

Adult donor treatment: Intensive care unit

Recommendations for the topic

Management and monitoring of adult organ donors with preserved heart function in intensive care units

Module — 3

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Contents

| | |
|---|-----------|
| 1.0 Summary | 4 |
| 1.1 Scope and objectives | 4 |
| 1.2 Ethical considerations | 4 |
| 1.3 Start of donor treatment | 4 |
| 1.4 Life-saving emergency measures during donor treatment | 5 |
| 1.5 End of donor treatment | 5 |
| 2.0 Point-by-point recommendations for donor treatment | 5 |
| 2.1 Volume therapy | 6 |
| 2.2 Haemodynamics | 8 |
| 2.3 Body temperature | 12 |
| 2.4 Diabetes insipidus | 12 |
| 2.5 Sodium | 13 |
| 2.6 Other electrolytes: K, Ca, Mg, Phosphate | 13 |
| 2.7 Blood glucose | 14 |
| 2.8 Haemoglobin | 14 |
| 2.9 Thrombocytes | 14 |
| 2.10 Blood coagulation | 15 |
| 2.11 Corticosteroids | 15 |
| 2.12 Dopamine | 16 |
| 2.13 Antibiotic therapy | 16 |
| 2.14 Feeding | 16 |
| 2.15 Ventilation | 16 |
| 3.0 Point-by-point recommendations for monitoring | 17 |
| 3.1 Standard monitoring | 17 |
| 3.2 Extended monitoring | 18 |
| 3.3 Standard laboratory tests | 19 |
| 3.4 Microbiology | 19 |
| 4.0 Specific tests for organ procurement | 20 |
| 4.1 Specific tests for organ procurement | 20 |
| 4.2 Specific laboratory tests for organ procurement | 21 |
| 4.3 Microbiology | 21 |

1.0

Introduction

1.1 Scope and objectives

The guidelines for adult donor treatment after brain death (donation after brain death – DBD) are intended for medical personnel (doctors, nurses/therapists) in intensive care units in Switzerland. The aim is to minimize the number of lost donors due to inadequate donor treatment and thus increase the quantity and quality of organs available for transplantation.

1.2 Ethical considerations

According to the Swiss Academy of Medical Sciences (SAMS), dignified dying has the priority over saving lives or restoring health when it comes to patients with a terminal diagnosis. This guiding principle also applies to patients who are being evaluated as potential organ donors, or are already being treated as organ donors, so that they are handled with dignity throughout the donation process. It is also important to support the relatives in this very difficult situation.

1.3 Start of donor treatment

Monitoring and actual treatment as a potential donor begins after brain death has been determined. However, the **continuation of organ preservation measures** – as described in chapters 2 and 3 below (the latter with the exception of subchapter 3.2) – are permitted from **before** death, until the patient's will has been clarified or brain death has been determined. After (brain) death, organ preservation measures may be continued for a maximum of 72 hours until the will of the donor has been clarified (e.g. decision of the relatives).

Comment: Preparatory medical measures (including, for example, the tests mentioned in chapter 3.2) must be clearly distinguished from the organ preservation measures mentioned above. According to the SAMS Guidelines on the "determination of death with regard to organ transplantation and preparation for organ procurement" of 16.05.2017, preparatory medical measures **prior** to death are only permitted if the patient has given his and her consent for these measures. In the absence of the patient's consent to preparatory medical measures, the relatives may consent to the implementation of such measures, provided that the following cumulative conditions are met:

1. There is no evidence that the patient would have refused the measures (presumed will).
2. The measures cannot expedite death or lead to a permanent vegetative state.
3. The measures are essential for a successful transplantation and involve only minimal risks and burdens for the donor. Measures that do not meet these criteria are listed in a negative list (Annex H of the SAMS Guidelines).

1.4 Life-saving emergency measures during donor treatment

If a brain-dead patient who has consented to organ donation suffers cardiac and circulatory arrest prior to organ procurement, resuscitation measures including defibrillation and cardiac massage are strongly recommended.

Comment: The SAMS guidelines of 16.05.2017 (Section H: Negative list) are against the use of mechanical resuscitation **before** death; the use of mechanical resuscitation **after** (brain) death is left open.

1.5 End of donor treatment

The monitoring and care of the organ donor ends with the cross-clamping of the aorta and procurement of the thoracic organs.

2.0

Point-by-point recommendations for donor treatment

Signs of adequate organ perfusion

- Mean arterial blood pressure 60 – 75 (maximum 90) mmHg
- Warm periphery
- Urine output $\geq 1.0 \text{ ml/kg/hr}$
- Lactate $\leq 2 \text{ mmol/l}$
- $\text{SvO}_2 > 65\%$ or $\text{ScvO}_2 > 70\%$

With the lowest possible dosage of vasoactive agents.

SvO_2 : mixed venous oxygen saturation; ScvO_2 : central venous oxygen saturation

Preliminary remark on the following chapters 2.1 (Volume therapy) and 2.2 (Haemodynamics):

Transplant medicine has different expectations regarding the balance between volume and vasoactive therapy: For heart transplantation, no / minimal doses of vasoactive agents should be used during donor treatment (instead, if necessary, more volume), for lung transplantation, on the other hand, a restrictive volume supply should primarily be observed. The therapeutic objective of **adequate perfusion of all organs at the lowest possible dosage of vasoactive agents**, as described above, optimally accommodates the conflicting expectations.

2.1 Volume therapy

Targets

- Mean arterial blood pressure 60 – 75 (maximum 90) mmHg
- Central venous pressure (CVP) 8 – 12 mmHg
- Pulmonary arterial wedge pressure (PAWP; if available) 10 – 15 mmHg; in case of refractory hypovolaemia/hypotension also possibly >15 mmHg
- Pulse pressure variation (PPV) <10%
- Urine output ≥ 1.0 ml/kg/hrs
- Lactate ≤ 2 mmol/l

Interventions

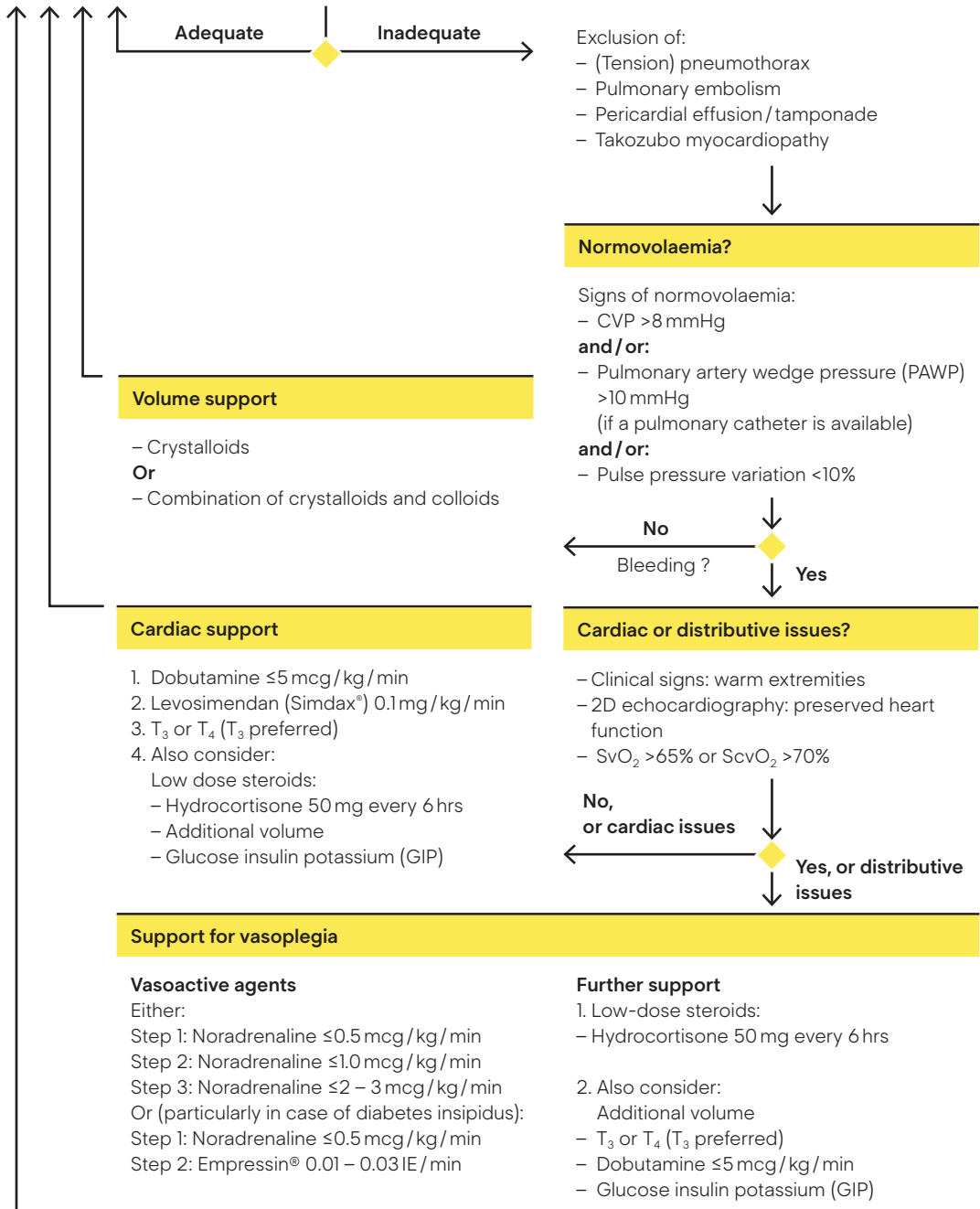
Hypovolaemia

- Crystalloids to normovolaemia (avoid hypervolaemia)
 - First choice: crystalloids (e.g. balanced solutions), avoidance of large amounts of NaCl 0.9%
 - Use of colloidal solutions (e.g. HES 130/0.4, albumin); at most in combination with crystalloids
 - In the presence of renal dysfunction, crystalloids are preferable to colloids (especially HES)
 - Administer warmed infusions if necessary

Hypervolaemia

- Diuretics
 - Furosemide, torsemide; consider thiazide diuretics in case of elevated sodium levels

Verification of adequate organ perfusion and sufficient blood pressure



2.2 Haemodynamics

Targets

Mean arterial blood pressure

- 60 – 75 (maximum 90) mmHg if organ perfusion is adequate

Heart rate

- 60 – 120 /min; <60 /min if an adequate organ perfusion is guaranteed

Mixed venous (SvO₂) or central venous (ScvO₂)

Oxygen saturation

- SvO₂: >65% or ScvO₂: >70%

Comments:

- The target values for SvO₂ / ScvO₂ were chosen as an indicator for adequate organ perfusion with regard to physiological oxygen extraction
- Due to the absence of cerebral oxygen extraction, higher values are recommended for ScvO₂ than for SvO₂
- SvO₂ / ScvO₂ can be measured either intermittently using blood samples or continuously using an optical module via a central venous catheter (ScvO₂) or pulmonary catheter (SvO₂)

Lactate

- ≤2.0 mmol/l

Pulmonary catheter

(PAC; preferably in case of pulmonary hypertension and /or cardiac dysfunction [especially of the right heart])

- Cardiac index (CI): ≥2.5 l / min / m²
- Pulmonary artery wedge pressure (PAWP): 10 – 15 mmHg; for refractory hypovolaemia also >15 mmHg
- Systemic vascular resistance (SVR):
No recommendations are made as this is a calculated value from measured cardiac output and measured mean arterial blood pressure

Pulse Contour Cardiac Output (PiCCO; preferably in case of a distributive issue)

- Cardiac index (CI): ≥2.5 l / min / m²
- Global end-diastolic volume index (GEDVI): 680 – 800 (possibly up to 950) ml / m²
- Pulse pressure variation (PPV): <10%
- Extra-vascular lung water index (EVLWI): <7 ml / kg (for refractory hypovolaemia / hypotension: up to 10 ml / kg)

Interventions

Hypotension

1. Check and correct any possibly existing hypovolaemia (e.g. due to [occult] bleeding, dehydration etc.). **Note:** Hypovolaemia is associated with a relevant loss of transplantable organs
2. Exclusion of an obstructive shock form such as pneumothorax/tension pneumothorax, pulmonary embolism, pericardial effusion/pericardial tamponade
3. Exclusion of Takotsubo cardiomyopathy
4. Establish whether the hypotension is due to a cardiac (inotropic) or distributive (vasoplegia) issue

In case of hypotension due to cardiac issues, this can be identified by:

- Clinical signs: cold extremities, marbled skin (cutis marmorata)
- 2D echocardiography: reduced heart function (e.g. LV-EF <45%)
- Increased oxygen extraction: SvO₂ <65% or: ScvO₂ <70%

In such cases the following cardiac support is recommended:

Cardiac support

1. Dobutamine ≤5 mcg/min/kg
2. Levosimendan (Simdax®) 0.1 mg/kg/min
3. T₃ or T₄ (T₃ preferred)
4. Also consider:
 - Low-dose hydrocortisone 50 mg every 6 hrs (or continuously 200 mg/24 hrs)
 - Additional volume with verified volume reactivity
 - Glucose insulin potassium (GIP)

In case of hypotension due to a distributive disorder, this can be identified by:

- Clinical signs: warm extremities (cool in case of sepsis, with massive hypovolaemia)
- 2D echocardiography: preserved heart function (possibly diffusely restricted in case of septic cardiomyopathy)
- Normal oxygen extraction: SvO₂ >65% or: ScvO₂ >70% (possibly increased in case of sepsis, with massive hypovolaemia)

In such cases the following support is recommended:

Support for vasoplegia

Vasoactive agents

| | |
|--|--|
| Either: | Or: |
| Step 1: Noradrenaline ≤ 0.5 mcg/kg/min | (particularly in case of diabetes insipidus) |
| Step 2: Noradrenaline ≤ 1.0 mcg/kg/min | Step 1: Noradrenaline ≤ 0.5 mcg/kg/min |
| Step 3: Noradrenaline $\leq 2 - 3$ mcg/kg/min | Step 2: Empressin® 0.01 – 0.03 IE/min |

Further support

1. Low-dose steroids:
Hydrocortisone 50 mg every 6 hrs¹
2. Also consider:
Additional volume T₃ or T₄ (T₃ preferred)
Dobutamine ≤ 5 mcg/min/kg

Comments:

- Vasopressin (Empressin®): infusion of 0.01 – 0.03 IE/min (check the ionized calcium, target >1.1 mmol/l)
- Triiodothyronine (T₃, preferred) or thyroxine (T₄):
T₃: (e.g. Thyrotardin®): bolus 4.0 mcg; infusion of 3 mcg/hrs
T₄: (e.g. Thyroxin Henning®: bolus 20 mcg; infusion of 10 mcg/hrs
alternatively a single bolus of 0.1mg TSH (Relefact®: synthetic thyrotropin-releasing hormone) can be administered

Comment: Intravenous administration of thyroid hormones (T₃ or T₄) is recommended for the treatment of decreased, refractory cardiac output and/or persistent, refractory hypotension for the treatment of brain-dead organ donors (with corresponding failure of the hypothalamic-pituitary axis). Currently, only the oral, not the intravenous forms of thyroid substitution are authorized in Switzerland. Intravenous dosage forms, for example from Sanofi-Synthelab Pharmazie, are available in Germany as L-Thyroxin Henning® Inject (T₄) or Thyrotardin® Inject N (T₃) and can be administered without approval. The same applies to Relefact® (synthetic thyrotropin-releasing hormone TSH).

¹ Alternatively, hydrocortisone can also be administered as a continuous infusion of 200 mg/24 hrs.

- Glucose insulin potassium (GIP): glucose 10% 1 ml/kg / hrs, in combination with Actrapid® or Novorapid® and potassium in one dose, in order to keep blood sugar and serum potassium within the targeted levels (see below)

Hypertension

- Nitroglycerin 0.5 – 8 mcg / kg / min
(if administered in high doses: monitoring of meth-haemoglobin)

Or:

Sodium-nitroprusside 0.5 – 5 mcg / kg / min

(if applied over a longer period of time: monitoring of cyanmethaemoglobin and / or cyanide level in whole blood)

- If in combination with tachycardia and high cardiac output:
 - Esmolol (Breviblock®):
Bolus 100 – 500 mcg / kg / min, followed by infusion: 100 – 300 mcg / kg / min
 - Or: labetalol (Trandate®):
Bolus: 20 – 50 mg i.v. followed by infusion: 0.2 – 2 mg / min
 - Or: metoprolol (Beloc Zok®):
Bolus: 3 – 5 mg up to 2 – 3 mg every 4 hrs
- Urapidil (Ebrantil®)
Bolus: 10 – 50 mg i.v. followed by infusion: 2 – 15 mg / hrs
- Clevedipin (Cleviprex®)
Infusion: 2 – 6 (up to 32) mg / hrs

Arrhythmias

Bradycardia

- Transjugular or external pacing. If not possible or as a temporary measure:
- Dobutamine up to 5 mcg / kg / min
Alternatively adrenaline or isoprenaline (Isuprel®) may be considered

Note:

Atropine is **not** effective in treating bradycardia arrhythmias in brain-dead patients.

Tachyarrhythmia

- Correction of any fluid and electrolyte disorders (potassium, magnesium), correction of hypothermia or hypoxaemia.
- Amiodarone; in case of hypertension with a high cardiac index, short-acting beta-blockers (e.g. esmolol) may be preferred.
- Possible electrical cardioversion (if possible, draw blood beforehand to determine the level of heart enzymes).
- Possible glucose insulin potassium (GIP) therapy: glucose 10% 1 ml/kg / hrs in combination with Actrapid® or Novorapid® and potassium in one dose, in order to keep blood sugar and serum potassium within the targeted levels (see below).

2.3 Body temperature

Target

Normothermia

Note:

During the determination of death (brain death diagnostics) the body core temperature must be $>35^{\circ}\text{C}$ (SAMS guidelines)

Interventions

Hypothermia

- Warm infusion solutions, warmed inspiratory gases, warm blankets etc.

Hyperthermia

- Search for possible infections (hyperthermia is rather unusual in brain-dead patients)
- Physical cooling methods (antipyretics are usually insufficient)

2.4 Diabetes insipidus

Occurs in up to 80% of all DBD donors

Diagnosis

- Urine output $>4\text{ ml/kg/hr}$
- Serum-sodium $\geq 145\text{ mmol/l}$ and increasing (note: may increase rapidly)
- Serum osmolality $\geq 300\text{ mosmol/l}$ and increasing
- Urine osmolality $\leq 200\text{ mosmol/l}$ and decreasing

Target

The target of the interventions is primarily based on the fluid status as well as the sodium concentration and osmolality in the patient's serum, and only secondarily on the urinary excretion, which should be kept between $1.0 - 4.0\text{ ml/kg/hr}$.

Interventions

- Desmopressin (Minirin®) $0.25 - 2.0\text{ mcg i.v. every 6 hrs}$
Or:
- Vasopressin (Empressin®) especially in case of hypotension as a continuous infusion of $0.01 - 0.03\text{ IE/min}$

2.5 Sodium

Target

130 – 150 mmol/l

Interventions

Hypernatremia

Note:

Hypernatremia can particularly damage the liver transplant:

- Stop infusions containing NaCl; look for other sources of sodium (e.g. colloidal solutions, penicillin antibiotics etc.) or reasons for osmotic diuresis (hyperglycaemia, elevated serum urea, mannitol therapy etc.)
- With concomitant diabetes insipidus: desmopressin or vasopressin (see point 2.4)
- For hypovolaemia (hypertonic hypovolaemia): infusion of glucose 5% or NaCl 0.45% or a combined infusion with glucose 5% and NaCl 0.9% in a ratio of 1:1 or 2:1
- For hypervolaemia (hypertonic hypervolaemia): first choice: natriuretic diuretics (e.g. hydrochlorothiazide); second choice: natriuretic diuretics combined with intravenous administration of free fluid (glucose 5%)

Note:

The supply of free water through an enteral probe increases the risk of aspiration due to the high gastric fluid levels. The lung transplant is therefore at risk.

Hyponatremia

- For hypovolaemia (hypotonic hypovolaemia): infusion of NaCl 0.9% with additional 100 – 200 mmol NaCl (e.g. from a 23.5% NaCl solution) over 4 – 6 hours (if necessary)
- For hypervolaemia (hypertonic hypervolaemia): fluid restriction, possibly diuretics

2.6 Other electrolytes: K, Ca, Mg, Phosphate

Target

The values should be kept within the normal range (if possible, the ionized values should be taken into account in each case).

Interventions

Correction or substitution of the corresponding electrolytes. Note: The intravenous administration of calcium should be performed slowly, as a too fast injection can lead to hypertension.

2.7 Blood glucose

Target

5 – 10 mmol/l

Interventions

Hyperglycaemia

Continuously adapted insulin infusion (e.g. with Actrapid® or Novorapid®)

Hypoglycaemia

Glucose 5% – 20% depending on fluid status

2.8 Haemoglobin

Target

≥70 g/l (≈haematocrit >25%)

Aim for 80 g/l when removing the heart.

Intervention

Erythrocyte concentrates (leucocyte-depleted, filtered). Transfusion of blood products whenever possible after taking blood samples for HLA typing and virological tests.

2.9 Thrombocytes

Target

>20 giga/l if there is no bleeding

>50 giga/l if there is active bleeding (also search for other coagulation disorders)

Intervention

- Thrombocyte concentrates (pooled, filtered)
- Transfusion of blood products whenever possible after taking blood samples for HLA typing and virological tests.

2.10 Blood Coagulation

Target

INR <2.0

Intervention

- Coagulation factors, e.g. Prothromplex® or Beriplex® especially if there is a risk of volume overload
- Fresh frozen plasma (FFP) only in exceptional cases due to the risk of a transfusion-associated acute lung injury (TRALI)
- Possible Vitamin K (Konakion®)
- Possible protamine hydrochloride with prior therapy with heparin
- Possible fibrinolysis inhibitors such as tranexamic acid (Cyclokapron®) or aprotinin (Trasylol®)

2.11 Corticosteroids

High-dose corticosteroids (intravenous methylprednisolone 15 mg / kg)

in the event of a planned procurement of lungs and / or liver.

Comment:

- The evidence for high-dose corticosteroids as preparation for lung and / or liver procurement is very limited and contradictory. In addition, these studies did not distinguish between anti-inflammatory effects of corticosteroids on the one hand, and substitution of relative or absolute adrenal cortex insufficiency on the other; the latter could be achieved with low-dose hydrocortisone (see below) alone. However, since in the environment of organ procurement / transplantation with subsequent obligatory immunosuppression no additional relevant side effects of high-dose methylprednisolone are to be expected during donor treatment, the possible advantages outweigh the potential risk.

Low-dose corticosteroids (intravenous hydrocortisone 50 mg Every 6 hrs = 200 mg / day)

Recommended for persistent hypotension and / or reduced cardiac output; a prior ACTH test (Synacthen® test) is only recommended in exceptional cases.

Alternatively, the 200 mg hydrocortisone can also be given in a continuous infusion over 24 hours.

2.12 Dopamine

Low-dose dopamine (4 mcg/kg/min intravenous) after death has been diagnosed

Low-dose dopamine – if administered for more than seven hours between the time of death and cold ischaemia – leads to better early function (fewer dialyses) and better transplant survival (post-hoc analysis) after kidney transplantation and better survival (reduced early mortality) after heart transplantation with no negative effects on the transplantation of other organs.

In case of haemodynamic side effects (hypertension, tachycardia), any other vasoactive agents should first be reduced or discontinued and only then – if hypertension/tachycardia persists, should the dopamine dosage be reduced to 2 mcg/kg/min or discontinued.

2.13 Antibiotic Therapy

No prophylactic antibiotic therapy: antibiotics only in case of confirmed or suspected infection

2.14 Feeding

- Continuation of existing enteral or parenteral feeding
- Continuation of the existing substitution of vitamins and trace elements

2.15 Ventilation

- Ensure adequate airway lavage (tracheal suction under sterile conditions) (may have been somewhat neglected in the previous treatment phase due to possible interactions with intracranial pressure [ICP]).
- Aspiration prevention, e.g. by elevating the head by at least 30°, sufficiently high cuff pressure (at least 25 mbar) etc.
- Ventilation therapy for an organ donor is performed as a lung-protective ventilation. For the setting of ventilation, this means accordingly: Tidal volume 4.0 – 7.7 ml/kg or driving pressure ≤ 15 mbar, inspiratory ventilation pressure ≤ 30 mbar and adequate PEEP of at least 5 mbar.
- In the presence of severe ALI/ARDS or other lung diseases where lung procurement is ruled out, the ventilation strategy can be reduced to sufficient oxygenation, for example $\text{PaO}_2 > 9$ kPa (≈ 70 mmHg) and $\text{SaO}_2 > 88\%$.
- **Caution:** It should be noted that in ventilated, brain-dead patients (after brain death diagnosis) the auto trigger phenomenon can occur, which simulates breathing by itself. In such cases the inspiratory trigger should be switched off or set to a less sensitive setting.

3.0

Point-by-point recommendations for monitoring

The following recommendations for monitoring are limited to the treatment of the organ donor and to the tests that must be carried out as part of the assessment of donor suitability. (Please also consult Module 7 of the Swiss Donation Pathway: "Organ and tissue procurement from DBD donors").

3.1 Standard monitoring

| Monitoring parameters | Measuring interval | Remarks |
|-------------------------------|--------------------|---------------------------------------|
| Vital signs | Continuously | Documentation ² every 1hrs |
| Fluid balance | Every 6 hrs | For diabetes insipidus every 1hrs |
| CVC / CVP | Continuously | Documentation ² every 1hrs |
| Peripheral venous catheter | | For high fluid or volume requirements |
| Arterial pressure measurement | Continuously | Documentation ² every 1hrs |
| Urine catheter | Continuously | Documentation ² every 1hrs |
| Feeding tube | | |
| Pulse oximetry | Continuously | |
| 3-channel ECG | Continuously | |
| 12-lead ECG | Every 24 – 48 hrs | |
| Chest X-ray | Every 24 – 48 hrs | |
| Temperature | Continuously | |

² Documentation in PDMS, deviating documentation obligation in the Swiss Organ Allocation System (SOAS) (see there).

3.2 Extended monitoring

| Monitoring parameters | Measuring interval | Remarks |
|--|---------------------------------|--|
| Combined venous /central venous saturation SO_2 ($SvO_2/ScvO_2$) | Continuously or every 2 – 4 hrs | For manifest /suspected organ hypoperfusion |
| PAC /PiCCO | | PAC: for manifest / suspected reduced cardiac output with left ventricular ejection fraction <40% PiCCO: for manifest / suspected distributive shock (SIRS /sepsis) with CVP >12 mmHg |
| TTE | Every 6 – 12 hrs | If EF <40% |
| Bronchoscopy BAL | On request | For diagnostics in case of suspected infection |
| CT-thorax /CT-abdomen | On request | For further diagnostics |

3.3 Standard laboratory tests

| Monitoring parameters | Measuring interval | Remarks |
|--|-----------------------------|---|
| Blood group ABO and Rhesus) | | Twice, if possible |
| Arterial blood gas analysis | Every 8 – 12 hrs | If unstable: every 2 – 4 hrs |
| Electrolytes (Na, K) | Every 4 – 8 hrs | If unstable: every 2 – 4 hrs |
| Creatinine, urea | Yes, once for normal values | |
| ASAT / ALAT / direct and total bilirubin | Every 8 – 12 hrs | |
| Blood sugar | Every 4 – 8 hrs | If unstable: every 2 – 4 hrs |
| Lactate | Every 8 – 12 hrs | If unstable: every 2 – 4 hrs |
| Troponin (I or T) | Once, if normal | Every 12 hours under therapy with desmopres- sin or vasopressin |
| Serum osmolality | Every 24 hrs | |
| Full blood count | Minimum 24 hrs | |
| Coagulation: INR, PT, PTT, fibrinogen, factor V | Once, if normal | |
| Urine analysis (spot and sediment) | Once, if normal | |

3.4 Microbiology

| Monitoring parameters | Measuring interval | Remarks |
|-----------------------|--------------------|---------|
| Blood cultures | If advisable | |
| Urine cultures | If advisable | |
| Tracheal secretion | If advisable | |

4.0

Specific tests for organ procurement

4.1 Specific tests for organ procurement

| Monitoring parameters | Measuring interval | Remarks |
|-----------------------|---|---------|
| Coronary angiography | On request | |
| 2D echocardiography | When collecting donor data (ideally without vasoactive agents) | |
| Abdomen sonography | When collecting donor data | |

4.2 Specific laboratory tests for organ procurement

| Monitoring parameters | Measuring interval | Remarks |
|--|-------------------------|--|
| Blood group (ABO and Rhesus) | | Confirmation by a reference centre |
| HLA typing | | By a reference centre |
| HIV, hepatitis B and C, CMV, syphilis, toxoplasmosis, EBV, HTLV I & II, herpes simplex & herpes zoster | | |
| Calcium, magnesium, phosphate, LDH, gammaGT, alc. phos., CPK, CK-MB, pancreatic amylase, lipase, EW, albumin, ammonia, CRP | Once, for normal values | |
| Arterial blood gas analysis (ABGA) | Every 4 hrs | With PEEP 5 mbar and FiO ₂ 0.4 for 10 min |
| Arterial blood gas analysis (ABGA) | Every 4 – 8 hrs | With PEEP 5 mbar and FiO ₂ 1.0 for 10 min |

4.3 Microbiology

| Monitoring parameters | Measuring interval |
|---|---|
| Blood and urine cultures, tracheal secretions | Standard <24 hrs before multi-organ procurement |

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Changes

| Date | Version | Changes |
|---------------|---------|---|
| February 2023 | 4.1 | Correction |
| December 2020 | 4.0 | Revision |
| March 2018 | 3.1 | New logo |
| April 2014 | 3.0 | Layout and title adapted Text adapted: chapters A, B, C; fusion chapter D and annex 1 |
| February 2011 | 2.0 | |
| December 2006 | 1.0 | Original version |

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