UNUSUAL INDICATIONS FOR ECMO

DAVE WILLIAMS D.O.

INTENSIVIST AT ABBOTT NORTHWESTERN HOSPITAL

APRIL 22ND, 2016

Allina Health

DISCLOSURE

There are no conflicts of interest or relevant financial interests in making this presentation and have indicated that my presentation does not include discussion of an unlabeled use of a commercial product, or an investigational use not yet approved for any purpose.

OBJECTIVES

- Sepsis
- Massive Pulmonary Embolism
- Toxicology

ECMO AND SEPSIS

- Facts to support ECMO
- Patient selection
- Circuit mode
- Case Review

ECMO IN ADULT SEPTIC SHOCK

- Bacteremia were considered relative contraindication
  - entrapping bacteria, function as culture medium
- Septic coagulopathy
  - increase risk of bleeding
- Minimal reports of use of ECMO in adult septic shock
- During last decade
  - improvement in technology
  - safety
  - indications are continuously being challenged

CASE SERIES

Authors and Journals	Case series titles	N and Survival	Study Time
Brechot N1, Luyt CE, Schmidt M, Leprince P, Trouillet JL, Léger P, Pavie A, Chastre J, Combes A. Crit Care Med. 2013 Jul;41(7)	Venoarterial extracorporeal membrane oxygenation support for refractory cardiovascular dysfunction during severe bacterial septic shock.	N = 14 71.4% Age: 28 - 66	2008 - 2011
Cheng A1, Sun HY, Lee CW, Ko WJ, Tsai PR, Chuang YC, Hu FC, Chang SC, Chen YC. J Crit Care. 2013 Aug;28(4):532.Epub 2013 Mar 19.	Survival of septic adults compared with nonseptic adults receiving extracorporeal membrane oxygenation for cardiopulmonary failure: a propensity-matched analysis	N = 108 24.4% Matched with 108 non-septic 34.9%	2001 - 2009
Huang CT1, Tsai YJ, Tsai PR, Ko WJ. J Thorac Cardiovasc Surg. 2013 Nov;146(5):1041-6. doi: 10.1016/j.jtcvs.2012.08.022. Epub 2012 Sep 7.	Extracorporeal membrane oxygenation resuscitation in adult patients with refractory septic shock.	N = 52 15%	2005 – 2010)
Park TK1, Yang JH2, Jeon Y3, Choi SH4, Lee GY5, Choi HC1, Chung CR3, Park CM3, Cho YH4, Sung K4, Suh GY3. Eur J Cardiothorac Surg. 2014 Nov 25.	Extracorporeal membrane oxygenation for refractory septic shock in adults.	N = 32 21.9%	2005 - 2013

Venoarterial Extracorporeal Membrane Oxygenation Support for Refractory Cardiovascular Dysfunction During Severe Bacterial Septic Shock*

Nicolas Bréchot, MD, PhD[1]; Charles-Edouard Luyt, MD, PhD[1]; Matthieu Schmidt, MD[1]; Pascal Leprince, MD, PhD[1]; Jean-Louis Trouillet, MD[1]; Philippe Léger, MD[1]; Alain Pavie, MD[1]; Jean Chastre, MD[1]; Alain Combes, MD, PhD[1]

- 14 patients with severe septic shock and refractory cardiac dysfunction
- All placed fem-fem VA ECMO
- Evidence of tissue hypoxia (mottling or elevated blood lactate (average 9))
- Confirmed intravascular volume repleate
- Severely suppressed LV function 10-30% (avg 16%)
- CI < 2.2L/min/m sq (avg 1.3)
- high-dose catecholamines
- Shock to ECMO interval: 24 hours (3 to 108 hrs)
- 10 of 14 survived

Parameters	Patients (n=14)
pre-ECMO cardiac index, L/min/m2	1.3 (0.7-2.2)
LVEF (%)	16 (10-30)
Catecholamine dose, µg/kg/min Dobutamine, n=4 Norepinephrine, n=7 Epinephrine, n=12	17.5 (6-30) 2 (0.5-4.9) 1.25 (0.1-4.2)
Inotrope score, µg/kg/min =Dobu+100*(Epi+Norepi)	250 (73-629)
Pre-ECMO systemic vascular resistance index, dynes/cm/m2, median (range)	3,162 (2,047–7,685)
pH	7.16 (6.68-7.39)
Blood lactate	9 (2-17)
Bicarbonate, mmol/L	15.8 (7.8-22)

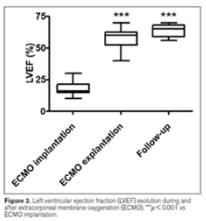


Figure 2. Left ventricular ejection fraction (LVEF) evolution during and after extracorporeal membrane oxygenation (ECMO). *p < 0.001 vs ECMO implantation.

Severe multiple organ failure with Refractory myocardial dysfunction

SAPS 3 84 (75-106)
SOFA 18 (8-21)

Predicted MORTALITY 80%

Bréchot, N, et al. Critical care medicine 2013

10/14 longtime survivors (71%)
Discharged home
2 MOF 48h after ECMO implantation
2 MOF due to MVAP after ECMO explantation

23/34 (67%)

Parameters	Patients (n=34)
pre-ECMO cardiac index, L/min/m2	1.4 (0.7-2.2)
LVEF (%)	15 (10-30)
Inotrope score, µg/kg/min =Dobu+100*(Epi+Norepi)	298 (73-1117)
pH	7.12 (6.68-7.44)
Blood lactate	9 (1-20)
SOFA	18 (10-22)
Anurie	21/34 (62%)

10/34 VA-VV ECMO
2/34 VA-VAV-VV-ECMO

ECMO=Bridge to recovery for all patients

Bréchot, N, et al. Critical care medicine 2013

Extracorporeal membrane oxygenation resuscitation in adult patients with refractory septic shock

Chun-Ta Huang, MD,[a,b] Yi-Ju Tsai, PhD,[c] Pi-Ru Tsai, RN,[d] and Wen-Je Ko, MD, PhD[a,d]

- Adult patients in refractory septic shock and requiring VA ECMO for support
- 52 patients
  - 75% had failure of at least 3 organ systems
  - 40% developed cardiac arrested then cannulated
- 8 of 52 (15%) survived. All 20 patients aged 60 or older died
- **TOO LATE**

Huang CT, et al. J Thorac Cardiovasc Surg. 2013

Survival of septic adults compared with nonseptic adults receiving extracorporeal membrane oxygenation for cardiopulmonary failure: A propensity-matched analysis☆

Aristine Cheng MD[a,b], Hsin-Yun Sun MD[b], Ching-Wen Lee MS[c], Wen-Je Ko MD[d], Pi-Ru Tsai BSc[d], Yu-Chung Chuang MD[b], Fu-Chang Hu ScD[e], Shan-Chwen Chang MD[b], Yee-Chun Chen MD[b,*]

- VV septic: 45.5% survival
- VA septic : 24.4% survival
- CPR pre- ECMO 32%
- CPR during ECMO 34%
  - TOO LATE
- Hyperdynamic/preserved LV function
  - Worse outcomes on VA vs VV reported

Cheng A, et al. J Crit Care 2013

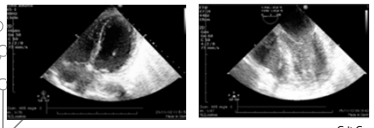
Actual incidence of global left ventricular hypokinesia in adult septic shock

Antoine Vieillard-Baron, MD; Vincent Caille, MD; Cyril Charron, MD; Guillaume Belliard, MD; Bernard Page, MD; François Jardin, MD

- Septic shock patients studied by TEE
- Global LV hypokinesia defined as LV ejection <45%
- Hx free of cardiac disease
- 26 of 67 on admission (40%)
- Additional 14 within 24-48hrs (60%) septic patients had LV dysfunction
- Acute and reversible; providing patient recovers

Circulating Myocardial Depressant Substance (MDS)

TNF-α
IL-1β
IL-6
NO



Crit Care Med 2008 Vol. 36, No. 6

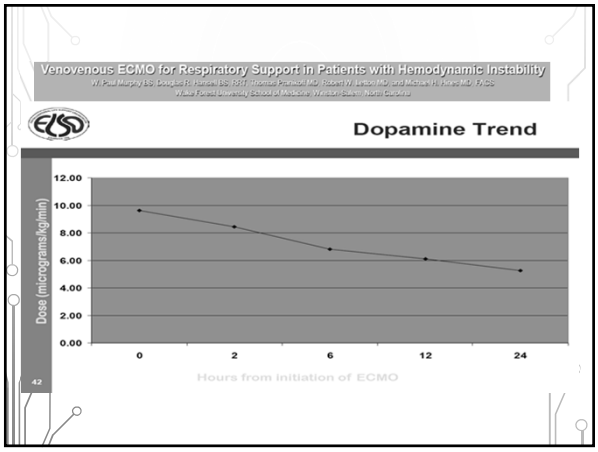
Table 2 Incidence of LV systolic dysfunction in septic shock according to the time of evaluation

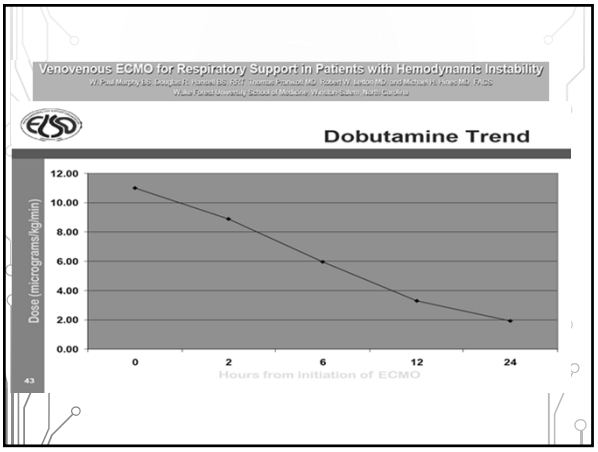
	Time of study/admission	Incidence of LV systolic dysfunction
Parker et al. [1] *PAC + radionuclide cineangiography*	Day 1	65%
Jardin et al. [2] *TTE*	0-6 hours	29%
Vieillard-Baron et al. [20] *TEE*	0-6 hours	18%
Vieillard-Baron et al. [25] *TEE*	Day 1, 2, 3	60%
Bouhemad et al. [16] *TEE*	?	20%
Etchecopar-Chevreuil et al. [22] *TEE*	12 hours	46%

PAC, pulmonary artery catheter; TTE, transthoracic echocardiography; TEE, transesophageal echocardiography.

MODE SELECTION: CONUNDRUMS IN ECMO

- VA ECMO is tempting to consider as a solution to all problems
- Example: respiratory failure with profound hemodynamic compromise, ongoing hypoxia despite advance mechanical ventilator settings, elevated intrathoracic pressures, worsening acidosis…
- Restoration achieved by both VA and VV





WHICH MODE

- **1. Cardiogenic shock (LV <30%) and sepsis: Peripheral VA ECMO**
- **2. ARDS and Hyperdynamic/preserved LV function: VV ECMO**
  - **Worse outcomes on VA vs VV reported (Cheng A, et al. J Crit Care 2013)**
  - **Reduction in vasopressor requirements usually dramatic**
- **3. Severe ARDS and depressed LV function: VA or VAV**
  - **Peripheral VA can result in deoxygenated blood being ejected by the LV, due to pulmonary dysfunction, minimizing appropriate oxygenation to the heart, brain and upper body**
  - **Central VA or VAV hybrid can be used to overcome this problem**

F. Sangalli et al. ECMO-Extracorporeal Life Support in Adults,Springer-Verlag Italia 2014.

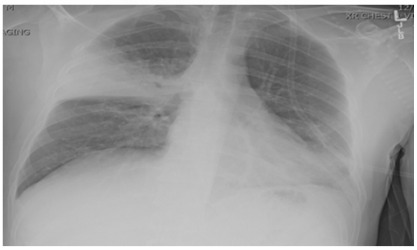
TAKE AWAY POINTS FOR SEPSIS AND ECMO

- Ideally initiate within first 24hrs of shock onset
- Confirm patient not fluid responsive
- Lactate <4.5
- SOFA score < 15
- LV dysfunction: EF< 30% will need VA vs VAV
- CPR pre-ECMO or during ECMO……..poor outcomes
- Support to LV recovery

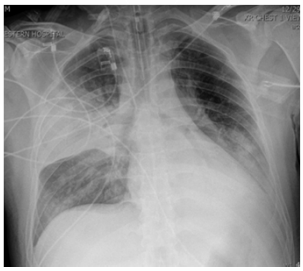
CASE 1

- 39 y.o. male was admitted septic shock (lactate 4.4, 3 pressors)
- Acute respiratory failure, lobar pneumonia after a 5day flu-like illness and acute renal failure
- Blood and sputum cultures were positive for Beta Streptococcus Group A.
- Echocardiogram initially showed mild decrease in LV and RV systolic function
  - 24hrs after admission showed severe biventricular systolic heart failure with LVEF < 20%.
- Evolving ARDS; Refractory hypoxia despite aggressive ventilator settings
- What type of ECMO should be considered?

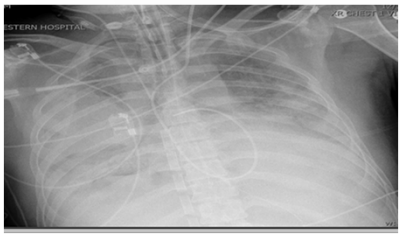
DAY 1: 630 AM



DAY 1: 1120 AM

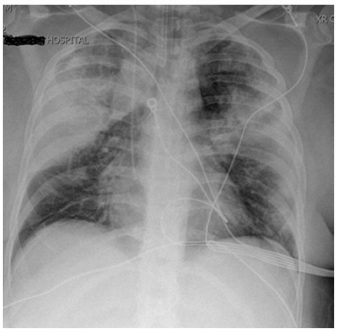


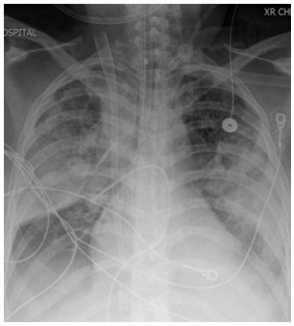
24HRS



CASE 2

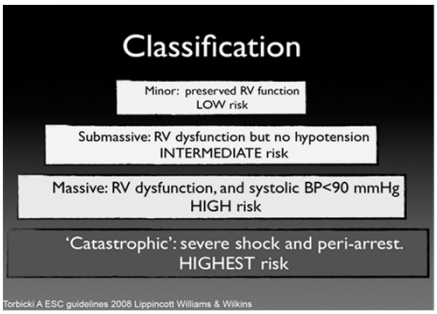
- 59 year old female with URI symptoms since early October treated with Augmentin and Levofloxacin
- Presented to OSH ED– O2 sat 82%, lactate 4.6,
- On admission Cr 5.5, ABGs 7.11/50/64/15
- Pt intubated and started on Flolan. Norepi, vasopressin, epi and phenylephrine
- Pt paralyzed on FiO2 100% - chest CT showed consolidation bilateral upper lobes and left lower lobe
- TTE hyperdynamic LV with EF>70%
- Blood culture from outside hospital + strep
- Which type of ECMO mode???





ECMO IN MASSIVE PE

- AHA define massive PE as sustained hypotension (systolic BP <90 mmHg or systolic pressure drop >40mmHg for 15 min) or requiring inotropic support
- Cardiogenic shock that results from pulmonary embolus has a high mortality rate (20% -30%)
- Impending or ongoing cardiac arrest
  - systemic thrombolysis or anticoagulation alone has not been always shown to be effective



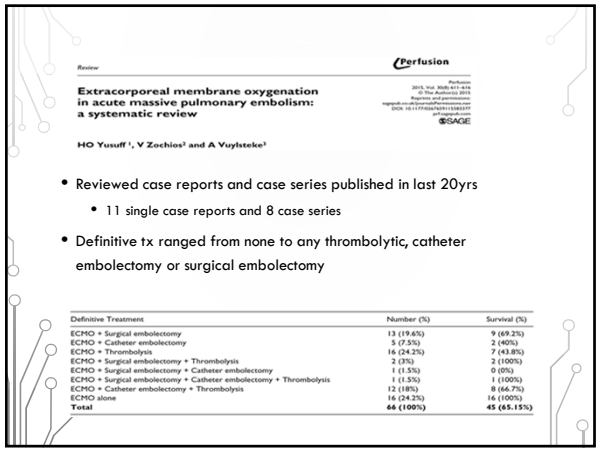
MASSIVE PE

- Treatment
  - Anticoagulation ???
  - systemic or intrapulmonary thrombolytic (6.2% mortality)
  - clot fragmentation, suction embolectomy (13.5% treatment failure including death)
  - surgical embolectomy (6% 30 day mortality)
- Hemodynamically unstable patients/ cardiac arrest
  - diagnostic and therapeutic options may be limited

Perfusion. 2015. Vol. 30(8) 611-616

RV FAILURE AND ECMO

- Rationale is to divert some blood from right atrium to the arterial circulation
- Unloading the RV and relieving its dilation
- ECMO relieves hypoxemia due to shunt and can provide therapeutic means by anticoagulation
- Massive pulmonary emboli will usually resolve or move into segmental branches within 48-72 hours of ECLS support



Review

Perfusion

Extracorporeal membrane oxygenation in acute massive pulmonary embolism: a systematic review

HO Yusuff [1], V Zochios[2] and A Vuylsteke[3]

- Reviewed case reports and case series published in last 20yrs
  - 11 single case reports and 8 case series
- Definitive tx ranged from none to any thrombolytic, catheter embolectomy or surgical embolectomy

Definitive Treatment	Number (%)	Survival (%)
ECMO + Surgical embolectomy	13 (19.6%)	9 (69.2%)
ECMO + Catheter embolectomy	5 (7.5%)	2 (40%)
ECMO + Thrombolysis	16 (24.2%)	7 (43.8%)
ECMO + Surgical embolectomy + Thrombolysis	2 (3%)	2 (100%)
ECMO + Surgical embolectomy + Catheter embolectomy	1 (1.5%)	0 (0%)
ECMO + Surgical embolectomy + Catheter embolectomy + Thrombolysis	1 (1.5%)	1 (100%)
ECMO + Catheter embolectomy + Thrombolysis	12 (18%)	8 (66.7%)
ECMO alone	16 (24.2%)	16 (100%)
Total	**66 (100%)**	**45 (65.15%)**

- VA approach in 88%, VV 1.6, VAV 10.2%
- Thrombolysis part of cardiac arrest algorithm when PE suspected
  - 55% cases presenting in cardiac arrest
  - 51.2% survival
- Overall survival was 70.1% and none of the definitive treatment modalities was associated with higher mortality

Definitive Treatment	Odds ratio	95% CI	P - value
Surgical embolectomy	0.44	(0.127 – 1.54)	0.20
Catheter embolectomy	1.01	(0.317 – 3.202)	0.99
Thrombolysis	0.99	(0.312 – 3.158)	0.99

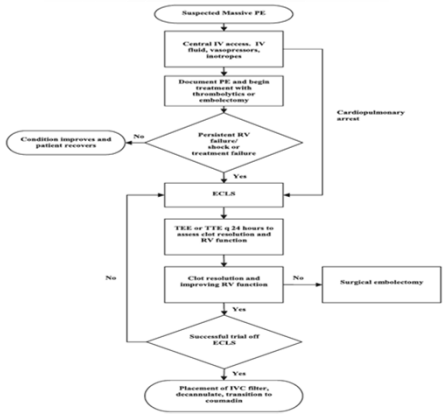
Perfusion. 2015. Vol. 30(8) 611-616

Extracorporeal Life Support for Massive Pulmonary Embolism

Paul Maggio, MD, Mark Hemmila, MD, Jonathan Haft, MD, and Robert Bartlett, MD

- 21 patients with MPE with profound shock and severe hypoxemia treated with ECLS
- Cardiac arrest due to PE (8 cases)
- Survival rate 62%
- Six patients had fibrinolytic therapy before requiring ECLS
- 10 of the 13 survivors required no additional therapy other than anticoagulation
  - Two patients underwent surgical pulmonary embolectomy after initial ECLS
  - TEE 4 days after ECLS demonstrated minimal clot dissolution and persistent RV failure

J Trauma. 2007;62:570 –576.



J Trauma. 2007;62:570 –576.

Percutaneous Cardiopulmonary Support for the Treatment of Acute Pulmonary Embolism: Summarized Review of the Literature in Japan Including Our Own Experience

Masahito Sakuma, MD,[1] Mashio Nakamura, MD,[2] Norikazu Yamada, MD,[2] Takeshi Nakano, MD,[2] and Kunio Shirato, MD,[2]

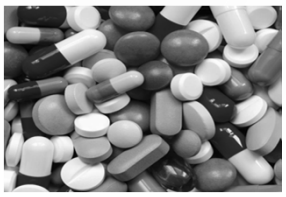
- 193 cases: overall 73% survival (65% in cardiac arrest)
- ECMO was combined with:
  - surgical embolectomy in 35% (68 of 193)
  - thrombolytic therapy in 62% (120/193)
  - catheter therapy in 24% (46/193).
- The survival rate breakdown:
  - 80% in surgical embolectomy
  - 71% in thrombolytic therapy
  - 76% in catheter therapy

Sakuma M. et al. Ann Vasc Dis 2:7-16

TIMING

- Bedside decision
  - Look at all factors
- Cardiac arrest
  - ?tpa vs no tpa
  - percutaneous vs cutdown
- Impending arrest
  - maintain hemodynamic stability for bridge to definitive therapy
    - Transport of patient to facility where surgical embolectomy could be feasible
  - Contra-indication for tpa

TOXICOLOGY



- Calcium channel blockers and beta-blockers represent more than 65% of deaths from acute drug intoxication (1)
- TOX-ACLS, 2001, "evidence to support the use of advance circulatory assist devices" (2).
- Beta blocker poisoning can result in fourfold cardiovascular toxicity
  - Myocardial depression, bradycardia
- impairs intracellular movement of calcium into muscle cells
- QRS widening, QT lengthening, especially with sotalol
  - Predisposes to VT, torsades de pointes, VF
- vasodilatation

1. F. Sangalli et al. ECMO-Extracorporeal Life Support in Adults,Springer-Verlag Italia 2014.

2. ANNALS OF EMERGENCY MEDICINE 37 : 4 APRIL 2001

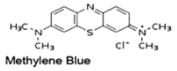
RESUSCITATION

- Insulin-glucose infusion
- Calcium……a lot
- Low threshold for S-G cath
- Rapid escalation of pressors
- Methylene Blue
  - inhibits the nitric oxide
  - decreasing vasodilatation
  - increasing responsiveness to vasopressors

Insulin-glucose infusion: Safety/Benefit in BB[8,9,10,20,21] as well as CCB[12,20,21] overdose

a. Initial IV bolus of 1 u/kg regular insulin plus 0.5 gm/kg glucose (100 mL of D50 in 100 kg patient)

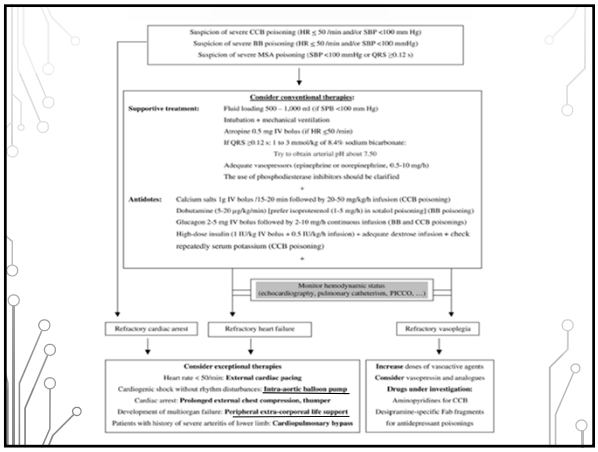
b. Began infusion of insulin at 1 u/kg/hr (100 u/hour in 100 kg adult) and increase rapidly (by 1 u/kg/hr every 10 min) up to 10 u/kg/hr[11,19,20,21] (1000 u/hr in 100 kg adult) as needed to raise systolic blood pressure > 90 mmHg or MAP > 65 mm



Methylene Blue

SEQUESTRATION THERAPY

- Fat emulsions (Intralipid® 20%) only for patients in ***extremis*** and not responding to other resuscitative measures……..
- bolus doses of 1.5 mL/kg over 1 minute,
- infusion of 0.25 mL/kg/min



FIRST REPORTED SERIES

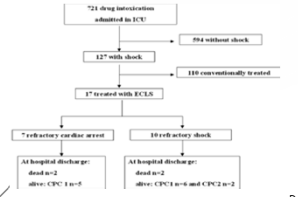
- Babatasi et al. 2001
- Six patient with cardiac arrest following intentional overdose of beta-blockers, calcium channel blockers
- Supported on fem-fem VA ECMO
- First two patients died of MSOF due to delay in installation
- Four patients survived without neuro or medical sequelae

Babatasi G et al. Severe intoxication with cardiotoxic drugs: values of emergency percutaneous cardiocirculatory assistance. Arch Mal Coeur Vaiss 94(12): 1386-1392.

Extracorporeal life support in severe drug intoxication: a retrospective cohort study of seventeen cases

Cédric Daubin[1], Philippe Lehoux[2], Calin Ivascau[3], Marine Tasle[2], Mehdi Bousta[1], Olivier Lepage[3], Charlotte Quentin[1], Massimo Massetti[3] and Pierre Charbonneau[1]

- Largest case series to date
- 721 patients admitted for drug intoxication, 17 with refractory cardiogenic shock (n=10) or cardiac arrest (n=7)
  - All fem-fem VA ECMO
- 13 survived and were discharged without significant cardiovascular or neurological sequelae



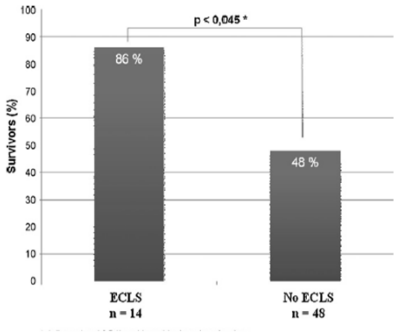
Daubin et al. Critical Care 2009, 13:R138

A comparison of survival with and without extracorporeal life support treatment for severe poisoning due to drug intoxication☆

Romain Masson[a], Vincent Colas[b], Jean-Jacques Parienti[c,d], Philippe Lehoux[e], Massimo Massetti[f], Pierre Charbonneau[a], Fabienne Saulnier[b], Cédric Daubin[a,*]

- compared poisoned cardiogenic shock patients treated with or without ECLS
- 10 persistent cardiac arrest and 42 with severe shock
- 14 patients were treated with ECLS and 48 patients with conventional therapies
- 12/14 ECLS survived; including all cardiac arrest

R. Masson et al. / Resuscitation 83 (2012) 1413– 1417



R. Masson et al. / Resuscitation 83 (2012) 1413– 1417

CASE 1

- 61 year old gentleman who has been having multiple psychosocial stressors
- Month supply metoprolol and norvasc
- Felt somewhat dizzy, nauseated.
- Emergency Department at 8 hours after ingestion
- Dopamine>norepi> High dose insulin> methylblue
- TTE preserved LV function, HR >65
- 26 hrs after ingestion: worsening shock, on/off epi, SG placed
  - RA=18; RV=51/17; PA=46/28, mean 37; PW=33; PA sat 80%; arterial sat 100%; EFCO/CI 8.06/3.36; SVR 546.
- Temp pacer as HR into 40s
- Emergent ECMO
- 73 hr. run time and successful decanulated

CASE 2

- 45 year old female found by her husband after having taken a months worth of atenolol and "handful of ambien".
- She was awake and talking when husband first arrived at home. Reported atenolol at 5pm followed by ambien at 10pm.
- Unresponsive in the ambulance and was intubated at OSH.
- 4hrs in the ED before developed hypotensive and bradycardic, responded to dopamine
- Delay in transfer due to weather

- Escalating multiple amps of epinephrine, and high dose epinephrine and norepinephrine infusions , and vasopressin.
- Worsening metabolic acidosis (Lactate 9.4), acute kidney injury.
- Bradycardia into 40s. Urgently taken to cath lab for transvenous pacing after transcutaneous pacing failed to capture.
- Heart rate 100 (paced), PA pressure 40/28 PCW 28 TD CO 2.47 CI 1.61 MVO2 48%
- Methylene blue given with improvement in SVR
- Discussions regarding intralipid
- STAT echocardiogram reveals globally depressed EF with apical ballooning wall motion abnormality pattern consistent with a takotsubo cardiomyopathy.
- VA ECMO remained as the best salvage therapy for her ongoing shock

CONSENSUS

- Earlier the better, delay of shock presentation given slow absorption
- Intralipid……not good for circuit
- IABP plays a role in less severe forms
- ECMO is crucial with severe cardiogenic shock
  - Gain time to recovery / washout
- Average ECMO duration 4.5 days; thus lower chance complications
- Drug poisoning appears to be one of the most favorable scenarios for ECMO support

THANK YOU

- **David.Williams@allina.com**