Les techniques en devenir

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19/10/2019

Changes in critically ill cancer patients' short-term outcome over the last decades: results of systematic review with meta-analysis on individual data

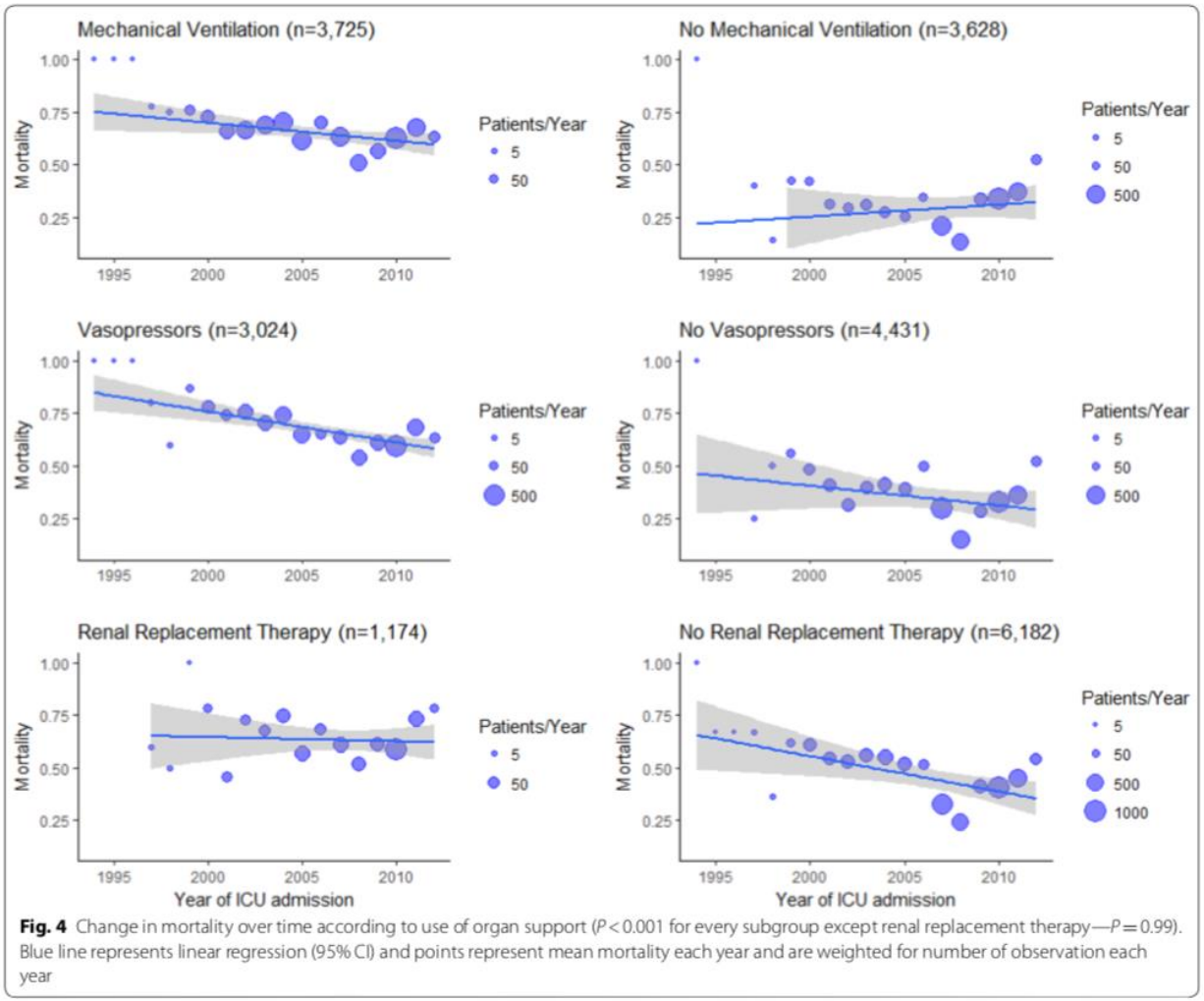


Fig. 4 Change in mortality over time according to use of organ support ($P < 0.001$ for every subgroup except renal replacement therapy—$P = 0.99$). Blue line represents linear regression (95% CI) and points represent mean mortality each year and are weighted for number of observation each year

Darmon *Intensive Care Med* 2019

Contexte global

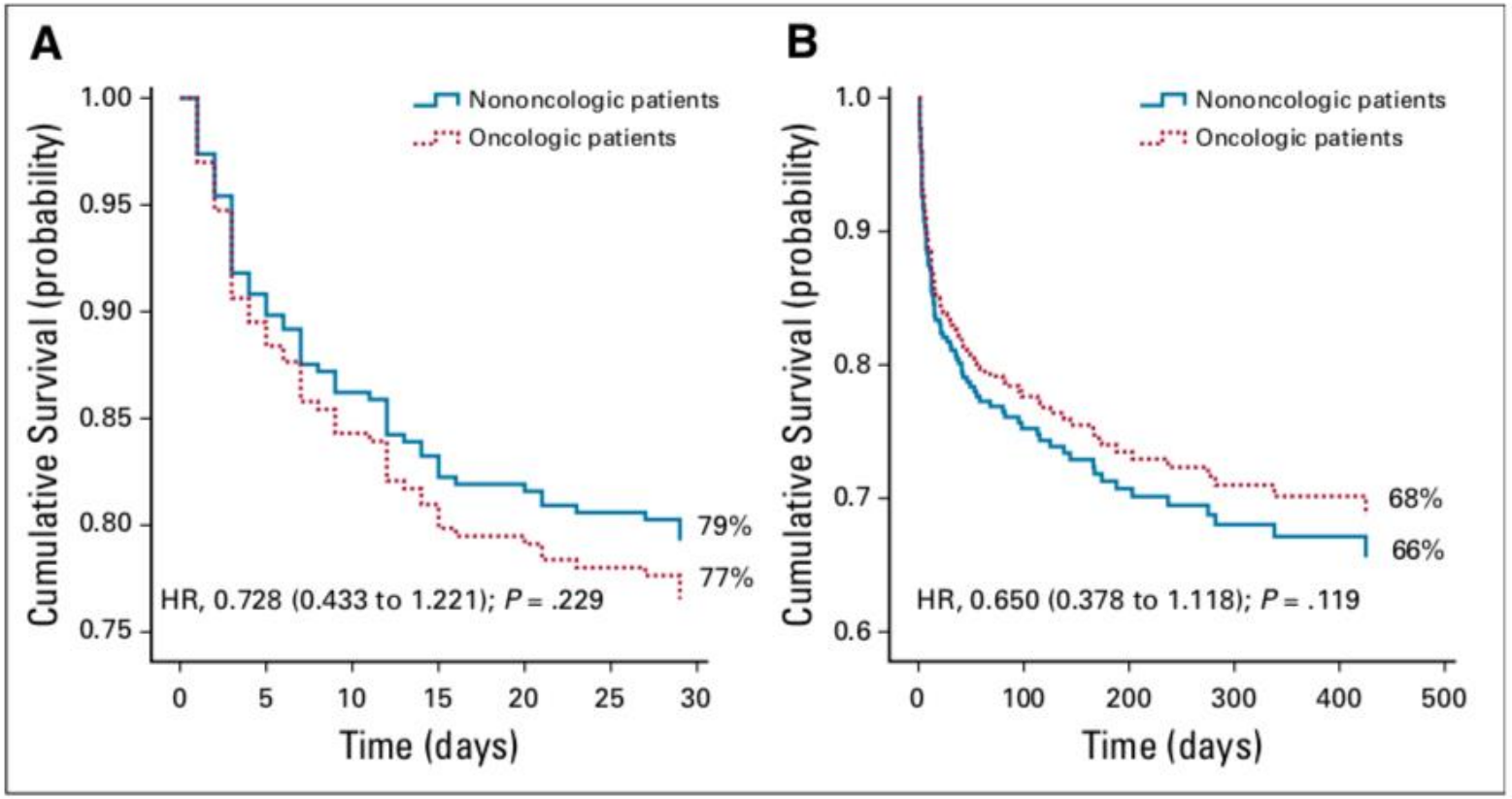


FIG 1. (A) Survival at day 28 between oncologic and nononcologic patients adjusted by Acute Physiology and Chronic Health Evaluation II (APACHE II) score. (B) Survival at end of follow-up between oncologic and nononcologic patients adjusted by APACHE II score and Charlson comorbidity index.

Lopéz *J Global Oncol* 2019

Contexte global

- Pronostic du patient oncologique / hématologique ↑
- Phase aiguë : devenir dépend supports mis en œuvre // patient tout venant
- Phase chronique : devenir dépend maladie de fond

→ admission aux soins intensifs pour support d'organes // patient tout venant
→ Principe du « test usi » (Azoulay)

Nouvelles techniques ?

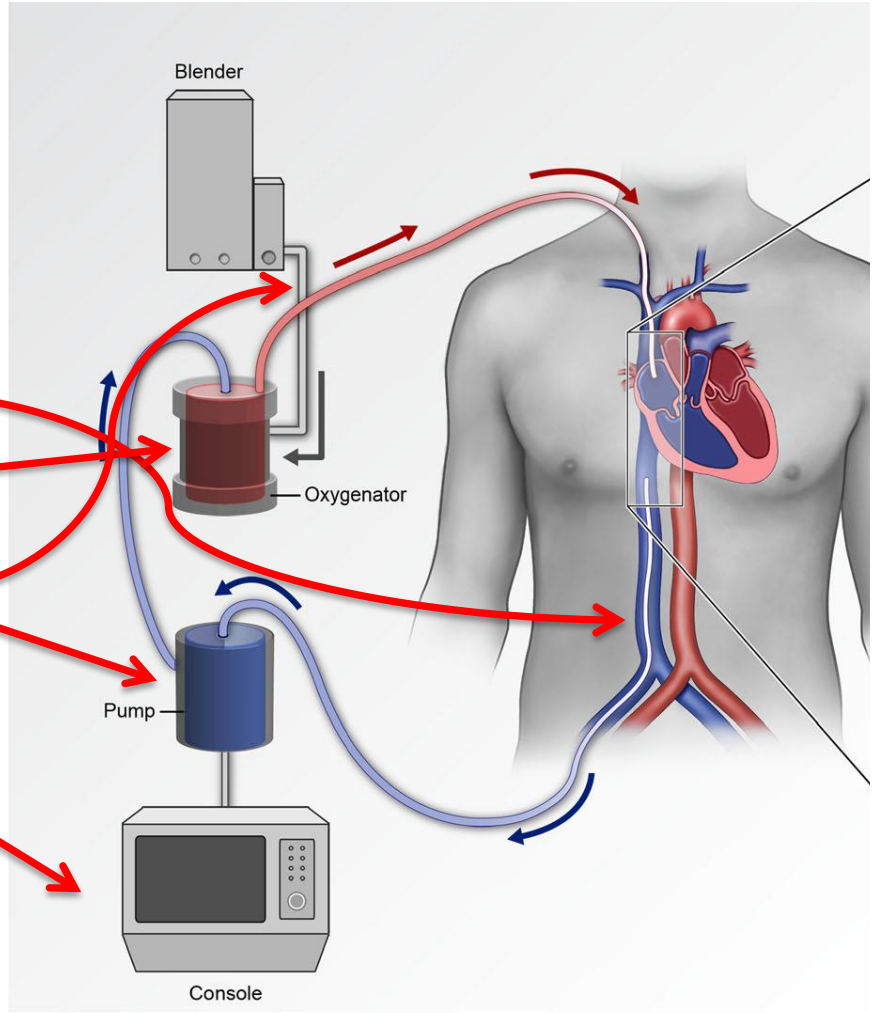
- Supports ventilatoires
  - *Ventilation non-invasive*
  - *Ventilation mécanique* : 6 ml/kg – PEEP élevée – fréquence élevée
  - *Décubitus ventral* = prone position (étude PROSEVA 2013 : 10% patients ont un cancer)
  - *ECMO = Extra corporeal membrane oxygenation*
    - Veino-veineuse
    - Veino-artérielle
  - *$ECCO_2R$*
- Techniques d'échange – support hépatique
- Support rénal

ECMO

(extracorporeal membrane oxygenation)

Principe

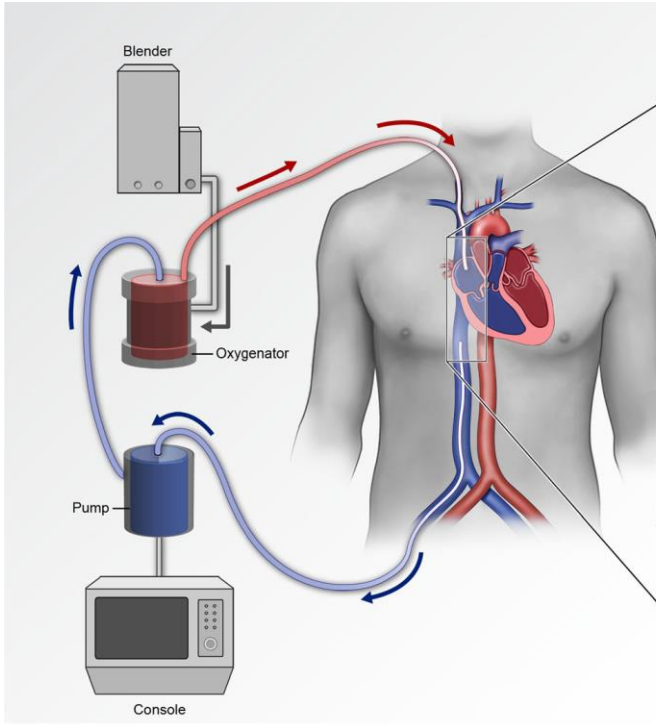
- ***Simple !***
  - 1 ***canule*** d'aspiration = ***veineuse***
  - 1 ***pompe***
  - 1 ***oxygénateur***
  - 1 ***canule*** de réinjection = ***artérielle***
  - 1 ***console de contrôle***



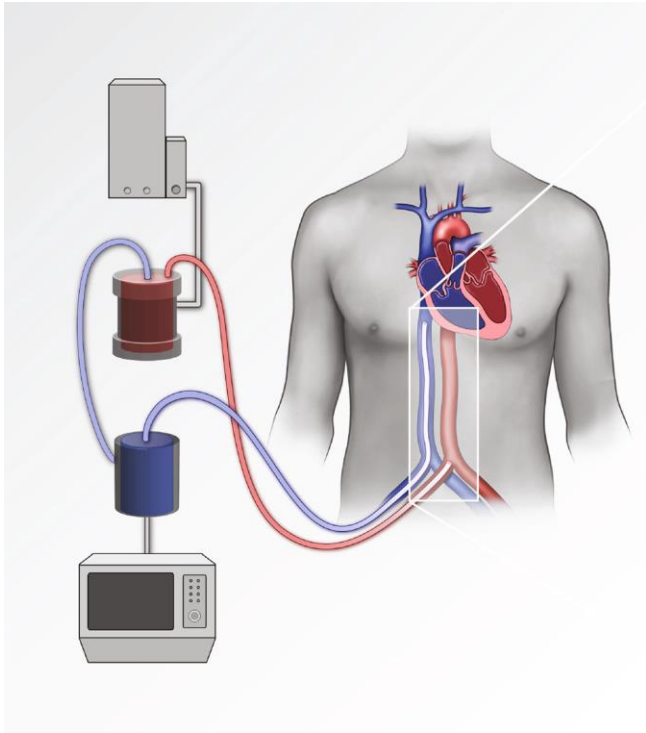
ECMO

types

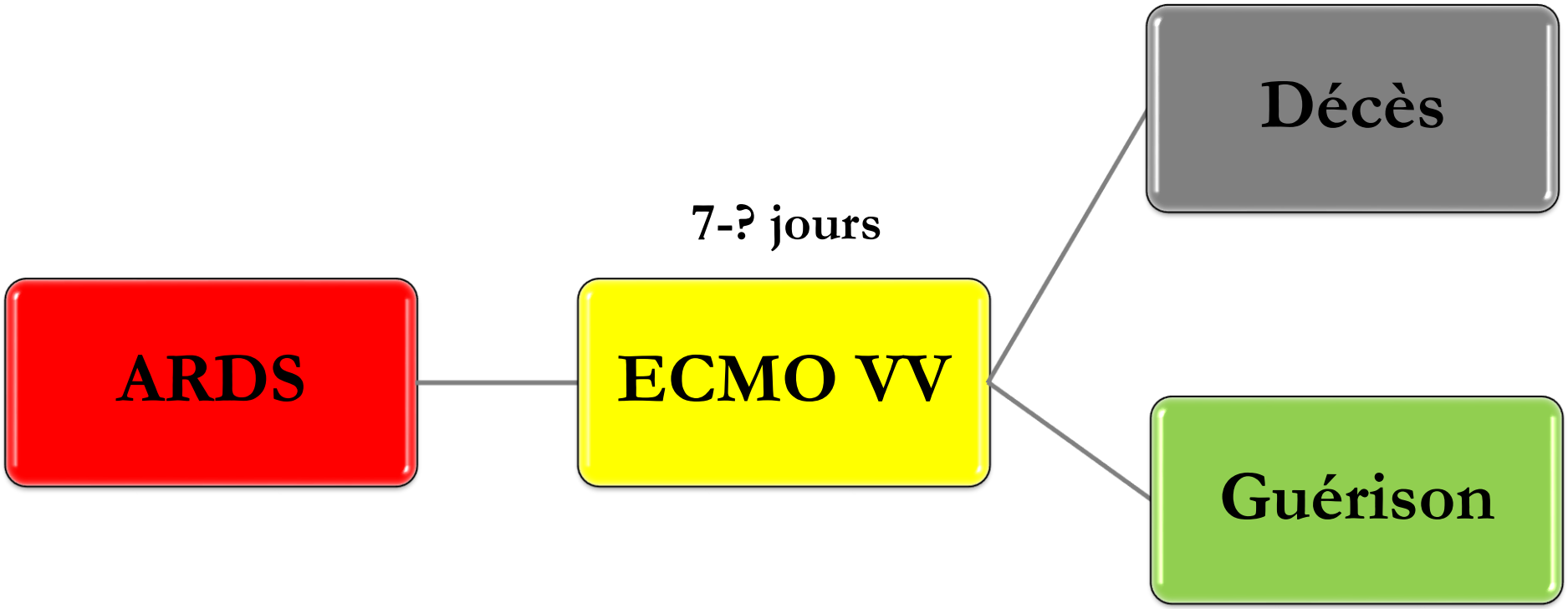
- ***ECMO VV =*** support ventilatoire + oxygénation



- ***ECMO VA =*** support circulatoire + oxygénation



But ? Gagner du temps !



Indications VV

- ***Insuffisance respiratoire hypoxémique***
  - ARDS
  - Asthme
  - BPCO
  - *Compression tumorale*

Indications VA

- ***Choc cardiogénique***
  - en phase aiguë infarctus
  - post cardiotomie (greffe)
  - myocardites (virale, bact, AI, à éosinophiles, peri-partum)
  - intox médicamenteuse (cardiotropes : antiarythmiques, betabloquants, digitaliques, bloquants Ca2+), complication chimio/radiothérapie
  - insuffisance cardiaque chronique décompensée (éligible pour Tx)
  - embolie pulmonaire massive – HTAPulm
- ***Arrêt cardiaque réfractaire***
- ***Hypothermie accidentelle***
- ***Choc septique ?*** si dépression myocardique sévère

Bénéfice

- ***Support respiratoire*** → oxygénation tissulaire adéquate
- ***Support circulatoire*** → perfusion adéquate des organes
- ***Support cardiaque*** → perfusion coronaire, cœur « au repos »
- Sous réserve !
  - temporaire
  - non thérapeutique mais supportif → facilite prise en charge / traitements

Réalité sur le terrain ?

ECLS Registry Report

International Summary

July, 2019

For July reports, the current year is reported as a partial year only

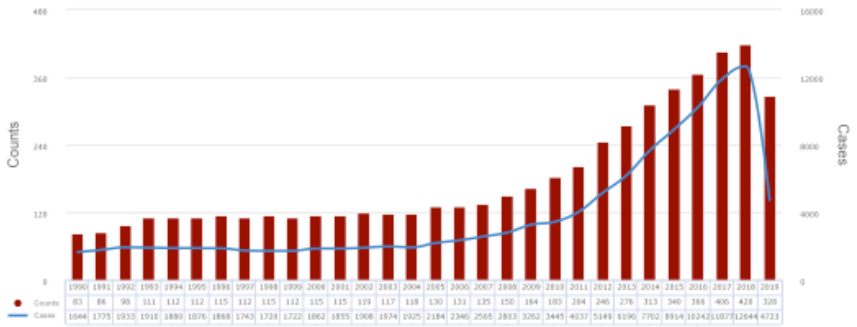
Extracorporeal Life Support Organization
2800 Plymouth Road
Building 300, Room 303
Ann Arbor, MI 48109

Overall Outcomes

	Total Runs	Survived ECLS		Survived to DC or Transfer	
Neonatal					
Pulmonary	31,923	28,050	87%	23,360	73%
Cardiac	8,498	5,874	69%	3,665	43%
ECPR	1,923	1,359	70%	812	42%
Pediatric					
Pulmonary	9,902	7,126	71%	5,879	59%
Cardiac	11,839	8,512	71%	6,251	52%
ECPR	4,608	2,760	59%	1,957	42%
Adult					
Pulmonary	21,874	15,159	69%	13,088	59%
Cardiac	22,193	13,177	59%	9,585	43%
ECPR	6,994	2,923	41%	2,074	29%
Total	119,754	84,940	70%	66,671	55%

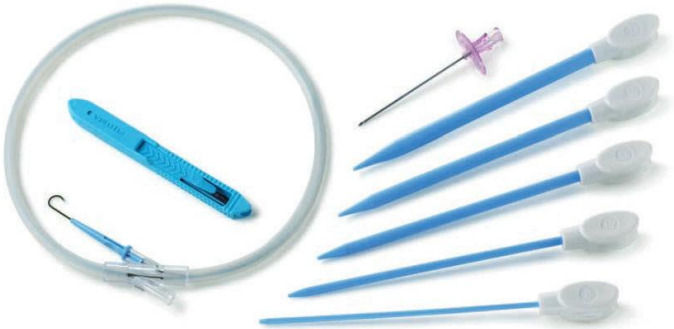
Centers

Centers by year



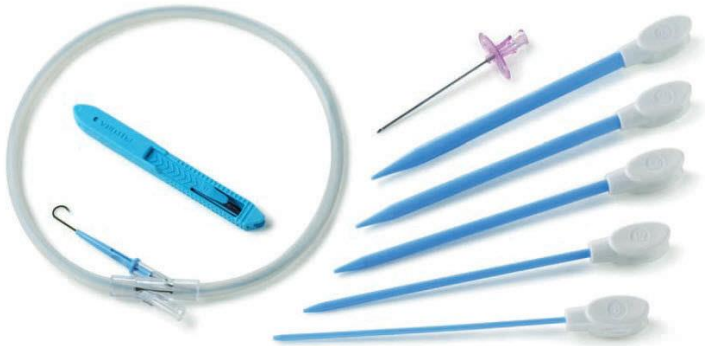
Matériel

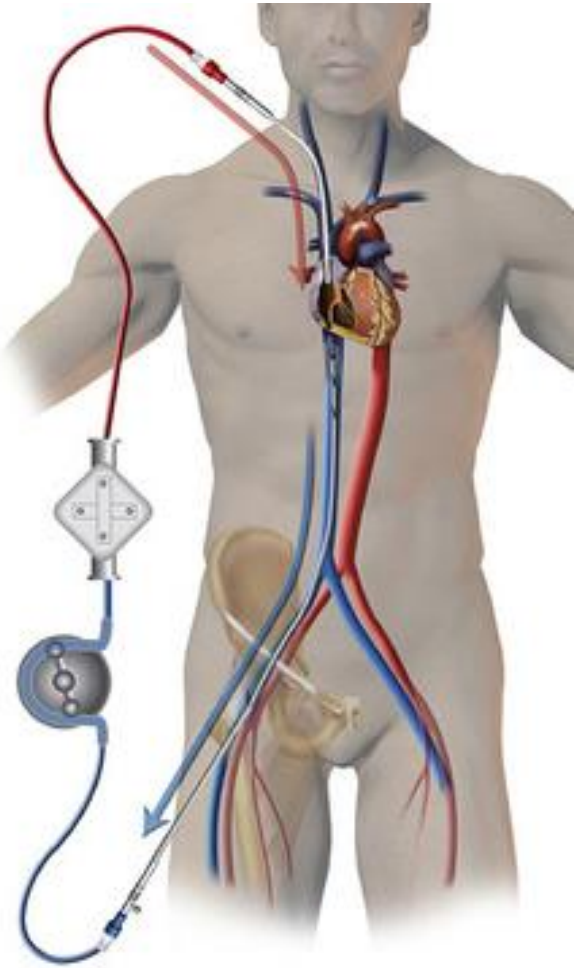
- ***Canule veineuse*** *:* longue (60 cm), multiperforée, diamètre 18 à 25 F
- ***Canule artérielle*** *:* courte (15-20 cm), diamètre 16 à 20 F

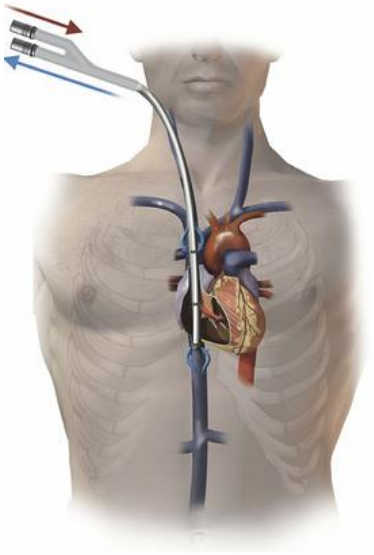


Technique de canulation

- ***Abord percutané***
  - Pction art + veine / contrôle écho
  - Insertion cathéter angio – guides
  - Dilatation
  - Insertion canules







ARDS réfractaire ?

- Échec du traitement « conventionnel »
  - Ventilation « protectrice » 6 ml/kg + Pplat < 30 cm H_20
  - Paralysie musculaire
  - Décubitus ventral = prone position

- Cœur pulmonaire aigu malgré ventilation protectrice

- Contre-indication au décubitus ventral

→ envisager support mécanique

Projet

Bridge to…	
Bridge to recovery (BTR)	Assistance en vue guérison
Bridge to decision (BTD)	Assistance en vue évaluation
Bridge to candidacy (BTC)	Assistance en vue éligibilité pour greffe
Bridge to transplantation (BTT)	Assistance en vue greffe
Destination therapy (DT)	Assistance définitive

ESC Guidelines *European Heart Journal* 2018

Facteurs pronostiques ?

- Âge > 65 ans
- Pplat (très) élevée
- Compliance effondrée
- Immunosuppression
- Durée de ventilation mécanique avant implantation ECMO > 7 jours
- Pathologie réversible ?

tous facteurs pronostiques **négatifs**

Support ventilatoire

Extracorporeal membrane oxygenation in adult patients with hematologic malignancies and severe acute respiratory failure

Table 1 Individual characteristics and outcomes

Patient number	Malignancy	Therapy status (days since therapy)	Etiology of ARF	SAPS II	LIS	ECMO days	Bleeding	ICU and hospital outcome
1	CNS NHL	Chemotherapy (51)	Pneumonia	45	3.7	9	Minor	Died
2	Hodgkin lymphoma	Allo SCT (111)	Pneumonia	34	3.3	28[b]	Major	Died
3	ALL	Consolidation (13)	Abdominal sepsis	78	2.3	4[c]	-	Alive
4	ALL[a]	Induction on ECMO	TRALI	62	3.3	3	-	Alive
5	Burkitt lymphoma	Induction (16)	Pneumonia	63	3.8	8	-	Alive
6	ALL	Allo SCT (31)	Pneumonia	39	3.5	7	Major	Died
7	Hodgkin lymphoma	Allo SCT (33)	Pneumonia	65	3.3	18	-	Died
8	ALL	Allo SCT (203)	Pneumonia	68	3.3	10	-	Died
9	DLBCL	Induction on ECMO	Pneumonia	102	4.0	4	-	Died
10	Multiple myeloma	Auto SCT (789)	Pneumonia	43	3.7	9	Major	Alive
11	Anaplastic T-cell NHL[a]	Induction on ECMO	Pneumonia	46	3.0	25[d]	Major	Alive
12	DLBCL[a]	Induction on ECMO	NHL	36	3.3	3[c]	-	Alive
13	AML	Consolidation (34)	Pneumonia	48	3.3	34	Major	Died
14	DLBCL[a]	Induction on ECMO	NHL	56	2.3	4[d]	-	Alive

ALL, acute lymphoblastic leukemia; allo SCT, allogeneic stem cell transplantation; AML, acute myeloid leukemia; ARF, acute respiratory failure; auto SCT, autologous stem cell transplantation; CNS, central nervous system; DLBCL, diffuse large B-cell lymphoma; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; LIS, lung injury score at ECMO baseline [30]; NHL, non-Hodgkin lymphoma; SAPS II, simplified acute physiology score at ICU admission [27]; TRALI, transfusion-related acute lung injury. [a]Diagnosis of hematologic malignancy on ECMO; [b]Two episodes of ECMO; [c]ventoarterial ECMO; [d]three episodes of ECMO.

- Etude cohorte rétrospective 2000-20013 Vienne, Autriche

Wohlfarth *Crit Care* 2014

Support ventilatoire

Extracorporeal membrane oxygenation in adult patients with hematologic malignancies and severe acute respiratory failure

Table 2 Cohort characteristics and outcomes

	All patients *N* = 14	Survivors *n* = 7	Nonsurvivors *n* = 7	*P* value
Characteristics during ECMO				
Venoarterial ECMO	3	3	0	0.19
Duration of ECMO therapy, days	8.5 (4–16)	4 (3–9)	10 (7–28)	0.08
Diagnosis of HM on ECMO	4	4	0	0.07
Chemotherapy on ECMO	5	4	1	0.27
Vasopressors	14	7	7	na
Hemofiltration	5	2	3	1.00
Major bleeding events	5	1	4	0.27
Number of packed red blood cell units	8 (4–14)	4 (3–8)	14 (6–27)	0.02
Number of platelet concentrates	5 (1–17)	2 (0–5)	23 (14–26)	0.01
Outcome				
ICU LOS, days	22 (14–42)	22 (21–77)	18 (11–40)	0.12
Hospital LOS, days	56 (44–101)	63 (49–110)	45 (15–133)	0.46
ICU and hospital survival, *n* (%)	7 (50%)			

Data are given as median and interquartile range or *n*, respectively; ARF, acute respiratory failure; CCI, Charlson comorbidity index [26]; HM, hematologic malignancy; ICU, intensive care unit; ECMO, extracorporeal membrane oxygenation; LOS, length of stay; na, not applicable; SAPS II, Simplified Acute Physiology Score at ICU admission [27]; SOFA score, Sequential Organ Failure Assessment Score at ECMO Baseline [29]; [a]microbiologic pathogen detected *or* histologic proof of HM in lung biopsy.

- **Survie 50%**

Wohlfarth *Crit Care* 2014

Support ventilatoire

Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*

- 12 USI (Allemagne, Autriche, Belgique, France, Norvège) – 2010-2015

TABLE 2. ICU and Extracorporeal Membrane Oxygenation–Related Characteristics and Outcome

Variable	All Patients ($n = 37$)	Nonsurvivors ($n = 30$)	Survivors ($n = 7$)	p
Characteristics at ICU admission				
Age, yr	37 (26–49)	36 (28–49)	38 (26–58)	0.69
Sex, female	17 (46)	15 (50)	2 (29)	0.42
Charlson Comorbidity Index (16)	0 (0–1)	0 (0–1)	1 (1–1)	0.36
Simplified Acute Physiology Score II score	56 (42–67)	55 (41–66)	56 (47–70)	0.61
Days from allogeneic hematopoietic stem cell transplantation to ECMO	146 (27–321)	100 (24–226)	485 (270–976)	0.011

Wohlfarth *Crit Care Med* 2017

Support ventilatoire

Characteristics and Outcome of Patients After Allogeneic Hematopoietic Stem Cell Transplantation Treated With Extracorporeal Membrane Oxygenation for Acute Respiratory Distress Syndrome*

- Paralysie : 50% - Décubitus ventral : 36% - NOi : 25%

Outcome				
Duration of ECMO therapy, d	15 (8–23)	15 (8–23)	10 (4–13)	0.20
ICU length of stay, d	28 (14–33)	22 (12–35)	28 (25–49)	0.28
ICU and hospital survival	7 (19)			

- Survie
  - usi : 9/37 = **24%**
  - hôpital : 7/37 = **19%**
  - « cut off » 240 j post greffe : 1/24 = **4% vs** 6/13 = **46%**

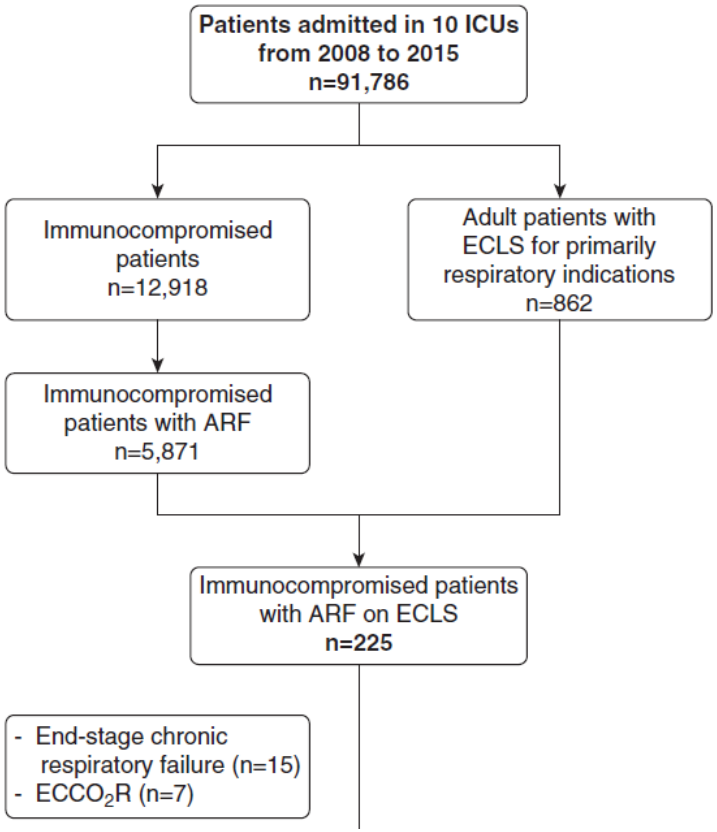
- Complication : hémorragies (38%) dont 16% évènements graves (3 hgies cérébrales fatales)

Wohlfarth *Crit Care Med* 2017

Support ventilatoire

Six-Month Outcome of Immunocompromised Patients with Severe Acute Respiratory Distress Syndrome Rescued by Extracorporeal Membrane Oxygenation

An International Multicenter Retrospective Study



Schmidt *Am J Respir Crit Care* 2018

Support ventilatoire

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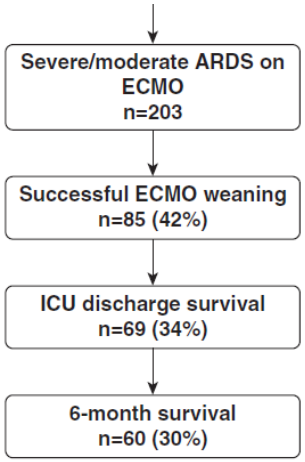
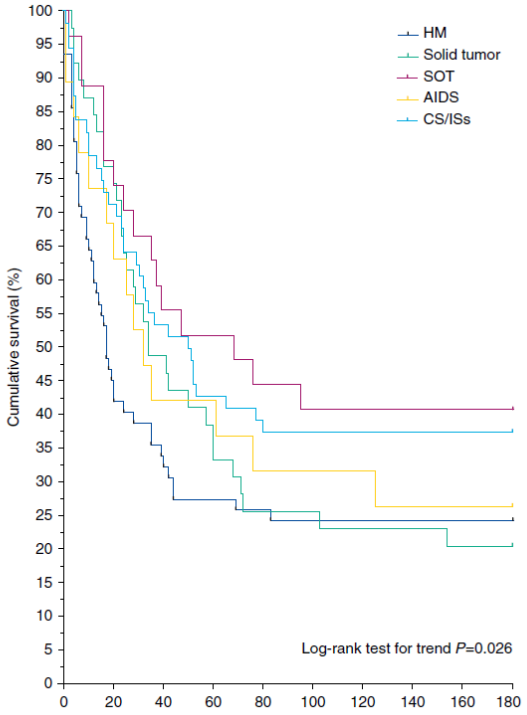


Figure 1. Flow chart of the study. ARDS = acute respiratory distress syndrome; ARF = acute respiratory failure; $ECCO_2R$ = extracorporeal CO_2 removal; ECLS = extracorporeal life support; ECMO = extracorporeal membrane oxygenation.



HM	62	26	20	17	16	15	15	15	15	15
Solid tumor	39	29	19	13	10	10	09	09	08	08
SOT	27	20	15	14	12	11	11	11	11	11
AIDS	19	12	08	08	06	06	06	05	05	05
CS/ISs	56	40	30	24	21	21	21	21	21	21

Figure 2. Kaplan-Meier estimates during the 180 days after ICU admission, depending on patients' underlying immunodeficiency. CS = corticosteroids; HM = hematological malignancies; IS = immunosuppressant use; SOT = solid-organ transplant.

Schmidt *Am J Respir Crit Care* 2018

Support ventilatoire

Six-Month Outcome of Immunocompromised Patients with Severe Acute Respiratory Distress Syndrome Rescued by Extracorporeal Membrane Oxygenation

An International Multicenter Retrospective Study

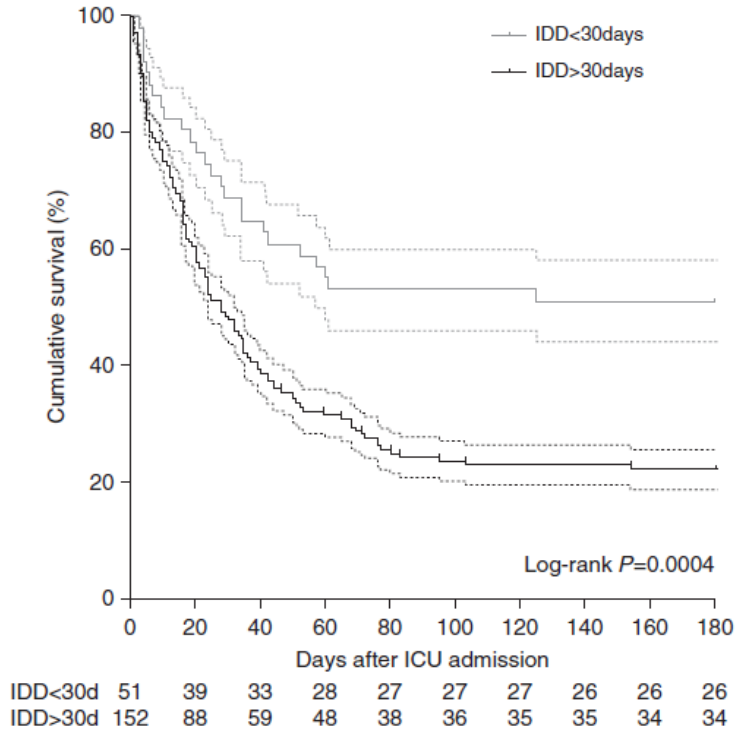
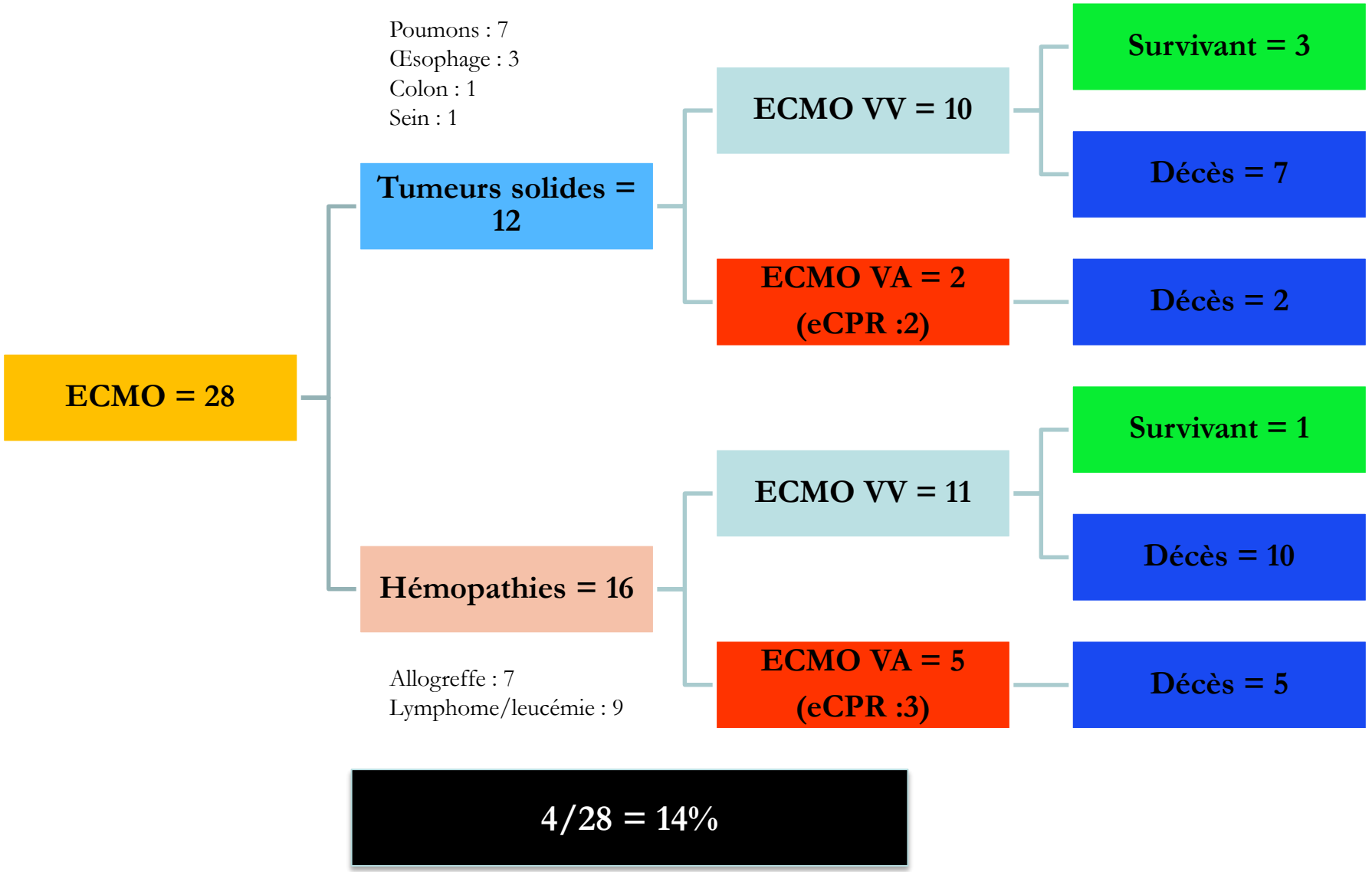


Figure 3. Kaplan-Meier survival estimates for immunocompromised patients with refractory acute respiratory distress syndrome on extracorporeal membrane oxygenation 180 days after ICU admission, according to the time of immunodeficiency diagnosis (IDD) (<30 or >30 d) (log-rank test; $P = 0.0004$). The dashed lines represent the 95% confidence interval.

- Complications :
  - Hémorragies : 36%
  - VAP : 50%
  - Infection canules : 10%

Schmidt *Am J Respir Crit Care* 2018

Erasme 2008 - 2019



$ECCO_2R$

- **Extracteur de CO_2 = $ECCO_2R$** = Extracorporeal carbon dioxide removal

- Aucune donnée dans la littérature pour les patients onco/hématologiques

- Complications attendues :
  - Hémolyse
  - Hémorragie
  - Thrombose

  → Besoin anticoagulation +++ → ECMO >> $ECCO_2R$???

Techniques d'échange

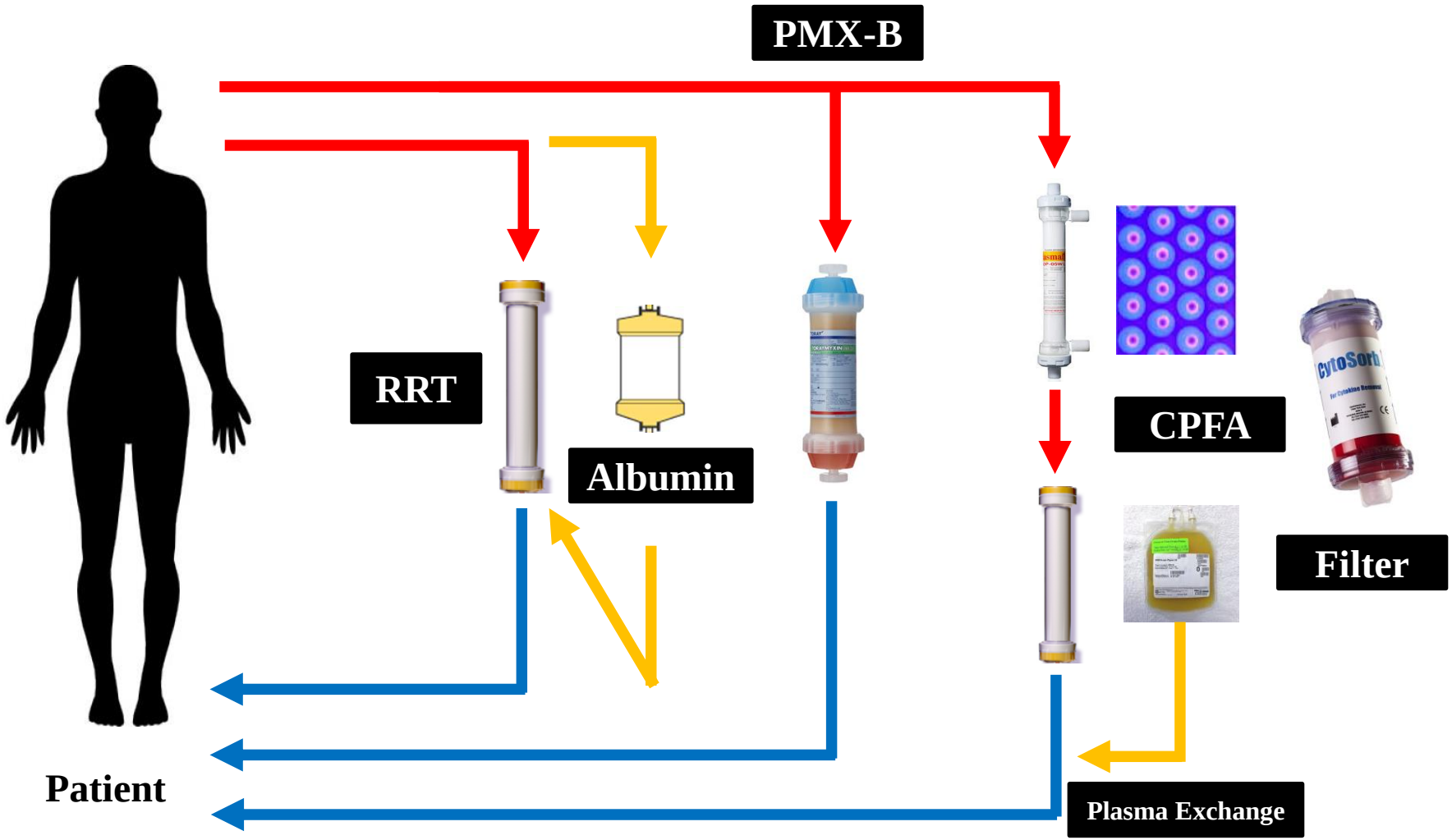
- ***Pourquoi ?***

  - Eliminer déchets – produits de dégradation < insuffisance rénale
  - Suppléer insuffisance hépatocellulaire
  - Eliminer des toxiques

  - Chez patient « aigu » : voies d'élimination rénale/hépatique déficientes
  - Nécessité haute doses médicaments : +/- toxiques → létales
  - Risque de coma prolongé

- ***Comment ?***
  - **Hémoperfusion** : échange de grands volumes sanguin du patient sur une surface adsorbante en vue de purifier le sang
  - Technique extra-corporelle
  - Adsorbants = résines ou charbon activé

Techniques d'échange



Techniques d'échange

- ***PMX-B = polymyxin B***
  - 2010-2016 – 55 usi
  - 146 vs 148 patients
  - Aucune différence sur mortalité 28j

Effect of Targeted Polymyxin B Hemoperfusion on 28-Day Mortality in Patients With Septic Shock and Elevated Endotoxin Level
The EUPHRATES Randomized Clinical Trial

Dellinger *JAMA. 2018*

- ***CPFA = Coupled Plasma Filtration Adsorption***
  - Peu de patients traités (90 pts)
  - 2 RCTs
  - Résultats controversés
  - CPFA et HVHF (85 ml/kg.h) équivalents
  - Diminution des taux plasmatiques de cytokines

→ pas de bénéfice clinique prouvé

Hu *Ren Fail. 2012*
Lentini *G Ital Nefrol. 2009*
He *J Clin Gastroenterol. 2013*
Mao *Int J Artif Organs. 2009*
Mao *Int J Artif Organs. 2011*
Ronco *Crit Care Med 2002*

Support hépatique

- Technique de MARS = molecular adsorbend recirculating system abandonnée au profit (?) d'échanges plasmatiques

- Echanges plasmatiques = plasma exchange

High-volume plasma exchange in patients with acute liver failure: An open randomised controlled trial

- Patients : 182
  - 90 SMT = standard medical treatment
  - 92 HPV = SMT + high plasma volume (15% IBW ≈ 8-10 L)
  - Exclusion : patients oncologiques

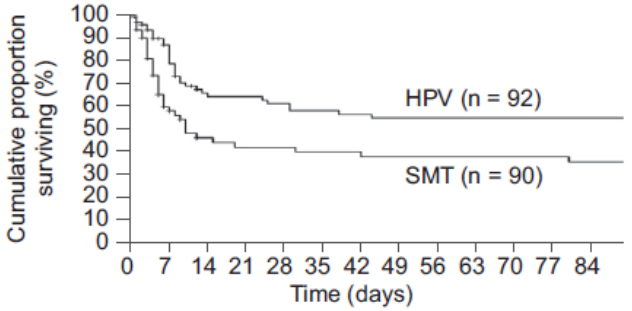


Fig. 1. Main results of the intention-to-treat analysis survival data in the standard medical treated group (SMT) compared to the high-volume plasma exchange (HVP) treated group (LogRank: $p = 0.0058$).

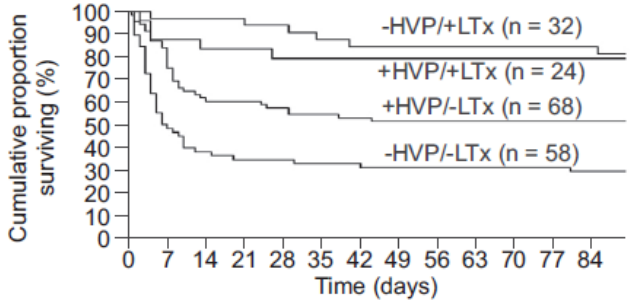


Fig. 2. Survival in the groups, in the two groups receiving SMT (standard medical treated group) with and without emergency transplantation (–HVP +LTx *vs.* +HVP–LTx) and the two group receiving SMT with and without emergency transplantation (–HVP–LTx *vs.* +HVP–LTx) (LogRank: $p = 0.0058$) and Cox proportional hazard: LTx: $p < 0.0001$; HVP: $p = 0.0076$).

Larsen *J Hepatol* 2016

Conclusion

- Patient onco/hémato aigüs = patient usi « tout venant »
- Peu de données avec réserve ++ sur certains sous-gpes (allogreffés)
- Nouvelles techniques tendent à se généraliser → en attente de plus larges cohortes de patients
- Intérêt de centres de référence !

Hôpital Erasme

ULB

Merci pour votre attention