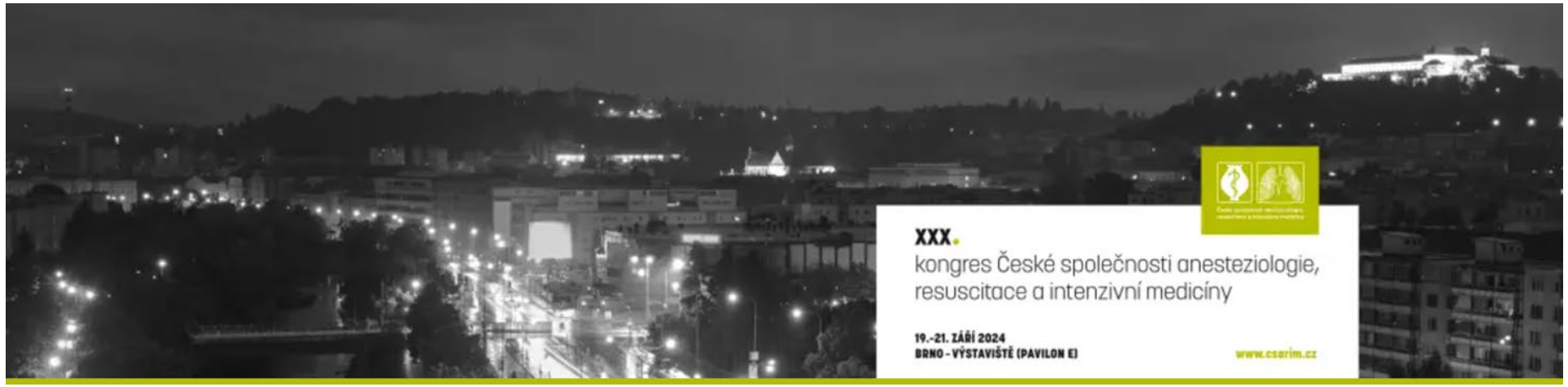
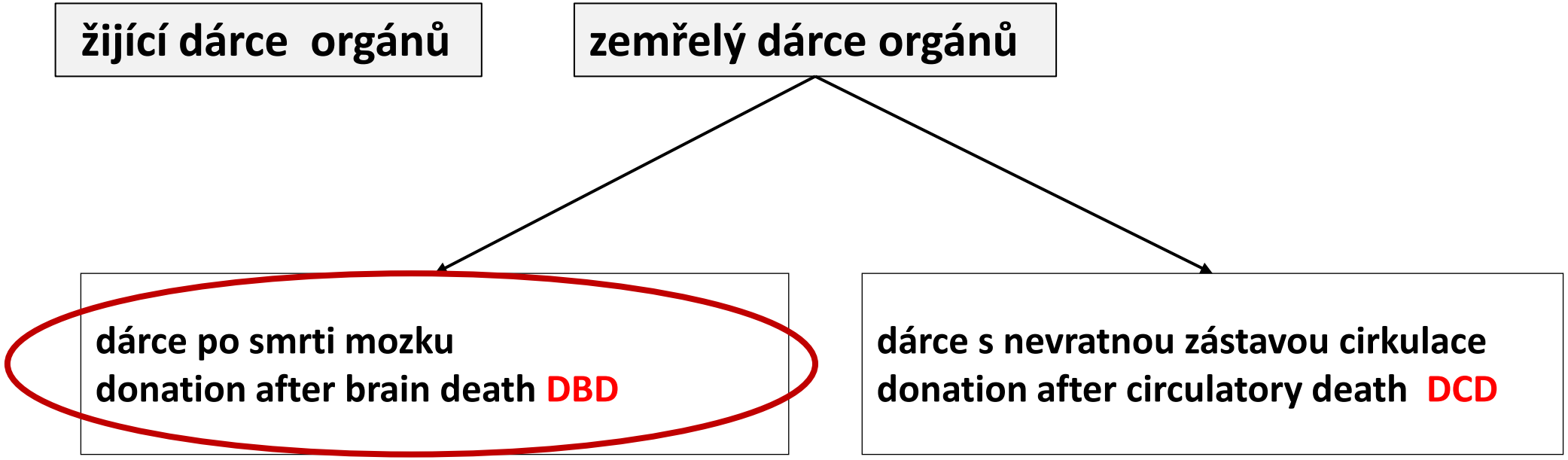
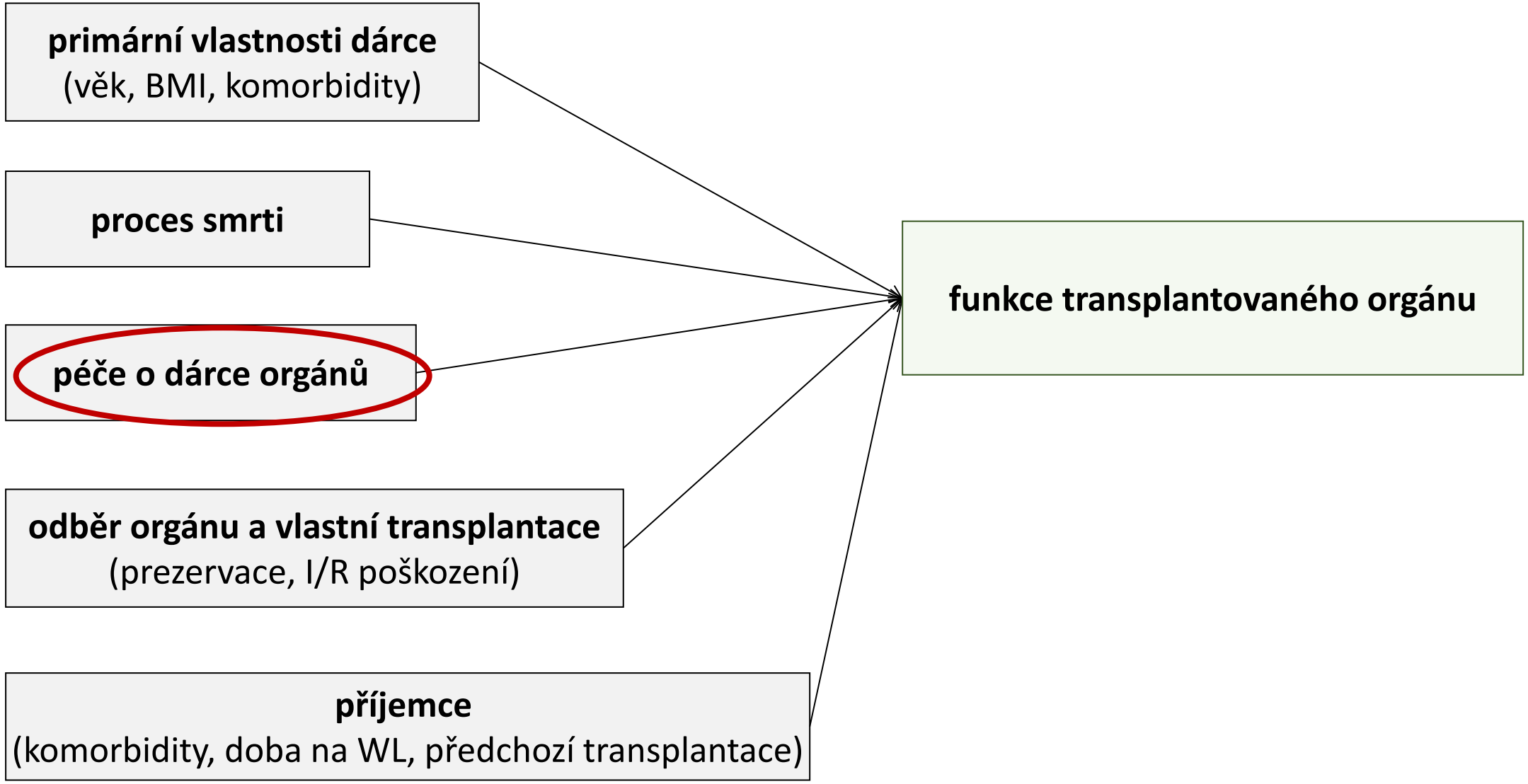


Optimalizace funkce orgánů odebraných od zemřelého dárce update 2024

Eva Kieslichová
Klinika anesteziologie, resuscitace a intenzivní péče IKEM
1. LF UK Praha
eva.kieslichova@ikem.cz

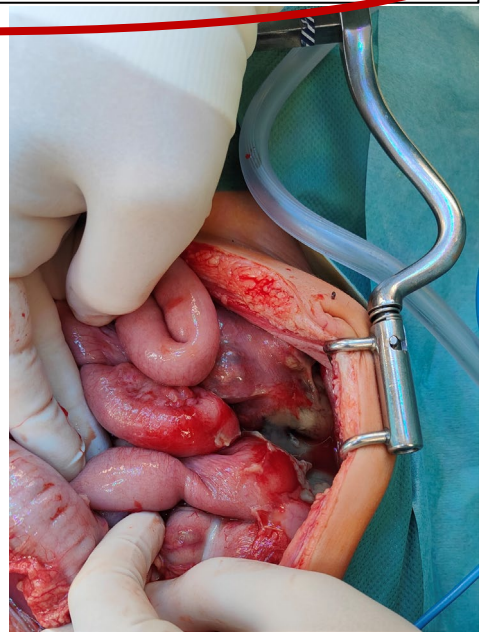

žijící dárce orgánů
zemřelý dárce orgánů
dárce po smrti mozku
donation after brain death DBD
dárce s nevratnou zástavou cirkulace
donation after circulatory death DCD


primární vlastnosti dárce
(věk, BMI, komorbidity)
proces smrti
péče o dárce orgánů
odběr orgánu a vlastní transplantace
(prezervace, I/R poškození)
příjemce
(komorbidity, doba na WL, předchozí transplantace)
funkce transplantovaného orgánu

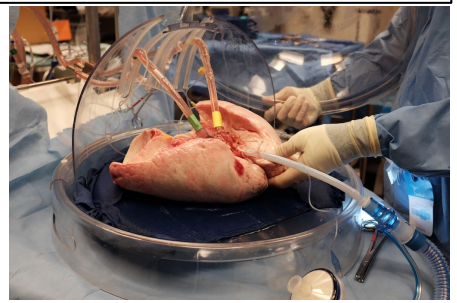
péče o dárce s dg smrti mozku = péče o kriticky nemocného

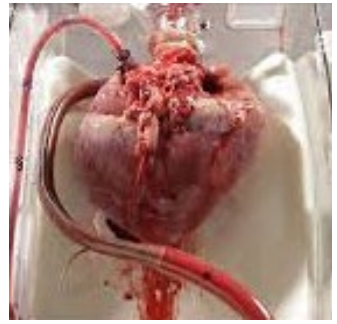
specifická opatření = patofyziologické změny po smrti mozku

In vivo cílená intenzivní péče o dárce



ex vivo rekondice orgánů





postupná ischemizace mozkového kmene rostro-kaudálně → typický sled patofyziologických změn

pontinní ischemie → smíšená vagová a sympatická stimulace → „**Cushingova odpověď**“ ↓*TF, hypertenze, nepravidelné dýchání*

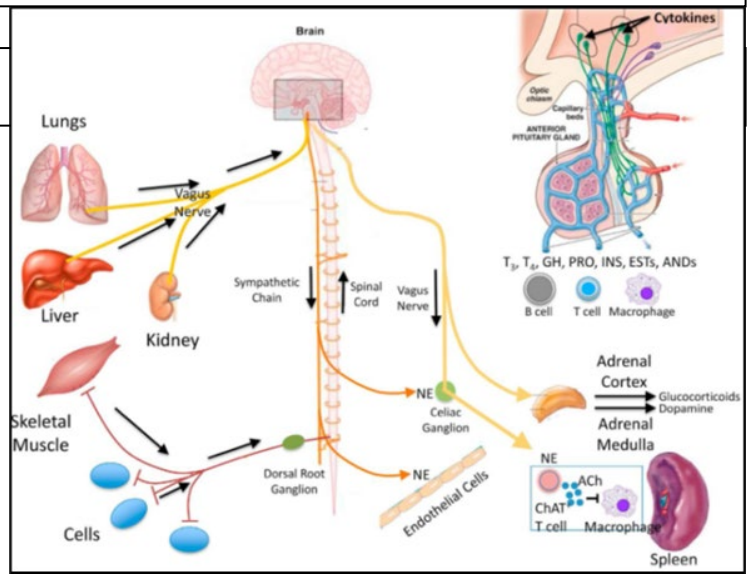
ischemie kaudální prodloužené míchy→ destrukce vagových jader→ neoponovaná převaha sympatiku **„sympatická bouře“**

pokračující herniace → kompletní **ischemie vazomotorických center v prodloužené míše a sympatických drah v krční míše**

ztráta sympatické aktivity → **progresivní hypotenze a kardiovaskulární kolaps** „neurogenní šok“

postižení hypotalamo–hypofyzárního regulačního systému, **ztráta homeostatických kontrolních mechanismů**

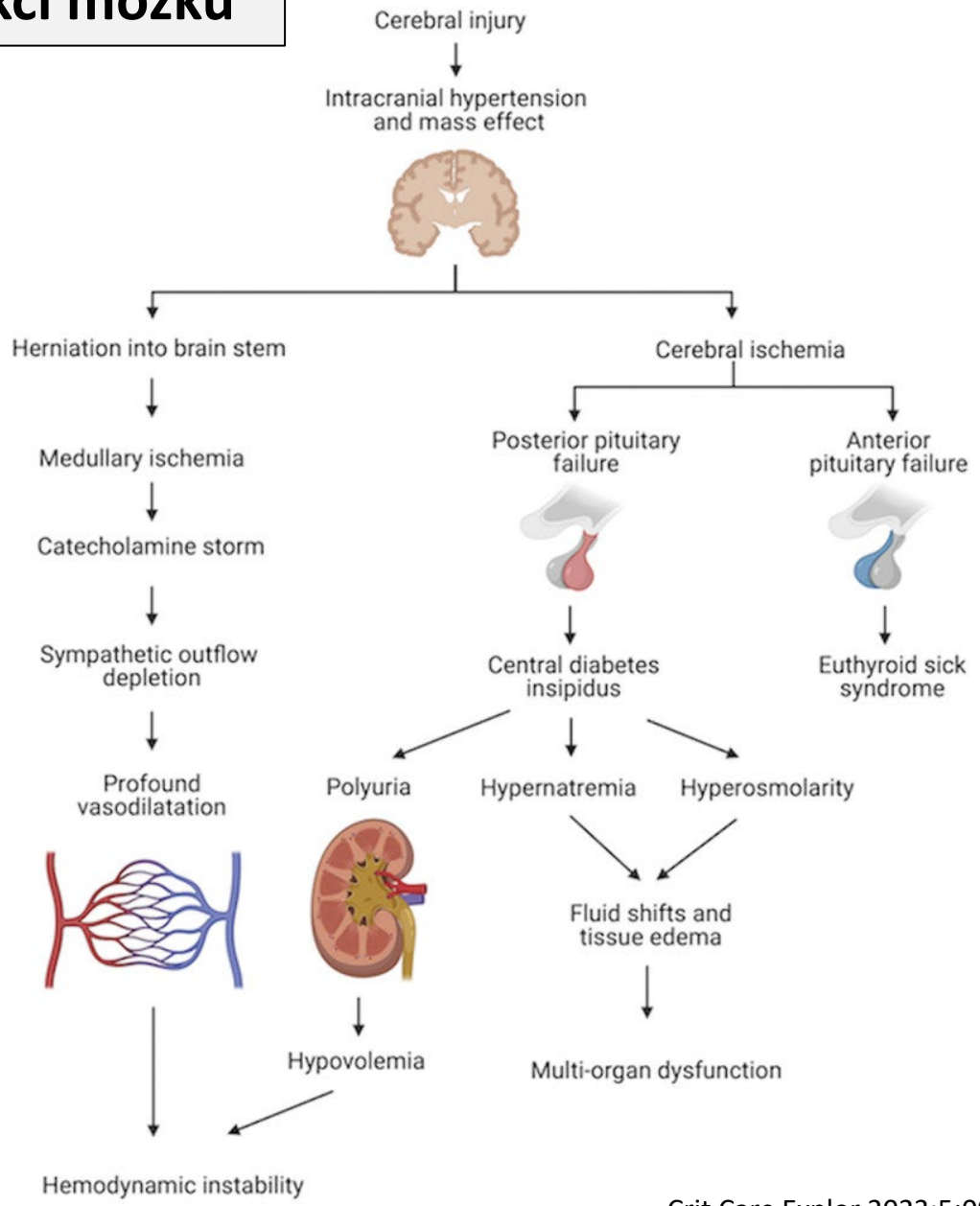
smrt mozku – generalizovaná zánětlivá odpověď a endoteliální poškození



↑ pro a anti imflamatorní cytokiny, IL-1, IL-6, TNF-α, CRP, PCT
↑ katecholaminy: noradrenalin, adrenalin
stupeň katecholaminové odpovědi koreluje s rychlostí zvýšení ICP

Patofyziologické změny při ireverzibilní ztrátě funkcí mozku

systém	důsledky smrti mozku/incidence
kardiovaskulární	hemodynamická nestabilita • hypertenze • **hypotenze 81–97 %** myokardiální poškození ztráta vaskulárního tonu **arytmie 25–32 %** hypovolémie
respirační	zvýšení kapilární permeability **neurogenní plicní edém 13–18 %**
endokrinní	hypothalamo/hypofyzární dysfunkce **hypotermie 100 %** **diabetes insipidus 46–78 %** hypernatrémie hyperglykémie
hematologický	**koagulopatie 29–55 %** DIC
imunitní	systémová zánětlivá reakce endoteliální poškození

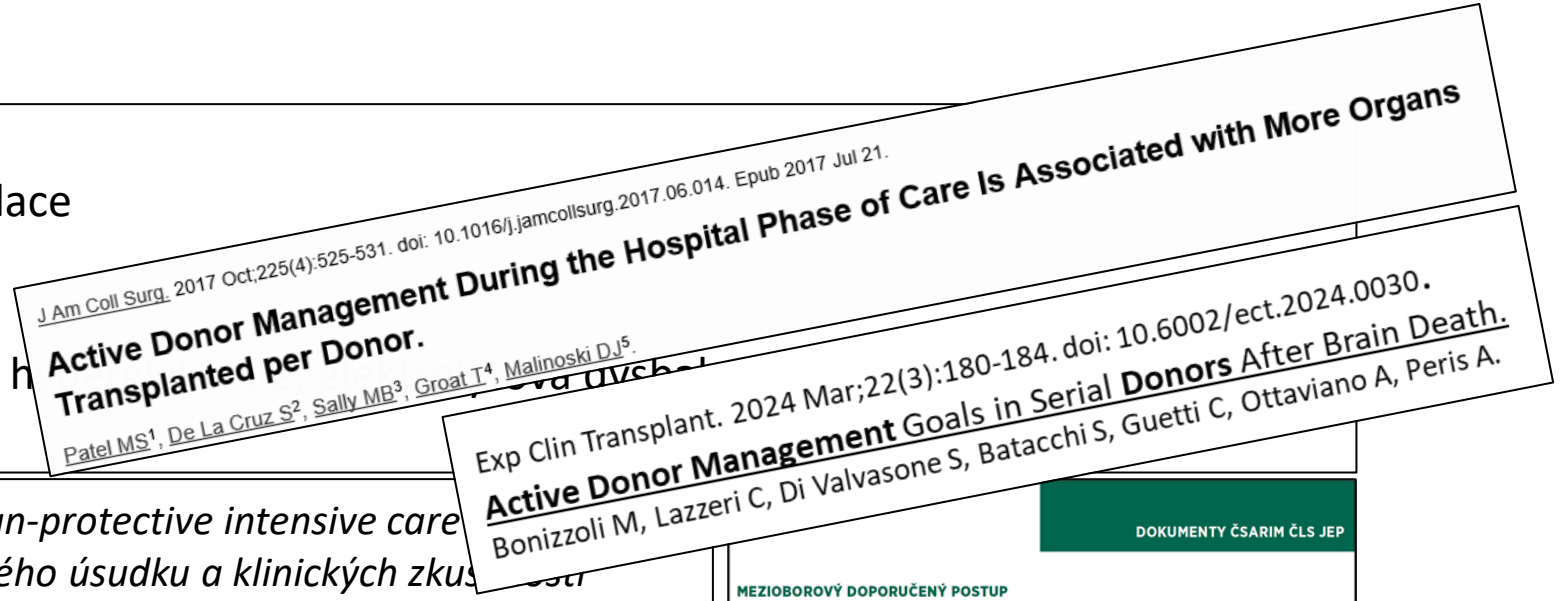


Br J Anaesth 2012; 108: i96, Anaesthesia 2020;75:1205

Crit Care Explor 2023;5:0907

Péče o dárce (DBD)

optimalizace hemodynamiky
péče o funkci plic – protektivní ventilace
normotermie
prevence a terapie infekcí
prevence komplikací: žilní trombóza, h… …vá dysbal…
…..



- *doporučení evidence based pro „organ-protective intensive care*
- *většina doporučení na úrovni odborného úsudku a klinických zku…*
- *extrapolace výsledků jiných studií v intenzivní medicíně*
- *doporučení odborných společností*

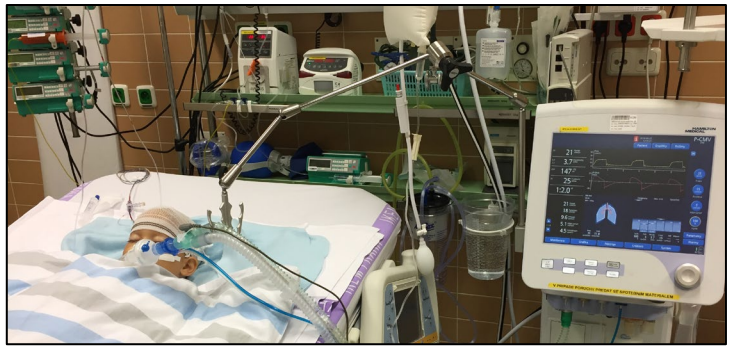
Intensive Care Med 2019;45:343
Intensive Care Med 2024;50:964
Anest Intenziv Med 2018,29:235

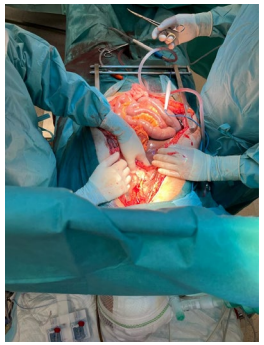
cílená intenzivní péče o dárce

péče o dárce v průběhu transportu

péče o dárce při odběru orgánů

preparace orgánů - perfuze - explantace





Hemodynamika

→ krátká hyperdynamická fáze **“catecholamine storm”** (hypertenze, arytmie)
→ **prolongovaná hypodynamická fáze** (hypotenze)

art katetr, CŽK, PMK
kapilární návrat, laktát, výdej moče, SvO2

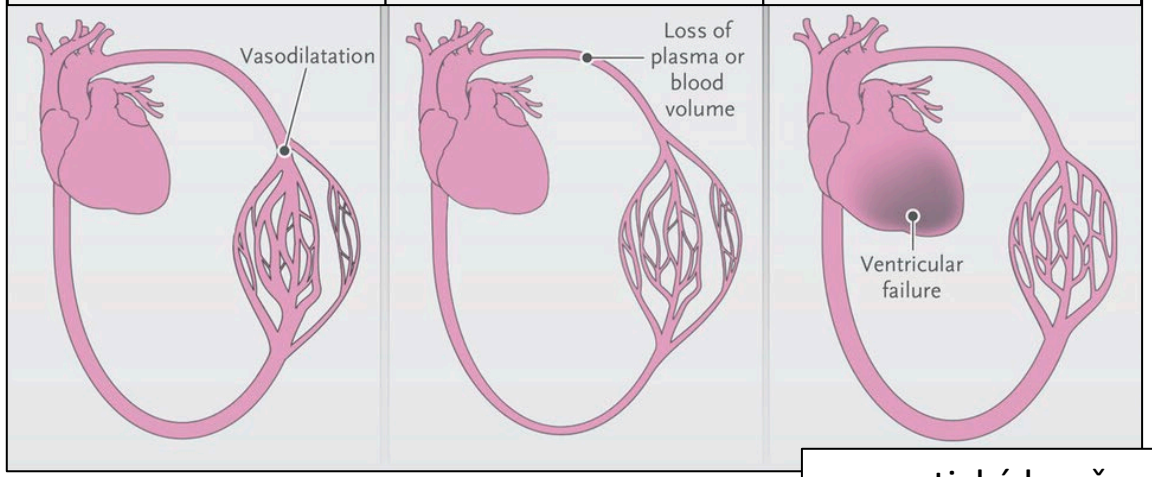
autonomní bouře
→ krátkodobě působící léky
esmolol
nitráty

euvolémie ~~(hyperhydratace)~~
MAP 60 – 70 mmHg
CVP 6 – 10 mmHg
výdej moče 1 – 3 ml/kg/hod
CI > 2.4 l/min/m^2

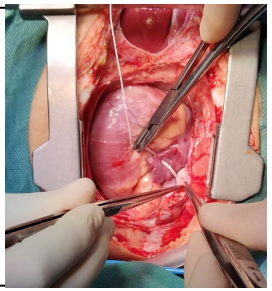
krystaloidy = 1. volba
balancované roztoky
hypotonické roztoky dle SNa
vazopresory/inotropika
terapie arytmie

SNa 135–145 mmol/l

distribuční šok	hypovolemický šok	kardiogenní šok



sympatická bouře
deplece hormonů
poruchy elektrolytů
ischemie myokardu
stresová KMP

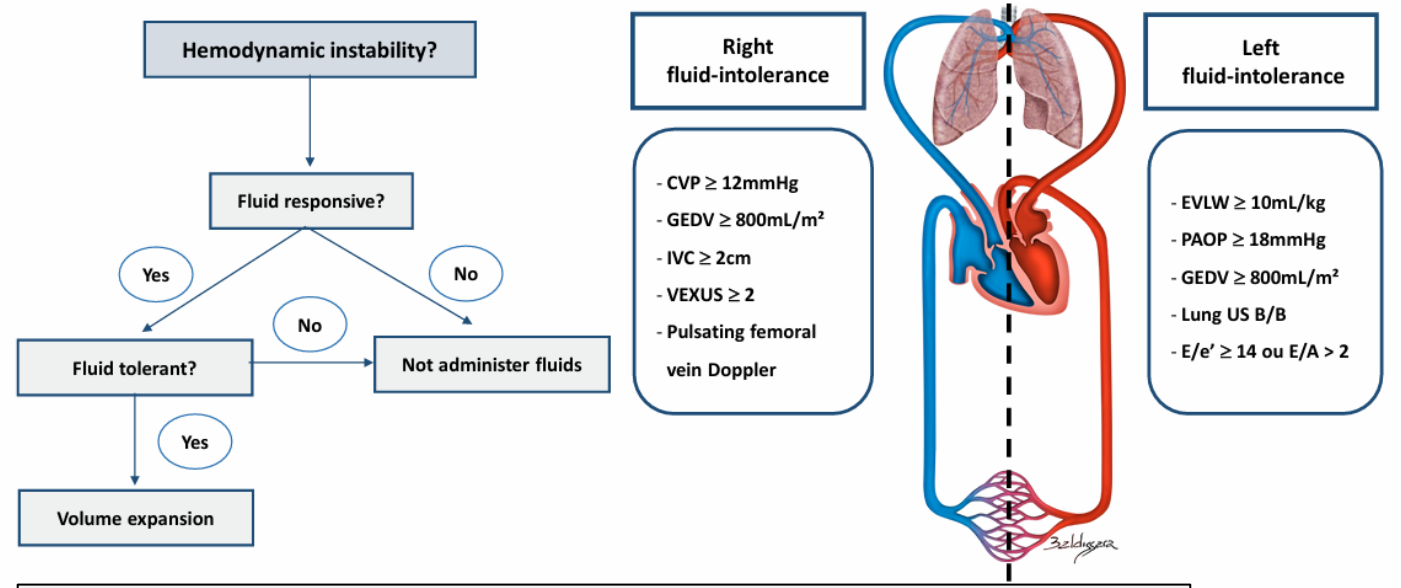


poškození myokardu: cca 20–25 % dárců s dg smrt mozku

Hypotenze:
vazoplegie - hypovolemie - myokardiální dysfunkce - endokrinní poruchy (diabetes insipidus, thyroidální dysfunkce)

Intensive Care Med 2024;50:964 NEJM 2013;369:1726 Ir J Med Sci 2019;188:1111

Tekutinová terapie



Hodnocení tolerance tekutin pro rozhodování o volumoexpanzi

Fluid responsiveness	Fluid tolerance	Hemodynamic management
Present	Present	Volume expansion
Absent	Present	Conservative fluid management
Absent	Absent	Resuscitation: diuretics and ultrafiltration
Present	Absent	Early use of vasopressors

Tekutinové přetížení a orgánová dysfunkce

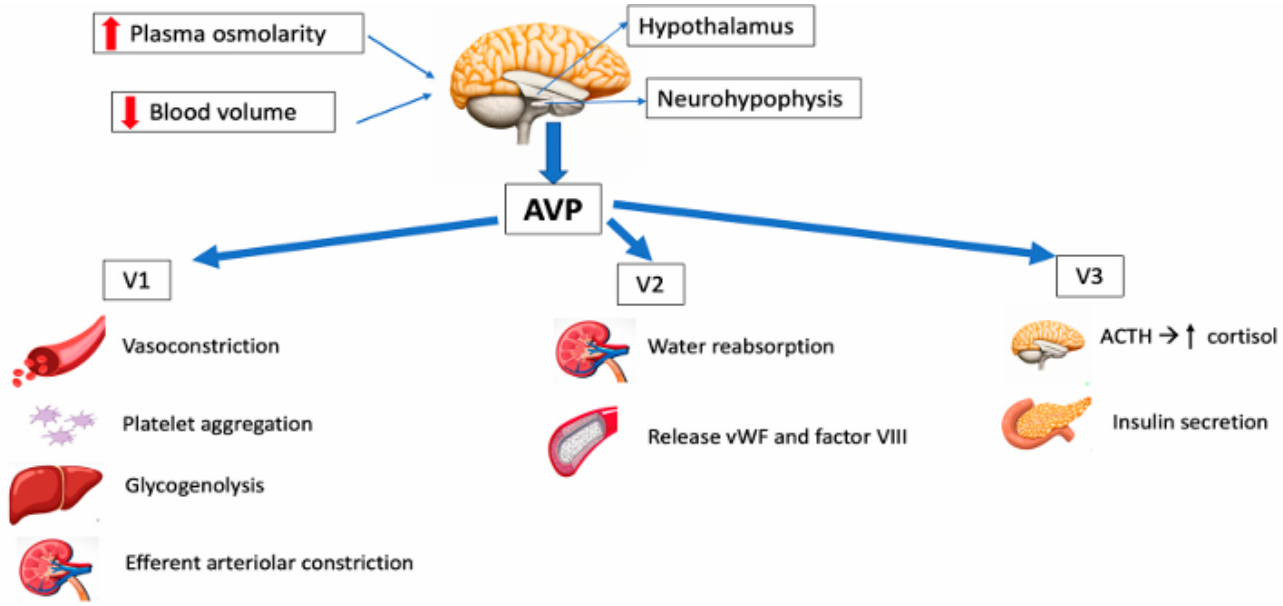
Body	Dysfunction
Lungs	Alteration in gas exchange
	Reduction in complacency
	Increased work of breathing
Heart	Conduction disorders
	Change in contractility
	Diastolic dysfunction
Brain	Cognitive dysfunction
	Delirium
Kidney	Increased interstitial pressure
	Reduction in renal blood flow
	Decreased glomerular filtration rate
	Uremia
	Retention of salt and water
Liver	Cholestasis
	Dysfunction of hepatic synthesis
Intestine	Ileum
	Malabsorption
Skin	Reduction in the healing process
	Pressure ulcer
	Wound infection

Crit Care Sci 2023;35:226

Hemodynamika – volba vazopresorů

podpora vazopresory 80–90% dárců

→ ~~Dopamin~~
→ **Noradrenalin**
→ **Vazopresin**
→ **Hydrokortizon**



NARRATIVE REVIEW

OPEN

Vasopressin Use in the Support of Organ Donors: Physiological Rationale and Review of the Literature

CONCLUSIONS: Despite potential impact on graft outcome and a protective effect through catecholamine support sparing, the benefit of vasopressin use in organ donors is based on low evidence. Well-designed observational and randomized controlled trials are warranted.

Crit Care Explor 2023;5:0907

0.01–0.04 IU/min IV

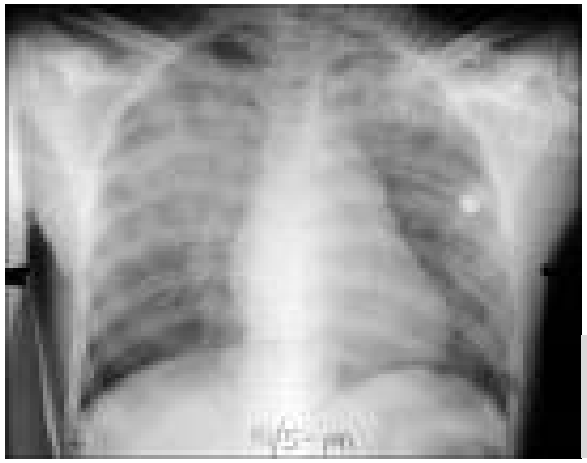
VASOPRESSIN AGONISTS	STRUCTURE	RECEPTOR AFFINITY	CLINICAL APPLICATION	HALF-LIFE (min)
ARGININE VASOPRESSIN (AVP)	8-Arginine vasopressin	V1, V2, V3	Sepsis, vasodilatory shock, cardiac arrest	5–15
DESMOPRESSIN ACETATE (DDAVP)	Deamino-Cys-D-Arg vasopressin	V2	Central diabetes insipidus, bleeding disorders	90–190
TERLIPRESSIN (TP)	N3-triglycyl-8-lysin vasopressin	V1	Portal hypertension, bleeding gastric and esophageal varices, septic shock	240–360
SELEPRESSIN	Phe-2-Ile-3-Hgn-4-Orn-8 vasopressin	V1	Septic shock Not approved for clinical use	10–30
ORNIPRESSIN	8-L-Ornithine vasopressin acetate	V1	Vasoconstricting agent during myomectomy in cirrhosis, as hepatorenal treatment	60–120

J Pers Med 2023;13:1548

Respirační systém

protektivní ventilace
prevence barotraumatu a derecriutmentu
pronační poloha

nižší FiO2 k paO2 ≥ 10 kPa
normokapnie (pH 7.35 – 7.45)
CPAP během testu apnoe
recruitment
CAVE plicní edém
toaleta DC (šetrné odsávání, FBS)



neurogenní plicní edém
↑VR, capillary leak

Br J Anaesth 2012; 108: i96, Anaesthesia 2020;75:1205, JAMA 2010

ORIGINAL CLINICAL SCIENCE

J Heart Lung Transplant 2021;40:120

Ventilation in the prone position improves oxygenation and results in more lungs being transplanted from organ donors with hypoxemia and atelectasis

Gary F. Marklin, MD,[a] Coby O'Sullivan, MS,[a] and Rajat Dhar, MD[b]

hypoxémie (PaO2/FiO2 < 300 mm Hg + atelektázy) 12 hodin a déle
→ více tx plic 45 vs 24 % (p=0.03)
X bez randomizace, nejednotná alokace

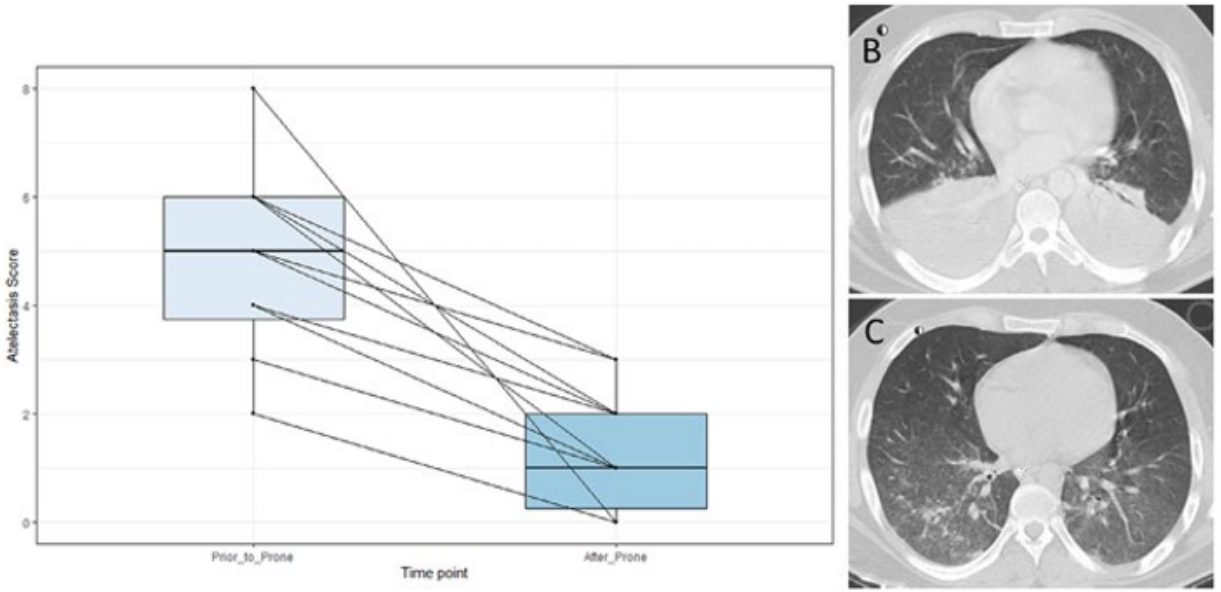
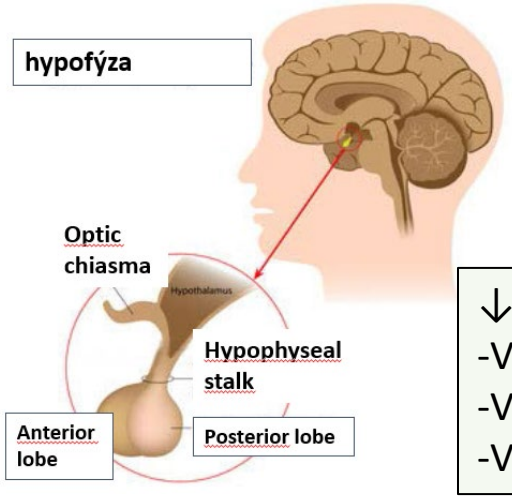


Figure 2 Improvement in atelectasis after ventilation in the prone position. (a) Change in median CT atelectasis scores before and after ventilation in the prone position. The severity of the atelectasis decreases with decreasing numerical scores. The amount of atelectasis decreased in every donor. (b, c) CT scan of a donor with bibasilar lobar atelectasis (b) before (PaO_2/FiO_2 of 105 mm Hg) and (c) after (PaO_2/FiO_2 of 452 mm Hg) 12 hours of ventilation in the prone position demonstrating resolution of the atelectasis and improved oxygenation. CT, computed tomography; FiO_2, fraction of inspired oxygen; PaO_2, partial pressure of arterial oxygen.

Endokrinní dysfunkce a hormonální terapie



↓ ADH
-V1: vasopresorický efekt
-V2: antidiuretický efekt
-V3: přední hypofýza

↓ ACTH ⇒ ↓ kortisol
⇒ ↓srdeční výdej
↓ TSH ⇒ ↓ T3free
⇒↓srdeční výdej

hladina kortizolu cca v normě
kapacita ke ↑ sekrece po stimulaci ACTH nižší

Diabetes insipidus:
polyurie > 4 ml/kg/hod
specifická hmotnost moče < 1010 kg/m^3
osmolalita moče < 200 mmol/kg
Na v moči < 25 mmol/l, SNa > 145 mmol/l
bez glykosurie
osmol plazmy > 300 mmol/kg
poměr močové/plazmatické osmolality < 1

Klinická manifestace

- hypotenze
- hypovolémie
- myokardiální dysfunkce
- elektrolytová dysbalance
- hyperglykémie
- hypotermie

- zhoršení acidózy a koagulopatie
- zvýšení rizika arytmií
- chladová diuréza
- posun disociační křivky kyslíku doleva

diabetes insipidus → náhrada tekutin + desmopressin (V2 receptory): 10–20 µg nazálně/2–4 µg iv
vasopressin (V1, V2, V3 receptory): vazoplegie 0.5.–2.4 IU/hod
glykemie → 6–10 mmol/l, optimálně kolem 8 mmol/l, inzulin kontinuálně, glukóza
kortikosteroidy → **ne rutinně**, hydrokortison u hemodynamicky nestabilních, metylprednisolon?
hormony štítné žlázy → **ne rutinně**

Kortikosteroidy

hydrokortison: ne rutinně, progrese oběhové nestability

vysoké dávky metyprednisolonu = blokáda zánětlivé reakce = protekce orgánové dysfce? **nedoporučeno k rutinnímu užití**

- riziko infekce
- hyperglykémie

Pinsard M, et al. Interest of low-dose hydrocortisone therapy during brain-dead organ donor re uscitation: the CORTICOME study. Crit Care 2014;18:R158

Dupuis S, et al. Corticosteroids in the management of brain-dead potential organ donors: a systematic review. Br J Anaesth 2014;113:346

Hormony štítné žlázy

nedoporučeno k rutinnímu užití

RESEARCH SUMMARY

N Engl J Med 2023;389:2029

Intravenous Levothyroxine for Unstable Brain-Dead Heart Donors

Dhar R et al. DOI: 10.1056/NEJMoa2305969

multicentrická RCT, levothyroxin během 24 hod po dg smrti mozku [838 DBD, T4 vs placebo]

Clinical TRANSPLANTATION

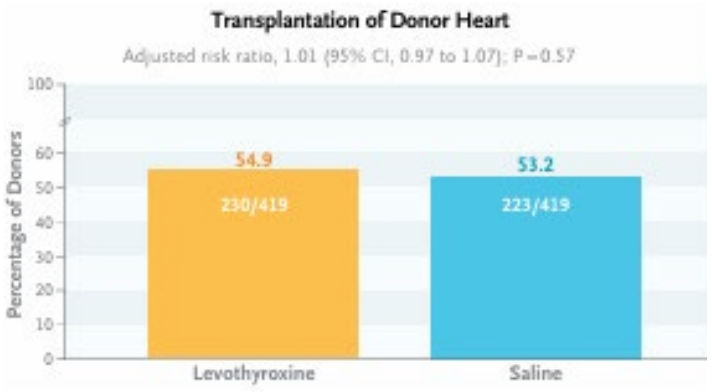
The Journal of Clinical and Translational Research

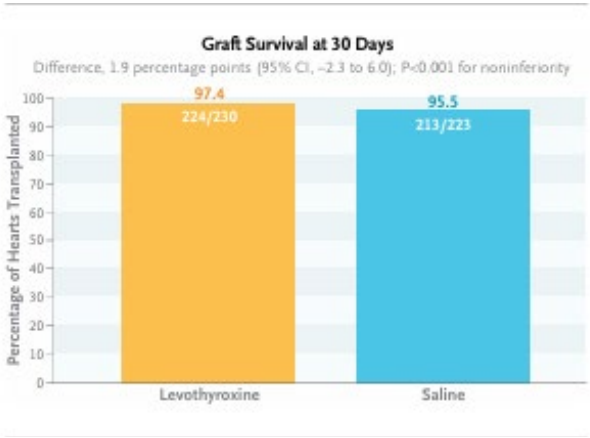
ORIGINAL ARTICLE | Full Access

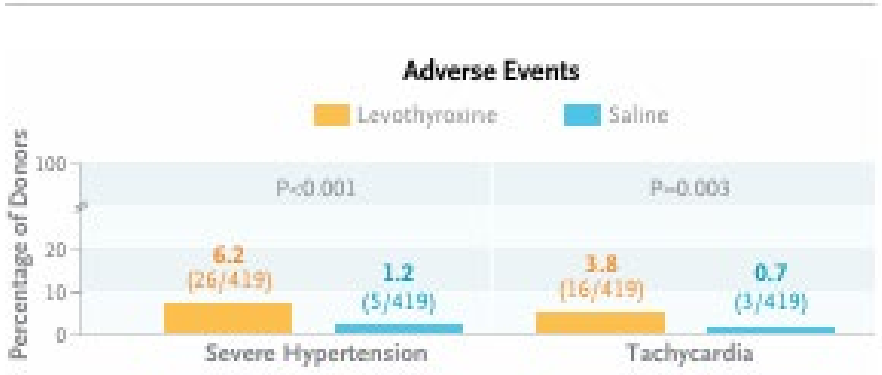
Donor thyroid hormone therapy is associated with an increased risk of graft dysfunction after heart transplantation

Yael Peled, Jacob Lavee, Yigal Kassif, Michael Arad, Alexander Kogan, Amir Peled, Amir Tirosh, Leonid Sternik, Eilon Ram

First published: 04 May 2020 | https://doi.org/10.1111/ctr.13887 | Citations: 5







Normotermie

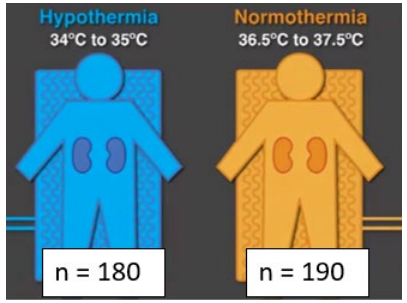
monitorace TT, aktivní ohřev
~~hypotermie?~~

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 JULY 30, 2015 VOL. 373 NO. 5

Therapeutic Hypothermia in Deceased Organ Donors and Kidney-Graft Function

Claus U. Niemann, M.D., John Feiner, M.D., Sharon Swain, M
Melissa Friedman, M.S.N., R.N., Megan Crutchfield, M.P.H., Kristi
John P. Roberts, M.D., and Darren Mali



34–35 °C→ ↓ DGF
HD nestabilita, koagulopatie → TT > 35°C

Table 2. Characteristics of the Organ Recipients.*

Variable	Recipient of Kidney from Hypothermia Group	Recipient of Kidney from Normothermia Group	P Value
Age			0.14
No. of recipients with data	238	238	
Mean — yr	52.3±13.5	53.4±15.4	
Sex — no./total no. (%)			0.40
Female	91/238 (38.2)	101/238 (42.4)	
Male	147/238 (61.8)	137/238 (57.6)	
Body-mass index			0.57
No. of recipients with data	224	225	
Mean	27.2±5.3	26.9±5.5	
Warm-ischemia time			0.11
No. of recipients with data	148	147	
Mean — min	34±19	38±21	
Cold-ischemia time			0.02
No. of recipients with data	281	286	
Mean — hr	13.9±7.3	15.6±8.3	
Delayed graft function — no. of recipients/total no. (%)	79/280 (28.2)	112/286 (39.2)	0.008

* Plus–minus values are means ±SD.

Relativní riziko DGF bylo o 38 % nižší u dárců s mírnou hypotermií než u dárců s normotermií.
Z hypotermie dárce profitovali příjemci štěpu od dárce s rozšířenými kritérii.

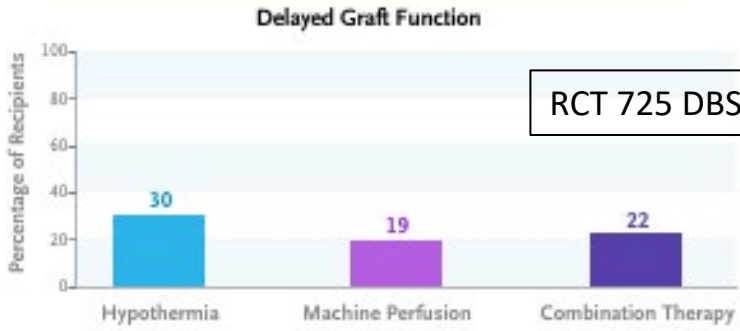
RESEARCH SUMMARY

Hypothermia or Machine Perfusion in Kidney Donors

Malinoski D et al. DOI: 10.1056/NEJMoa2118265

CLINICAL PROBLEM

The use of hypothermia in brain-dead organ donors has been shown to reduce the incidence of delayed graft function in kidney recipients. A similar effect has been estimated for ex situ hypothermic machine perfusion of donor kidneys, but this intervention involves substantial logistic and cost hurdles. Whether donor hypothermia is as effective as machine perfusion in protecting against delayed graft function is unclear.



RCT 725 DBS, 1349 tx ledvin

CONCLUSIONS

Hypothermia in brain-dead kidney donors was inferior to ex situ hypothermic machine perfusion of the kidney in reducing delayed graft function after transplantation. The combination of hypothermia and machine perfusion was not superior to machine perfusion alone.

NEJM 2023;388:418

Prevence a léčba infekce

mikrobiální screening dárce, známky infekce
kontrolovaná infekce/sepse není KI odběru a transplantace

ATB terapie dle nálezů, nově při známkách infekce
CAVE přenos infekce na příjemce

Tromboprofylaxe

smrt mozku → SIRS→ protrombogenní stav
RCT data nejsou

profylaxe LMWH nejsou-li KI
cíl před odběrem INR < 1.5, trombocyty > 50 000/mm^3

Nutriční podpora

RCT data nejsou

kontrola glykémie
při protrahované péči zvážit podání glukózy, nutrientů

Intensive Care Med 2024; 50:964

Schock 2017;47:12

Intensive Care Med 2019;45:343

Transfuzní přípravky

restriktivní transfuzní politika u DBD

významná anemizace [Hb < 70g/l]→ EK v zájmu příjemců orgánů

deleukotizované

DO_2 (index) = CI x CaO_2 x 10)

CaO_2 = (Hb x 1,34 x SaO_2) + (0,003 x PaO_2)

substituce koagulačních faktorů a/nebo trombocytů

krvácení, antikoagulancia, antiagregancia

Transplantation Res 2013;2:4

TRANSPLANTATION RESEARCH

RESEARCH Open Access

Blood transfusion in deceased donor kidney transplantation

Karim Marzouk[1,4], Joseph Lawen[1,5] and Bryce A Kiberd[2,3*]

Abstract

Background: Given the unpredictable timing of deceased donor organs and the need for blood transfusion, this study was carried out to determine the rate and risk factors for transfusion in order to identifying a low-risk cohort in the face of a critical blood shortage.

Methods: This retrospective chart review examined 306 consecutive deceased solitary kidney transplant recipients from January 2006 to August 2012.

Results: Records show that 80 (26.1%) patients were transfused with a total of 300 units (0.98 units/transplant) during their first hospital stay. Transfusions were higher in patients on warfarin (8/14, 57%, 5.1 units/transplant) and antiplatelet agents (46/136, 33.8%, 1.1 unit/transplant) compared to no anticoagulants (74/156, 16.7%, 0.47 units/transplant). In a multivariable logistic regression analysis warfarin (odd ratio (OR) 8.2, 95% confidence interval (CI) 2.5–27, *P*=0.001), antiplatelet agents (OR 2.9, 95% CI 1.6–5.3, *P*=0.001), recipient age ≥55 years (OR 2.2, 95% CI 1.2–3.9, *P*=0.008), recipient male (OR 0.36, 95% CI 0.2–0.64, *P*=0.001) and preop hemoglobin ≥115 g/L (OR 0.32, 95% CI 0.18–0.57, *P*<0.001) were independent predictors of blood transfusion. Lower bleeding cohorts with transfusion rates <5% could not be identified.

Conclusion: The need for blood is significantly higher in subjects on either warfarin or antiplatelet agents. These patients might be avoided if kidney transplantation is to occur during a critical blood shortage. Unfortunately even patients not on anticoagulation are at some risk.

Keywords: Warfarin, Anticoagulation, Blood shortage, Antiplatelet agents, Transfusion

Medicine 2022;101:e32353

Observational Study

Medicine OPEN

Evaluation of red blood cell transfusion threshold in the management of brain-dead organ donors

Sungjeep Kim, MD, PhD[a], Kyunghak Choi, MD[a], Min Ae Keum, MD[a], Min Soo Kim, MD[b], Sun Geon Yoon, MD[b], Kyu-Hyouck Kyoung, MD, PhD[a]

Abstract

The disparity between the demand and supply of organs has necessitated an expansion of the criteria for organ donation. Consequently, numerous guidelines have been proposed for managing brain-dead organ donors (BDODs) to improve their organ function and the organ procurement rate. Therefore, we aimed to evaluate the previously recommended threshold for red blood cell transfusion in BDODs. Medical records of BDODs were retrospectively reviewed from January 2012 to December 2021. We enrolled BDODs who stayed for more than 24 hours at an hospital organ procurement organization. We analyzed their organ function and the rate of organ procurement according to the hemoglobin concentration. A total of 111 BDODs were enrolled and divided into the following 2 groups: hemoglobin (Hb) ≥ 10 g/dL (45.0 %) and Hb < 10 g/dL (55.0 %). There were no significant differences between the groups in the total bilirubin, creatinine, arterial blood lactate, and the rate of organ procurement. A correlation analysis did not reveal any association between the hemoglobin concentration and organ function of the BDODs. Hemoglobin concentration of 10 g/dL cannot be considered a threshold for red blood cell transfusion. Furthermore, organ function is not correlated with a hemoglobin concentration > 7 g/dL. Restrictive transfusion strategy is appropriate for BDOD management.

Abbreviations: BDODs = brain-dead organ donors, HOPO = hospital organ procurement organization, RBC = red blood cell, TRICC = transfusion requirements in critical care, VIS = Vasoactive-inotropic score.

Keywords: brain-dead organ donors, graft function, hemoglobin concentration, organ transplantation, transfusion threshold

GENERAL THORACIC

The Effect of Blood Transfusion in Lung Donors on Recipient Survival

Check for updates

Sayf A. Said, MD, MPH, Toshihiro Okamoto, MD, PhD, Amy S. Nowacki, PhD, Hiromichi Niikawa, MD, PhD, Kamal S. Ayyat, MD, PhD, Ichiro Sakanoue, MD, James J. Yun, MD, PhD, and Kenneth R. McCurry, MD

Department of Inflammation and Immunity, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio; Department of Thoracic and Cardiovascular Surgery, Cleveland Clinic, Cleveland, Ohio; Transplant Center, Cleveland Clinic, Cleveland, Ohio; and Department of Quantitative Health Sciences, Lerner Research Institute, Cleveland Clinic, Cleveland, Ohio

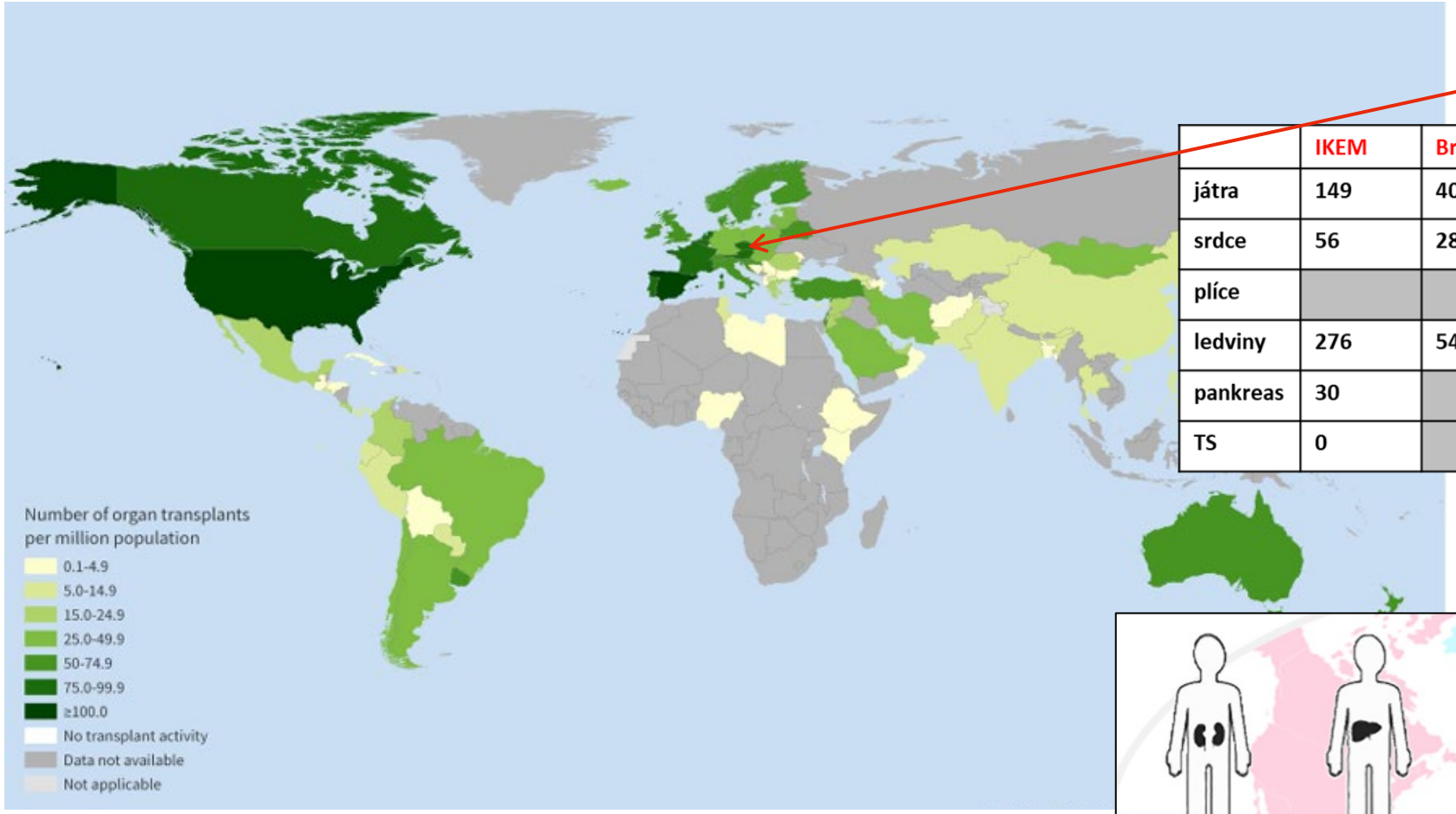
Background. Blood transfusion can have detrimental effects on the pulmonary system, leading to lung injury and respiratory decompensation with subsequent increased morbidity and mortality in surgical and critically ill patients. How much of this effect is carried from a lung donor to transplant recipient is not fully understood, raising questions regarding transplant suitability of lungs from transfused donors.

Methods. United Network for Organ Sharing data were reviewed. Lung transplants from adult donors and known donor transfusion status were included; multi-organ transplants and retransplants were excluded. Recipient mortality was evaluated based on donor and recipient characteristics using a Kaplan-Meier survival estimate, Cox proportional hazards, and logistic regression models. We further assessed whether recipient mortality risk modified the donor transfusion effect.

Results. From March 1996 to June 2017, 20,294 transplants were identified. Outcome analysis based on transfusion status showed nonsignificant difference in 1-year mortality ($P = .214$). Ninety-day recipient mortality was significantly higher with transfusion of >10 units (U) vs 1-10 U or no transfusion (8.5%, 6.1%, and 6.0%, respectively, $P = .005$). Multivariable analysis showed increased 90-day mortality with transfusion of >10 U compared to no transfusion (odds ratio 1.62, $P < .001$), whereas 1-10 U showed no difference (odds ratio 1.07, $P = .390$). When stratified by recipient transplant risk, transfusion of >10 U was associated with increased mortality even with the lowest-risk recipients, while transfusion of 1-10 U showed no mortality increase even in the highest-risk recipients.

Conclusions. Donor transfusion of >10 U of blood was associated with increased 90-day recipient mortality even in low-risk transplants. This risk should be considered when evaluating donor lungs.

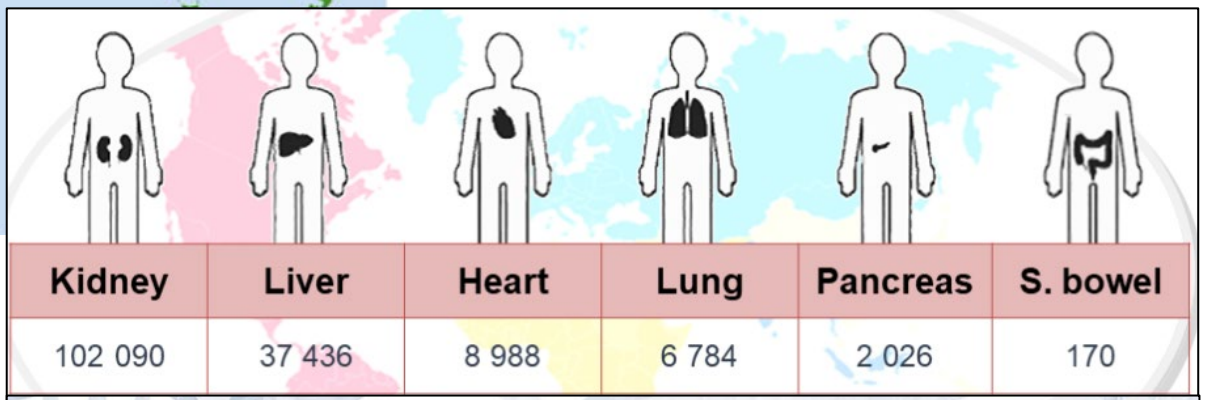
Ann Thorac Surg 2021;112:1109



Česká republika 2023

	IKEM	Brno	Motol	Hradec	Plzeň	Ostrava	Olomouc
játra	149	40					
srdce	56	28	0				
plíce			67				
ledviny	276	54	16	34	37	51	20
pankreas	30						
TS	0						

KOORDINAČNÍ STŘEDISKO TRANSPLANTACÍ



Kidney	Liver	Heart	Lung	Pancreas	S. bowel
102 090	37 436	8 988	6 784	2 026	170

Information of 91 Member States on organ transplantation activities (75 % of the global population)
2023

INTERNATIONAL REPORT ON
Organ Donation and Transplantation Activities

World Health Organization

- ≈ 157 494 solid organ transplants
- ≈ 9.1% increase vs 2021
- ≤ 10% of global needs
- 39 % living kidney transplants
- 24% living liver transplants
- 41 792 deceased donors (32 248 DBD and 9 544 DCD donors)*