CLINICAL PROTOCOL

OF SURGICAL AND DIAGNOSTIC INTERVENTION

**EXTRACORPOREAL MEMBRANE OXYGENATION
AS A METHOD OF TREATMENT FOR SEVERE FORMS OF CARDIAC AND RESPIRATORY FAILURE**

Approved by the Expert Council

**Republican State Enterprise on the Right of Economic Management
"Republican Center for Healthcare Development"
of the Ministry of Healthcare and Social Development of the Republic of Kazakhstan**

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Protocol No. 18

INTRODUCTORY SECTION

Protocol title:
Extracorporeal membrane oxygenation as a method of treatment for severe forms of respiratory and cardiac failure.

Protocol code:
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ICD-10 Codes:

C38 – Malignant neoplasm of heart, mediastinum and pleura
I05 – Rheumatic mitral valve diseases
I06 – Rheumatic aortic valve diseases
I07 – Rheumatic tricuspid valve diseases
I08 – Multiple valve diseases
I09 – Other rheumatic heart diseases
I10 – Essential (primary) hypertension
I13 – Hypertensive heart and renal disease
I24 – Other acute ischemic heart diseases
I25 – Chronic ischemic heart disease
I34 – Non-rheumatic mitral valve disorders
I35 – Non-rheumatic aortic valve disorders
I36 – Non-rheumatic tricuspid valve disorders
I41 – Myocarditis in diseases classified elsewhere
I42 – Cardiomyopathy
I43 – Cardiomyopathy in diseases classified elsewhere
I46.0 – Cardiac arrest with successful resuscitation
I48 – Atrial fibrillation and flutter
I49 – Other cardiac arrhythmias

I50 – Heart failure
I51 – Complications and ill-defined heart diseases
I52 – Other heart disorders in diseases classified elsewhere

I97 – Circulatory system complications following medical procedures, not classified elsewhere
Excludes: Postoperative shock (T81.1)

I97.0 – Postcardiotomy syndrome

I97.1 – Other functional disturbances after cardiac surgery.
Heart failure following cardiac surgery or related to the presence of a cardiac prosthesis

I99 – Other and unspecified circulatory system disorders

J10–J18 – Influenza and pneumonia
J20–J22 – Other acute lower respiratory tract infections

J80–J84 – Other respiratory diseases primarily affecting the interstitial tissue

J96.0 – Acute respiratory failure
J96.1 – Chronic respiratory failure
J96.9 – Respiratory failure, unspecified

K44 – Diaphragmatic hernia

O74 – Complications related to anesthesia during labor and delivery
Includes: maternal complications caused by general or regional anesthesia, analgesics or sedatives during labor and delivery

O75.0 – Maternal distress during labor and delivery
O75.1 – Maternal shock during or after labor and delivery

O75.4 – Other complications caused by obstetric surgical interventions and procedures, including cardiac arrest after cesarean section or other obstetric operations and procedures, including delivery, NOS

P24.0 – Neonatal meconium aspiration

Q20 – Congenital malformations of cardiac chambers and connections
Q21 – Congenital malformations of cardiac septa
Q22 – Congenital malformations of pulmonary and tricuspid valves
Q23 – Congenital malformations of aortic and mitral valves
Q24 – Other congenital heart malformations
Q25 – Congenital malformations of great arteries
Q26 – Congenital malformations of great veins
Q27 – Other congenital malformations of peripheral vascular system
Q28 – Other congenital malformations of the circulatory system

S26 – Injury of heart

T81.1 – Shock during or following a procedure, not classified elsewhere

T86 – Failure and rejection of transplanted organs and tissues

T86.2 – Failure and rejection of heart transplant with artificial cardiac device (T82.5) or heart-lung transplant (T86.3)

T86.3 – Failure and rejection of heart-lung transplant

Date of protocol development: 2015

Patient category: adults, children

Protocol users: cardiologists, cardiac surgeons, anesthesiologists, intensivists, arrhythmologists, interventional cardiologists, transplantologists, internists/pediatricians, general practitioners, pulmonologists, clinical pharmacologists, physiotherapists, social workers

METHODS, APPROACHES AND PROCEDURES FOR DIAGNOSIS AND TREATMENT

Assessment of the level of evidence of recommendations

Levels of evidence scale:

A – High-quality meta-analysis, systematic review of randomized controlled trials (RCTs), or large RCTs with very low risk of bias (++), the results of which can be extrapolated to the relevant population.

B – High-quality (++) systematic review of cohort or case-control studies, or high-quality (++) cohort or case-control studies with very low risk of bias, or RCTs with low risk of bias (+), the results of which can be extrapolated to the relevant population.

C – Cohort or case-control study or controlled study without randomization with low risk of bias (+).
Results may be extrapolated to the relevant population, or RCTs with very low or low risk of bias (++ or +), the results of which cannot be directly extrapolated.

D – Case series description, uncontrolled study, or expert opinion.

GPP – Good pharmaceutical practice.

Definition

Extracorporeal membrane oxygenation (ECMO) or **extracorporeal life support (ECLS)** is the use of mechanical devices for temporary (from hours to days or months) support of cardiac and/or pulmonary function (partially or completely) during cardiopulmonary failure, until recovery of function or transplantation.

Most commonly, ECMO as a prolonged extracorporeal circulation procedure is used in patients with acute, potentially reversible respiratory, cardiac, or cardiorespiratory failure that does not respond to full standard therapy.

Types of ECMO

Veno-arterial ECMO (VA ECMO) – a type of ECMO in which blood is drained from the venous system, oxygenated in the oxygenator, and returned to the arterial circulation. Used to support both heart and lungs.

Veno-venous ECMO (VV ECMO) – a type of ECMO in which blood is drained from the venous system, oxygenated in the oxygenator, and returned to the venous circulation. Used when only pulmonary support is required.

NOMENCLATURE OF PERIPHERAL CANNULATION CONFIGURATIONS FOR ECLS

Configuration Variants

Variant	VV (ECMO)	VA (ECMO)	VVA (ECMO)	AV ($ECCO_2R$)
Flow direction	From → oxygenator → To	V–V, VV–V	V–V	V–A, VV–A
			V–VA	V–AV
Configuration	Single-lumen cannulas	Dual-lumen cannula	Single-lumen cannulas	Single-lumen cannulas from V–V
			Dual-lumen cannula from V–V	Single-lumen cannulas from V–V
			Single-lumen cannulas	

Level 1: Hierarchy

Uppercase = high-flow cannula
Lowercase = low-flow cannula

- Vcep–V
- (dl)V–V
- (ca)V–V
- (bc)Vcep–V
- V–Ad
- (dl)VV–Ad
- Vv–VAd
- (dl)V–VA
- V–AdV
- (pl)A–V

Level 2: Cannulation Site (indexed)

- Vf–Vj
- (dl)Vf–V
- (ca)Vjcep–V
- Vj–Af
- VjVf–Afd
- Vj–Acar
- Vf–VjAf
- (bc)Vj–VAfd
- Vj–AfVf
- (pl)Afl–Vfr

Level 3: Cannula Tip Position (indexed)

- Vivc–Va
- Vjacep–Vf
- Vfsvc–Vf
- Vja–Aflidpvntal
- Vja–Asrg
- Vj–Ai
- Vf–VfivcAf
- Vf–VjAi
- (ca)Vj–VAslc
- Vjavc–AfrdpVfr
- (pl)Afri–Vfli

Level 4: Cannula Size

OD/Length
Length is not specified
OD is always specified

- V21/50–V17
- V21f–V17fivc
- V23/25a–V17f
- (dl31)V–V
- (ca32)Vjcep–V
- V25/25–A17/18

- V29fa–Afdt
- V25flsvc–Afl19dp
- V25/38j–Vf
- A19/18fdt
- (dl23)V–VAf
- V25/25java–A21frdpV17/50fr
- (pl)A15/17fr–V15fl

Legend

- "–" — oxygenator
  bc — bicaval dual-lumen cannula
  ca — cavo-atrial dual-lumen cannula
  dl — dual-lumen cannula
  $ECCO_2R$ — extracorporeal carbon dioxide removal
  VA, V–A — veno-arterial
  VV, V–V — veno-venous
  VVA — veno-veno-arterial

Level 1 Abbreviations

A — arterial
cef — cranial drainage
d — distal perfusion line of the cannulated limb
P — pulmonary artery
pl — pumpless
V — venous
vnt — cardiac drainage

Level 2 Abbreviations

car — carotid artery
f — femoral
g — vascular graft (chimney)
j — jugular
l — left
r — right
s — subclavian

Level 3 Abbreviations

a — atrium (Va: index "a" indicates the tip of the venous cannula positioned in the right atrium;
vntal — index "al" ("ar") indicates the drainage catheter positioned in the left (right) atrium)

c — left ventricle (vntc: index “c” indicates drainage catheter position in the left ventricle)

i — iliac vein/inferior vena cava or iliac artery
ivc — level of hepatic veins in the inferior vena cava
l — left
p — ankle (dp, index “p” indicates distal retrograde ankle perfusion of the cannulated limb)
r — right
svc — superior vena cava
t — thigh/groin (dt, index “t” indicates distal perfusion via cannula placed at the femoral cannulation site)

Level 4

OD — outer diameter of the cannula in Fr
(1 Fr = 1/3 mm)

PURPOSE OF THE PROCEDURE / INTERVENTION

The primary purpose of ECMO is to maintain hemodynamic and/or respiratory status in patients with acute, potentially reversible respiratory, cardiac, or cardiorespiratory failure resistant to standard therapy, until:

- recovery of organ function
- transplantation
- diagnostic clarification
- prolonged “bridge” to heart transplantation (implantation of a left ventricular assist device, LVAD)

INDICATIONS AND CONTRAINDICATIONS FOR THE PROCEDURE / INTERVENTION

Indications for ECMO

Respiratory indications

In children and adults — pulmonary failure despite maximal respiratory support:

- $FiO_2 = 1.0$
- Pinsp = 35 cmH_2O

Oxygenation Index (OI):

(OI) = (MAP × FiO_2 × 100) / PaO_2

MAP — mean airway pressure

OI ≥ 40 in **3 of 5 arterial blood gas analyses within 2 hours**

Alveolar–arterial oxygen gradient:

$AaDO_2 = FiO_2 \times (760 - 47) - (PaCO_2 / 0.8) - PaO_2$

where 47 = partial pressure of water vapor

$AaDO_2$ > 605–620 mmHg for **at least 4–12 hours**

Acute deterioration:

- Murray Score > 3

Arterial blood gas parameters:

- PaO_2 < 50 mmHg for 4 hours
- PaO_2 < 40 mmHg for 2 hours
- pH < 7.2 for 2 hours
- $PaCO_2$ > 55–60 mmHg for 2–12 hours
- Barotrauma at MAP > 15–18 cmH_2O

Cardiac indications

As an adjunct to cardiopulmonary resuscitation (excluding cases listed in "Contraindications"), provided circulation can be restored via ECMO within 30 minutes:

- witnessed cardiac arrest of any etiology with response to CPR but unstable hemodynamics
- cardiac arrest without response to CPR including direct cardiac massage for 5 minutes
- cardiogenic shock (CI < 2 L/min/m^2)
- hypotension: SBP < 90 mmHg (adults)
- postcardiotomy shock

Maximal inotropic support:

- Dobutamine* 15 μg/kg/min
- Epinephrine 0.2 μg/kg/min
- Dopamine 10 μg/kg/min
- Norepinephrine* 0.3 μg/kg/min

- Levosimendan* 0.2 μg/kg/min
- PAWP > 18 mmHg

Selection criteria for neonates

- gestational age ≥ 34 weeks
- birth weight ≥ 2000 g
- absence of coagulopathy or uncontrolled bleeding
- absence of significant intracranial hemorrhage
- mechanical ventilation < 7–10 days
- reversible lung injury
- absence of lethal congenital malformations
- absence of uncorrectable congenital heart defects

In Transplantology

- ex vivo / ex situ organ perfusion to reduce ischemic time during long-distance transport and to expand transplant indications from extended-criteria donors through treatment and comprehensive assessment during ex vivo/ex situ perfusion
- ex vivo / ex situ organ perfusion for targeted therapy using high (systemically toxic) drug doses and/or surgical treatment of difficult-to-access areas of organs (lungs, liver, heart) to expand indications for autotransplantation
- lung transplantation under ECMO support

Hemodynamic and/or respiratory support for high-risk procedures/operations

- extensive bronchoalveolar lavage
- surgery on the tracheobronchial tree or mediastinum
- interventional procedures on coronary arteries and/or cardiac valves
- reconstructive surgery for congenital diaphragmatic hernia

CONTRAINDICATIONS

Absolute contraindications

- contraindication to anticoagulation (uncontrolled severe coagulopathy or thrombocytopenia);
- asystole as the primary rhythm when an unconscious patient is found;
- terminal condition;
- unwitnessed cardiac arrest;
- uncontrolled metabolic acidosis;
- severe central nervous system injury;
- sepsis caused by multidrug-resistant microorganisms (MRGN 3,4).

Relative contraindications

- mechanical ventilation for more than 5–7 days;
- $PaO_2/FiO_2 < 100$ for more than 5 days;
- severe pulmonary hypertension: mean pulmonary artery pressure > 45 mmHg or > 75% of systemic arterial pressure;
- prolonged (more than 30 minutes) cardiopulmonary resuscitation ("low-flow" state);
- uncontrolled immunosuppression;
- age > 70 years;
- multiple organ failure (≥ 2 systems).

LIST OF MAIN AND ADDITIONAL DIAGNOSTIC MEASURES

Main laboratory investigations

- complete blood count;
- urinalysis;
- assessment of acid–base status and blood gas composition;
- **biochemical blood analysis:** total protein, blood glucose, creatinine, urea, total bilirubin, direct bilirubin, ALT, AST, LDH, CRP;
- coagulation tests (PT, INR, fibrinogen, aPTT, thrombin time);
- thromboelastography;
- activated clotting time;
- HIT testing;
- blood group;
- Rh factor;
- blood test for HIV;
- blood test for hepatitis B and C markers;
- microreaction test for syphilis;
- bacteriological examination of blood, sputum/BAL, urine, throat swab, wounds;
- determination of free hemoglobin in blood and urine.

Additional laboratory investigations

(for exclusion of concomitant pathology and treatment monitoring)

- fecal occult blood test;
- biochemical blood analysis (ferritin, serum iron, transferrin, GGT, alkaline phosphatase);
- procalcitonin (as indicated);
- determination of antibacterial drug concentrations;
- determination of immunosuppressant concentrations;

- determination of myocardial injury markers (CK-MB, troponin, myoglobin);
- sputum analysis for *Mycobacterium tuberculosis* (qualitative) by PCR;
- pregnancy test (as indicated).

Main instrumental investigations

- electrocardiography;
- coronary angiography;
- Holter monitoring;
- echocardiography (transthoracic);
- echocardiography (transesophageal);
- chest radiography (two projections);
- fibroesophagogastroduodenoscopy;
- fibrobronchoscopy;
- computed tomography of the chest, abdominal segments, and brain (including contrast-enhanced studies).

Additional instrumental investigations

(to clarify concomitant pathology)

- endomyocardial biopsy;
- MRI of the abdomen and brain (including contrast-enhanced studies);
- aortography;
- colonoscopy;
- abdominal ultrasound examination;
- EEG.

INDICATIONS FOR SPECIALIST CONSULTATIONS

- **Arrhythmologist consultation** — presence of cardiac rhythm disturbances (paroxysmal atrial tachycardia, atrial fibrillation and flutter, sick sinus syndrome), clinically diagnosed and confirmed by ECG and Holter ECG monitoring;
- **Neurologist consultation** — history of seizures, paresis, hemiparesis, or other neurological disorders;
- **Infectious disease specialist consultation** — signs of infectious disease (pronounced catarrhal symptoms, diarrhea, vomiting, rash, changes in biochemical blood parameters, positive virological or bacteriological test results);
- **Otolaryngologist consultation** — epistaxis, signs of upper respiratory tract infection, tonsillitis, sinusitis;
- **Hematologist consultation** — anemia, thrombocytosis, thrombocytopenia, coagulation disorders, other hemostatic abnormalities;
- **Nephrologist consultation** — signs of renal failure, decreased diuresis, proteinuria;

- **Pulmonologist consultation** — presence of concomitant lung pathology, decreased pulmonary function;
- **Ophthalmologist consultation** — fundoscopic examination;
- **Surgeon consultation** — to exclude acute surgical pathology;
- **Endocrinologist consultation** — presence of concomitant endocrine disorders;
- **Psychotherapist / psychologist, social worker consultation.**

REQUIREMENTS FOR PERFORMING THE PROCEDURE / INTERVENTION

- compliance with safety measures and anti-epidemic regime according to the Sanitary Rules
  "Sanitary and epidemiological requirements for healthcare facilities", approved by the Resolution of the Government of the Republic of Kazakhstan dated January 17, 2012 No. 87;
- infusion of fresh frozen plasma (5–20 ml/kg), cryoprecipitate, platelet concentrate, and replacement with packed red blood cells is performed **strictly according to indications**
  (in accordance with Order No. 666 of the Ministry of Healthcare of the Republic of Kazakhstan
  "On approval of the Nomenclature, rules for collection, processing, storage and distribution of blood and its components, as well as rules for storage and transfusion of blood, its components and products", and its appendices);
- the decision to implant ECMO must be made jointly by a multidisciplinary team including a cardiologist/cardiac surgeon, cardiac anesthesiologist, and perfusionist;
- ECMO implantation is performed by specialists who have undergone appropriate training and hold certification for working with patients of this profile;
- ECMO procedures are performed in intensive care units, operating rooms, and as an adjunct to CPR, including in non-medical facilities, by ECMO specialists.

REQUIREMENTS FOR EQUIPMENT AND CONSUMABLES FOR ECMO

- extracorporeal membrane oxygenation (ECMO) system;
- centrifugal pump and tubing system;
- cannulas for central or peripheral cannulation, sizes 8 Fr to 29 Fr;
- oxygenator;
- gas blender;
- air bubble, pressure, and flow sensors/detectors;
- heat exchanger (HCU);
- hemodialysis and hemodiafiltration system;
- intra-aortic balloon pump;
- expert-class ultrasound diagnostic system with Doppler;
- computed tomography scanner;

- angiography system;
- blood salvage and autotransfusion system;
- stationary X-ray unit;
- mobile radiography system;
- thromboelastograph;
- activated clotting time measurement device.

REQUIREMENTS FOR PATIENT PREPARATION

- preparation of operative fields immediately prior to the procedure (axillary regions, anterior chest wall and abdomen, groin areas);
- patient position: **supine**.

PROCEDURE / INTERVENTION TECHNIQUE

Anesthetic Management

Patient Monitoring

- ECG (5 leads);
- invasive and non-invasive arterial blood pressure;
- pulse oximetry;
- central venous pressure;
- measurement of central hemodynamics (PAP, WP, CO, CI, PVR);
- capnography.

Gastric mucosal protection

- proton pump inhibitors — **Nexium 40 mg**, **Omez 20 mg**;
- H_2-histamine receptor blockers — **Famotidine 20 mg**.

Induction of anesthesia

Opioid analgesics

- fentanyl 50–150 μg/kg IV;

Sedatives

- diazepam 0.3–0.5 mg/kg IV;
- ketamine 1–2 mg/kg;
- Dormicum (midazolam) 1–2 μg/kg/min;

Neuromuscular blocking agents

- pipecuronium bromide 70–80 μg/kg IV;
- rocuronium bromide 0.1 mg/kg;

Maintenance anesthesia

Opioid analgesics

- fentanyl 10–25 μg/kg every 20–30 minutes;

Inhalational anesthetic

- sevoflurane, low-flow anesthesia up to 2 L/min;

Sedation

- propofol 4–7 mg/kg/h;

Neuromuscular blockade

- rocuronium bromide 0.5 mg/kg every 60–90 minutes;
- pipecuronium bromide 70–80 μg/kg IV;

Additional agents

- ketamine 2–8 mg/kg IV.

Mechanical ventilation settings

- respiratory rate: 10–20 breaths/min;
- FiO_2 = 0.21–0.80;
- Pinsp = 15–25 cmH_2O;
- PEEP = 3–15 cmH_2O.

Inotropic and cardiotonic support

- norepinephrine* 0.01–0.5 μg/kg/min;
- epinephrine 0.01–0.3 μg/kg/min;
- dopamine 3–15 μg/kg/min;
- dobutamine* 3–15 μg/kg/min;
- milrinone* 0.1–0.5 μg/kg/min;
- levosimendan* 0.05–0.2 μg/kg/min.

PHARMACOTHERAPY

Medications used for bleeding control

No.	INN name	Single dose	Frequency	Route	Duration	Notes
1	Coagulation factors II, VII, IX and X (combined)	0.9–1.9 ml/kg or 3,000 IU	Once daily	IV	Single dose	Dose calculation is mainly empirical: 1 IU of factor II or X per 1 kg body weight increases plasma activity of factor II or X by 0.02 and 0.017 IU/ml respectively
2	Heparin	30–50 IU/kg/h	Continuous	IV	Until ECMO weaning	Under ACT control 180–200 sec

Medications for reduction of pulmonary hypertension

No.	INN name	Dose	Frequency	Route	Duration	Notes
3	Nitric oxide*	10–40 ppm	Continuous	Inhalation via ventilator circuit	Until weaning from MV	Methemoglobin level must not exceed 2.5%. If >4% reduce NO concentration by half; if >7% stop inhalation
4	Iloprost*	10 µg/ml	6–9 times/day	IV / inhalation	4.6–10.6 min	IV dose adjusted individually; inhalation for pulmonary hypertension
5	Sildenafil	25–300 mg/day	As prescribed	Enteral	As determined	Dose adjusted depending on pulmonary artery pressure

Inotropic agents

No.	INN name	Dose	Frequency	Route	Notes
6	Dobutamine*	2.5–10 µg/kg/min (up to 20–40 if required)	Continuous via infusion pump	IV	Dose individualized; requires continuous monitoring of BP, CVP, PAP, HR, ECG, urine output, electrolytes

7	Dopamine	2.5–10 μg/kg/min (up to 15–25)	Continuous	IV	Initial dose 1–5 μg/kg/min
8	Norepinephrine*	0.01–0.3 μg/kg/min (up to 0.6)	Continuous	IV	Do not mix with other drugs; BP and HR monitoring required
9	Epinephrine	0.01–0.2 μg/kg/min	Continuous	IV	Individualized
10	Milrinone*	0.1–0.5 μg/kg/min (up to 0.8)	Continuous	IV	Loading dose 50 μg/kg over 10 min; daily dose ≤1.13 mg/kg
11	Levosimendan*	0.05–0.2 μg/kg/min	Continuous	IV	Infusion 24 h; effects persist up to 9 days

SEDATIVES, ANESTHETICS AND NEUROMUSCULAR BLOCKING AGENTS

Sedatives and anesthetics

No.	INN name	Dose	Frequency	Route	Duration	Notes
12	Fentanyl	0.05–0.1 mg (in combination with droperidol 2.5–5 mg) in adults; 0.002 mg/kg in children	As prescribed	IV	Preoperative: 10–15 min before anesthesia; during surgery every 20–30 min	Administration under anesthesiologist supervision with appropriate anesthesia equipment
13	Propofol	4–12 mg/kg/h for maintenance of general anesthesia; 4 mg/kg/h in elderly or debilitated patients	Continuous infusion	IV	As clinically indicated	Used only by anesthesiologists; continuous monitoring for hypotension, airway obstruction, hypoventilation, hypoxemia
14	Ketamine	Adults: 1–3 mg/kg; children: 0.5–3 mg/kg; average anesthetic dose 2 mg/kg	As prescribed	IV slowly (>60 s) or IM	As determined	Individual dosing; anesthesiologist supervision required

15	Midazolam *	Individualized	As prescribed	Enteral / IV / IM / rectal	As determined	Dose selected individually based on age, condition, and concomitant therapy
16	Diazepam	Individualized	As prescribed	IV	As determined	Use under anesthesiologist supervision

Neuromuscular blocking agents

No.	INN name	Dose	Frequency	Route	Notes
17	Rocuronium bromide	1 mg/kg (induction); maintenance 0.05–0.1 mg/kg	As prescribed	IV	Dose adjusted based on anesthesia method, expected surgery duration, ventilation duration, and patient condition
18	Pipecuronium bromide	Initial and intraoperative: 0.06–0.08 mg/kg; maintenance: 0.01–0.02 mg/kg every 60–90 min	As prescribed	IV	Consider anesthesia method, ventilation duration, drug interactions

Inhalational anesthetic

No.	INN name	Use	Frequency	Route	Notes
19	Isoflurane	Maintenance of general anesthesia	Continuous	Inhalation	Dose titrated to effect considering MAC 0.5–3%

Gastroprotective agents

No.	INN name	Dose	Frequency	Route	Notes
20	Esomeprazole	20–40 mg	Once daily	IV	Duration determined by clinical condition

Antibiotic therapy

Antibiotic therapy is administered according to approved protocols for the underlying disease (sepsis, pneumonia, etc.) and based on bacteriological culture results.

BLOOD PRODUCTS

- packed red blood cells 20 ml/kg if Hct < 35%, Hb = 120–150 g/L;
- cryoprecipitate 1 IU/kg if fibrinogen < 150 mg/dL;
- fresh frozen plasma 10 ml/kg if PT > 17;
- albumin if serum level < 25 g/L;
- platelet count should be > 100,000/μL.

FLUID BALANCE AND DIURESIS

During the first 24–48 hours of ECMO, oliguria and acute tubular necrosis may occur due to capillary leak and intravascular volume loss, as contact with foreign surfaces induces systemic inflammatory response, resulting in fluid retention. After 48 hours, a diuretic phase begins.

- target urine output: **1 ml/kg/hour**;
- if oliguria persists for 48–72 hours, hemodialysis or hemofiltration should be integrated into the ECMO circuit.

CANNULATION AND ECMO TECHNIQUE

Cannulation using the Seldinger technique

Veno-arterial ECMO

- drainage via the right internal jugular vein from the right atrium → return to the common carotid artery;
- drainage from the femoral vein → return to the contralateral femoral artery;
- drainage via the right atrium → return to the aorta.

Veno-venous ECMO

Cannulation schemes for VV ECMO

Site of drainage (desaturated blood)	Site of return (oxygenated blood)
Right/left femoral vein → inferior vena cava	Right internal jugular vein → superior vena cava
Left femoral vein → inferior vena cava	Right femoral vein → right atrium
Right internal jugular vein → superior vena cava	Left femoral vein → inferior vena cava
Right femoral vein → right atrium	

Right internal jugular vein → venae cavae → right atrium	

Femoro-femoral (bifemoral) configuration

Drainage of desaturated blood from the inferior vena cava with return of oxygenated blood to the right atrium (veno–right atrial circulation). Both cannulas are inserted via the common femoral veins.

The return cannula tip must be positioned in the right atrium immediately above the inferior vena cava orifice to avoid atrial injury; the drainage cannula should be positioned 10–15 cm lower to prevent recirculation.

Femoro-jugular configuration

Drainage from the inferior vena cava with return to the right atrium (veno–right atrial circulation). The return cannula is inserted via the right internal jugular vein; drainage via the common femoral vein (preferably on the right).

The return cannula tip should be placed just below the superior vena cava orifice; the drainage cannula at the inferior vena cava orifice level.

Jugular dual-lumen cannula configuration

Bicaval–right atrial circulation. Cannulation via the right internal jugular vein. Drainage from both venae cavae; return of oxygenated blood into the right atrium via an opening opposite the tricuspid valve.

MANAGEMENT OF A PATIENT ON ECMO

Flow rates during ECMO

- neonates: **120–150 ml/kg/min**;
- children: **100–120 ml/kg/min**;
- adults: **70–80 ml/kg/min**;
- ECMO blood flow up to **70–80% of cardiac output**;
- fresh gas flow to blood flow ratio: **1:1**.

Mechanical ventilation parameters

- respiratory rate: **10–20 breaths/min**;
- FiO_2 = **0.21–0.80**;

- Pinsp = **15–25 cmH_2O**;
- PEEP = **3–15 cmH_2O**.

Hemodynamics

- neonates: mean arterial pressure **35–60 mmHg**;
- children and adults: mean arterial pressure **45–70 mmHg**.

If required, correction is achieved using sedation, analgesia, neuromuscular blockade, vasopressors, and antihypertensive agents.

Central nervous system assessment

- in neonates — cranial ultrasound before cannulation and after 24 hours due to high risk of intraventricular hemorrhage.

Patient care

- adherence to hospital care protocols;
- use of gel cushions;
- bilateral patient rotation;
- centered head positioning;
- change of body position every 2 hours to redistribute pressure load.

INDICATORS OF PROCEDURE EFFECTIVENESS

- restoration of organ function.

ECMO weaning protocol (within 6–24 hours)

- gradual reduction of ECMO performance by **5–10% per hour** to **25%**, but not less than **250 ml/min**;
- stop ECMO flow for **5–10 minutes**;
- assessment of cardiorespiratory function;
- vascular reconstruction if required.

PARAMETERS FOR WEANING FROM ECMO

Echocardiographic parameters

- left ventricular ejection fraction **> 35–40%**;
- LV end-diastolic diameter **< 55 mm**;

- velocity time integral **> 10 cm**;
- complete opening of the aortic valve;
- absence of left ventricular dilation.

Mechanical ventilation parameters

- PaO_2 / FiO_2 ≥ **300**;
- PEEP ≥ **5 cmH_2O**;
- lung compliance ≥ **80 ml/cmH_2O**;
- Murray Score **< 3**.

Blood gas laboratory parameters

- PaO_2 < 40 mmHg for 2 hours;
- pH < 7.2 for 2 hours;
- $PaCO_2$ > 55–60 mmHg for 2–12 hours.

ORGANIZATIONAL ASPECTS OF PROTOCOL IMPLEMENTATION

Protocol developers

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Conflict of interest

None declared.

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Conditions for protocol revision

Revision of the protocol after **3 years** and/or upon the emergence of new diagnostic or treatment methods with a higher level of evidence.

LIST OF REFERENCES

APPENDIX 1

Abbreviations Used in the Protocol

AV block — atrioventricular conduction block

AH — arterial hypertension

BP — blood pressure

ARVD — arrhythmogenic right ventricular dysplasia

CABG — coronary artery bypass grafting

ALT — alanine transaminase

ALT — alanine aminotransferase

ARA II — angiotensin II receptor antagonists

AST — aspartate aminotransferase

aPTT — activated partial thromboplastin time

BB — beta-blockers

ALVSD — asymptomatic left ventricular systolic dysfunction

CCB — calcium channel blockers

IVRT — isovolumetric relaxation time

HIV — human immunodeficiency virus

ICA — internal carotid artery

SCD — sudden cardiac death

HCM — hypertrophic cardiomyopathy

RG — respiratory gymnastics

DPAP — diastolic pulmonary artery pressure

PCWP — pulmonary capillary wedge pressure (left ventricular filling pressure)

PAWP — pulmonary artery wedge pressure

DCM — dilated cardiomyopathy

ACE inhibitors — angiotensin-converting enzyme inhibitors

CHD — coronary heart disease

MV — mechanical ventilation

CPB — cardiopulmonary bypass

LVEDVI — left ventricular end-diastolic volume index

MI — myocardial infarction

BMI — body mass index

IUF — isolated ultrafiltration

CAG — coronary angiography

LVEDV — left ventricular end-diastolic volume

LVEDD — left ventricular end-diastolic diameter

QoL — quality of life

CrCl — creatinine clearance

LVESV — left ventricular end-systolic volume

LVESD — left ventricular end-systolic diameter

LDH — lactate dehydrogenase

LV — left ventricle

PVR — pulmonary vascular resistance

PT — physical therapy

MAC — minimum alveolar concentration

INR — international normalized ratio

MRI — magnetic resonance imaging

CBC — complete blood count

UA — urinalysis

ICU — intensive care unit

AMI — acute myocardial infarction

AKI — acute kidney injury

PT — prothrombin time

VD — peripheral vasodilators

PEEP — positive end-expiratory pressure

PICS — postinfarction cardiosclerosis

RCA — right coronary artery

PCR — polymerase chain reaction

RAAS — renin–angiotensin–aldosterone system

RIA — radionuclide angiography

RCM — restrictive cardiomyopathy

GR — graft rejection

sPAP — systolic pulmonary artery pressure (calculated)

CRT — cardiac resynchronization therapy

SBP — systolic blood pressure

DM — diabetes mellitus

GFR — glomerular filtration rate

LM — light microscopy

HF — heart failure

HF — heart failure

HFpEF — heart failure with preserved systolic function

HFpEF — heart failure with preserved ejection fraction

CO — cardiac output

CRP — C-reactive protein

Stress Echo — stress echocardiography

LVEF (preserved) — preserved left ventricular ejection fraction

PWLV — posterior wall thickness of the left ventricle

TMDF — transmitral diastolic flow

IVST — interventricular septal thickness

TPG — transpulmonary gradient

HTx — heart transplantation

EF — ejection fraction

FC — functional class

FS — fractional shortening

CHF — chronic heart failure

HR — heart rate

ECG — electrocardiography

ECMO — extracorporeal membrane oxygenation

PM — pacemaker

EMB — endomyocardial biopsy

Echo — echocardiography

BNP — B-type natriuretic peptide

CI — cardiac index

CVP — central venous pressure

FiO_2 — fraction of inspired oxygen

IBP — invasive blood pressure

LVAD — left ventricular assist device

PAP — pulmonary artery pressure

PVR — pulmonary vascular resistance

SpO_2 — oxygen saturation

WP — wedge pressure

TC — total cholesterol

β-blockers — beta-adrenergic blockers

***** — single-use import permitted within the territory of the Republic of Kazakhstan