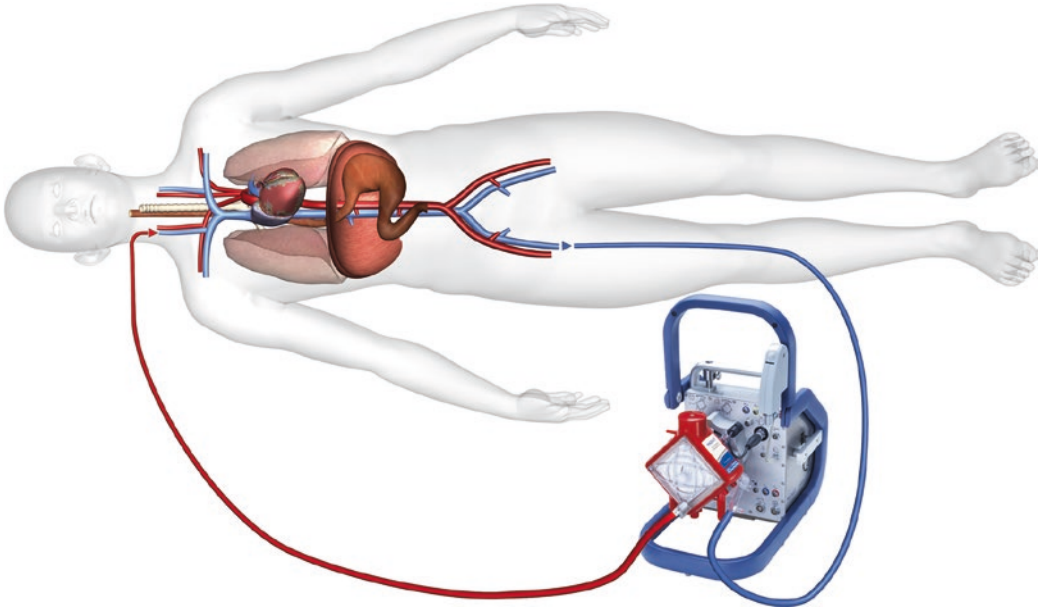


Fig. 6.16 Femorojugular venovenous ECMO (Courtesy of Maquet)

for its application and ultimately to better results (Muller et al. 2009; Schmid et al. 2009).

In myocardial pump failure, a cardiac index of 2.0–2.3 L/min/m^2 or lower defines today's indication for mechanical circulatory support with a ventricular assist device. Accordingly, refractory medical treatment for cardiac failure is an accepted indication for va-ECMO therapy. Postcardiotomy circulatory failure offers more therapeutic options. In case of myocardial contractile failure, the usual primary attempts for cardiovascular stabilization include augmented catecholamine administration followed by an intra-aortic balloon pump placement. Only after failure of both combined and an expected recovery of myocardial pump function, va-ECMO is indicated. If there is no recovery potential, assist devices for long-term support are the better choice (see ► Chapter «Cardiac Assist Devices and Total Artificial Heart», Sect. 38.4).

While va-ECMO is indicated for emergency treatment of primary myocardial failure, replacing the function of the lungs also, vv-ECMO is to replace the impaired gas exchange in primary pulmonary failure (endpoints: recovery, transplantation, or death), thereby preventing secondary cardiac failure also. Since these therapies require a high logistic effort, considerable resources, and a high skill level, vv-ECMO in adults is not widespread. As for va-ECMO, criteria when to install vv-ECMO are not well defined and differ among centers. In a prospective study in 1979, two indications for pulmonary support with ECMO were proposed (Zapol et al. 1979):

1. A pO_2 < 50 mmHg at an FiO_2 of 1.0 requires immediate ECMO placement.
2. Whereas a pO_2 < 50 mmHg at an FiO_2 > 0.6 and a PEEP > 5 cmH_2O for more than 12 h was defined as slow entry criterion.

Nowadays, emergency ECMO placement for pulmonary support is indicated when the predicted risk for conventional respirator management is high. Such a high risk is seen with an oxygenation index [(mean airway pressure × FiO_2 × 100)/pO_2)] >40 and with a pO_2/FiO_2 < 60–80. In this regard there is no difference between venovenous and venoarterial ECMO. However, prior to an ECMO installation, all other treatment options should be considered, and a lung protective ventilation aspired (tidal volume 6 mL/kg, PIP < 35 cmH_2O, FiO_2 < 0.6, cmH_2O and pO_2 goal: arterial pO_2 > 60 mmHg) (Schmid 2009).

A special type of ECMO is $ECCO_2R$ (extracorporeal carbon dioxide removal). Here, carbon

Table 6.7 Indications for va-ECMO and vv-ECMO (Schmid et al. 2009)

Indication	va-ECMO	vv-ECMO
Urgent	Cardiac index <2.0 L/min/m^2 (catecholamines ↑, IABP)	PaO_2/FiO_2 <80 mmHg; (FiO_2 = 1.0)
		Protective ventilation impossible
Emergency	Resuscitation with insufficient cardiac function	PaO_2/FiO_2 <60 mmHg; (FiO_2 = 1.0; PEEP = 20 cmH_2O), severe respiratory acidosis

dioxide is eliminated with an ECMO pump flow of 1–2 L/min, whereas oxygenation is achieved by the native lung by endotracheal/bronchial oxygen insufflation without significant ventilation.

There are only few absolute contraindications for ECMO. These are mainly situations, where recovery of end-organ function (late tumor stage, significant cerebral disease/damage) cannot be expected. All other contraindications are relative, i.e., in every case benefit and risk have to be weighed such as peripheral vascular disease and abdominal aortic aneurysm with thrombus formation. This is also true for the bleeding risk in polytraumatized patients, when an ECMO with heparin coating is used (Arlt et al. 2010). Yet, maintenance of ECMO without heparin administration is only possible for a few days. The carbon dioxide-lowering properties can also be beneficial for neurosurgical patients (Bein et al. 2002). A septic patient can be supported with ECMO too, but loss of peripheral resistance with a consecutive increase of cardiac output may not be fully mastered with peripheral ECMO systems, if at all (Table 6.7).

6.3.5 Physiological Consequences and Problems

The main goal of mechanical support with ECMO is to allow for recovery of heart and/or lung function. This works well as long as there is no total loss of cardiopulmonary function, i.e., if the ECMO supports but not replaces heart and lung, although this may be initially the case. A total loss of cardiac pump function can be compensated with a peripheral ECMO in small patients with large vessels only. Otherwise, the left heart is not sufficiently unloaded and distends. Consecutively, an additional vent may become necessary, which can be inserted into the left atrium with several approaches: on the right side into or between the pulmonary veins and on the left side through the left atrial appendage. The LV apex may be cannulated for drainage also. A transition from peripheral to central cannulation can be helpful too. An alkalotic hyperoxygenation by lowering pH/pCO_2 and pulmonary vascular resistance is a further means to benefit the right ventricle.

A recovery of myocardial pump function with persistent respiratory impairment can cause problems during femorofemoral venoarterial perfusion. The lower half of the body is well perfused with arterialized blood, whereas the upper body including the brain and coronary arteries is provided with hypoxemic blood from the native (malfunctioning) lung only. Diagnosis can be established by percutaneously measuring oxygen saturation at a right-sided finger or directly with a radial artery blood gas drawn. Therapeutic options consist of a transition to central cannulation or of a relocation of the arterial cannula into the right subclavian artery.

Major complications are bleeding and thrombosis at the cannula sites, followed by ischemic complications at the respective extremities. Therefore, it is advisable to anastomose a (6–8 mm) Dacron graft for cannulation to the arterial vessel if the latter is small in size. Most institutions follow that strategy always when accessing the subclavian artery due to the risk of deleterious complications. At the femoral artery, a separate small cannula placement for distal perfusion is another option.

Further problems arise during long-term support. Patient mobilization and physiotherapy are difficult. The patients are usually bedridden and tethered to the bed by the tubing. A successful extubation to benefit lung function and to prevent respiratory infections hardly facilitates mobilization. The use of a solitary double-lumen cannula for venovenous ECMO inserted into the jugular vein increases the mobility but may limit pump output (Chimot et al. 2013).

6.3.6 Long-Distance Transport on ECMO

Critically ill patients with cardiac and/or pulmonary failure may not have access to all therapeutic means in a primary care center; they have to be referred to a tertiary care center or a specialized heart and lung failure unit. However, the clinical state of patients being on high-dose inotropes or being maximally ventilated is rather unstable, and conventional patient transport is associated with a high risk.

With the availability of the miniaturized ECMO systems (see above ► Sect. 6.2.2), patient transport became safe, both in a venovenous and venoarterial configuration. Prerequisites are a hub and a radio system for the participating hospitals as well as an on call system in the hub hospital/unit which can be organized in various ways. An incoming request for ECMO transportation demands immediate response: (1) Verifying that the patient is an appropriate candidate for ECMO treatment with further definitive therapeutic options to be offered. The cause of heart failure, reversibility of cardiac dysfunction, end-organ failure, neurology, tumor, and other terminal diseases should be asked for to judge whether the patient may be weaned from ECMO, can undergo conventional open-heart surgery, or will need long-term mechanical support. (2) Availability of staff and equipment. ECMO transport teams usually include an anesthesiologist or an intensivist, a cardiac surgeon, a perfusionist, and a paramedic. Depending on the organizational structure and individual skill level, the team can be reduced to two staff members, as the space in most helicopters and ambulance cars is limited. (3) Availability of ICU capacity. In Europe, adult ECMO transportation is a new mission, predominantly created by cardiac surgeons. Therefore, not only the staff but also ICU capacity is shared. Shortness of ICU beds is common.

After arrival at the distant hospital, the patient's clinical condition is reviewed again. If the patient unexpectedly is no longer a candidate for ECMO according to (1), the mission is aborted. If the patient, now with specialists support available, can be stabilized for normal patient transfer, ECMO is not installed either. For ECMO placement, the size of the femoral vessels can be measured by ultrasound, and appropriate cannulas are chosen to minimize the risk of limb ischemia (arterial 15–17 Fr, venous 17–23 Fr). For va-ECMO, the tip of the arterial cannula is positioned in the common iliac artery or the distal abdominal aorta; the tip of the venous cannula was placed in the inferior vena cava. A so-called distal perfusion can be established but is frequently omitted. Central cannulation is not performed. In cases of vv-ECMO, outflow was achieved via the femoral vein, and inflow was gained by cannulation of the right internal jugular vein and thereafter into the superior vena cava. Before vessel cannulation 5000 IU heparin is administrated intravenously, except when the partial thromboplastin time (PTT) value is ≥1.5 times above normal range. With a heparin-coated circuit, no further anticoagulation is needed during transport. After starting the ECMO, circulatory state and respirator settings are optimized in a brief period. A dramatic reduction of catecholamine requirement is common; a mean systemic blood pressure of 50–70 mmHg is sufficient. The patient is transferred to the helicopter or ambulance car, and monitoring is established in the vehicle. Monitoring includes continuous electrocardiographic surveillance, invasive blood pressure measurement, pulse oximetry, and capnography. Tissue perfusion and oxygen delivery are assessed by pulse oximetry and estimation of arterial blood gas exchange and mixed venous oxygen saturation if available. Minimal requirements are electrocardiogram, blood pressure, pump flow (3–5 L/min), and right radial arterial saturation. During transport, low flow situations are treated with crystalloid infusions and impaired oxygenation with airway toilet and increased oxygen supply. An ischemic leg cannot be treated, but will not become a clinical problem for the few hours in the air/on the road. Upon arrival, the patient is immediately referred to the cardiac ICU, and further treatment options are discussed and applied (Arlt et al. 2008).

6.3.7 ECMO Resuscitation

Acute cardiovascular collapse is life threatening and mandates immediate action. In most instances, an appropriate drug therapy is sufficient to stabilize the patient; some, however, may require chest compressions/external heart massage and artificial ventilation. Further treatment options are usually not available except in institutions offering ECMO placement during resuscitation. Systems for ECMO as a resuscitation tool

include mobile larger devices and light-weight portable systems.

For ECMO resuscitation, femoral artery and vein—preferably on opposite sides—are punctured percutaneously during brief periods of halting external cardiac massage. With Seldinger's technique, a borderline small arterial cannula (e.g., 15 Fr) and a long venous cannula (21 Fr or 23 Fr) are inserted and connected to the ECMO circuit after careful de-airing. When ECMO is started, both cannulas are fixed to the patient, and echocardiography is performed to assess cardiac function and filling/unloading. Ventricular fibrillation is terminated with defibrillation. Inotropic drug support and volume administration are optimized, and the pH is normalized. The afterload of the heart is lowered to prevent cardiac distension, and the respirator is set to lung protective ventilation, if possible. The time period needed to establish mechanical support is about 15–20 min.

Recent studies showed that longer pre-ECMO resuscitation duration was associated with poor prognosis. The same was true for patients with pulseless electrical activity or asystole as compared to ventricular tachycardia or ventricular fibrillation as the initial rhythm. These finding suggests that the main factors associated with outcome are baseline condition, underlying cause, and the rapid response of the resuscitation team. Overall, a survival of about 30 % with resuscitation periods up to 1 h has been reported (Chen et al. 2008). It has been suggested that applying mild hypothermia (34 °C) for 24 or 48 h after ECMO initiation may add a benefit to the patient, as therapeutic hypothermia is currently recommended after cardiac arrest. Survival among the elderly supported on ECMO is lower than that for younger adult patients; however, age should not be a principle contraindication for the use of ECMO in older patients (Mendiratta et al. 2013).

Several important issues have to be considered when performing ECMO resuscitation. (1) The complication rates from femoral vessel cannulation are high including limb ischemia, severe vessel laceration, retroperitoneal and thigh bleeding, and placement of a cannula in a wrong vessel. Once the patient is stabilized, these problems have to be fixed. (2) As the effectiveness of resuscitation is never known, patients may end up being invalidated by severe cerebral injury. If the family and the treating physicians do not share the same opinion with regard to maintenance or withdrawal of therapy, ethical debates are difficult. (3) If ECMO resuscitation was successful and the patient denies consecutive necessary treatment such as VAD therapy, mechanical support must be terminated.

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