

UITNODIGING

ACUTE INTOXICATIONS: EEN UPDATE MEET THE EXPERTS

➤ 6^{de} Lage Landen Symposium Intoxicaties
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Management of cardiovascular toxicity

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I declare no conflict of interest

Poisonings with cardiotoxics

In the USA: AAPCC-NPDS 2022

Cardiovascular agents: 6th cause of exposures (2.7%) increasing each year and 2nd cause of death (fatality rate: ~0.3%)

Gummin DD. *Clin Tox* 2023

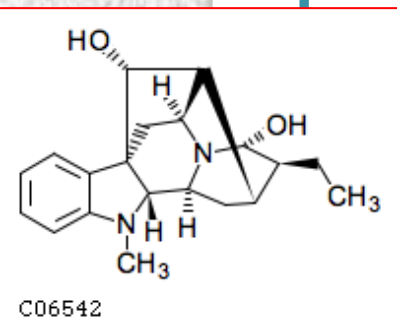
- **Cardiovascular pharmaceuticals**
 - Sodium-channel blockers (Class I)
 - Beta-blockers (class II)
 - Potassium channel blockers (sotalol) (class III)
 - Calcium-channel antagonists (class IV)
 - Cardioglycosides (class V)
- **Non-cardiovascular pharmaceuticals**
- **Drugs of abuse**
- **Industrial toxicants**
- **Plants, household and over-the-counter toxicants**



The prognostic value of the ingested dose: The example of ajmaline poisoning

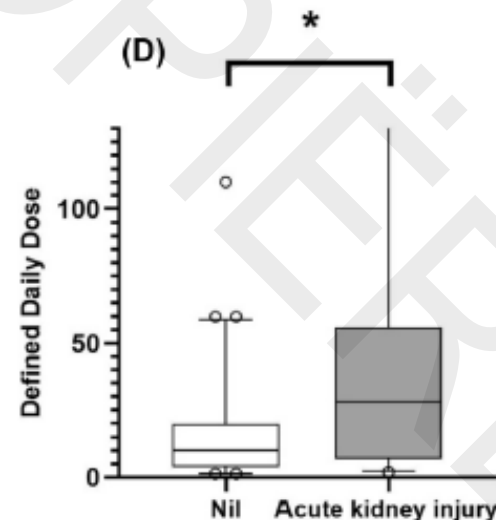
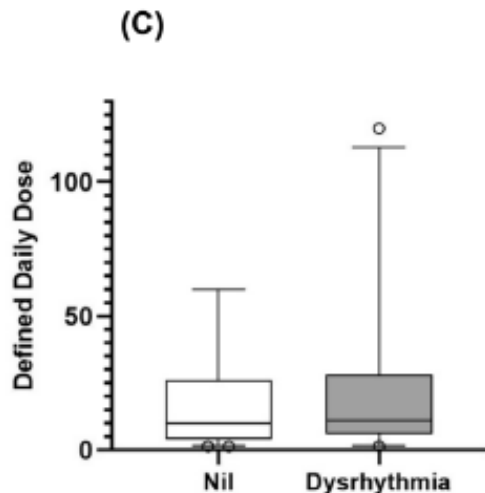
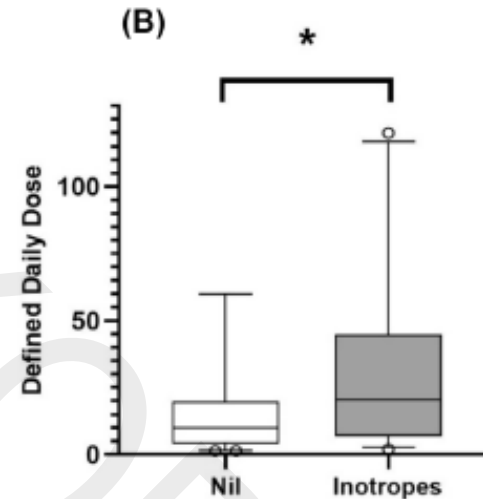
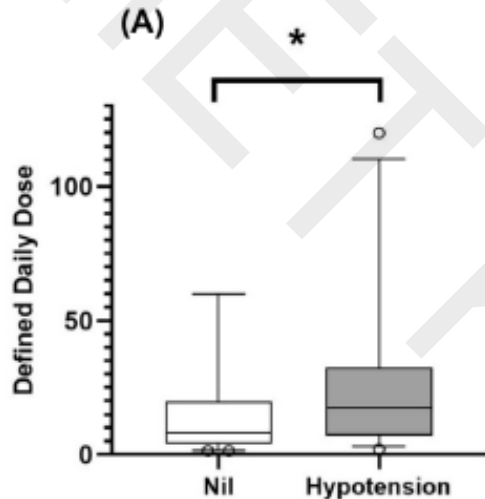
Delay for symptom occurrence: 1 - 3 h
All patients in cardiac arrest died

Ingested tablets	N	Cardiac arrest
1 g	7	0
2 g	13	1
3 g	16	8



Conso F. *Press Med* 1980

Dose and occurrence of specific CCB overdose complications

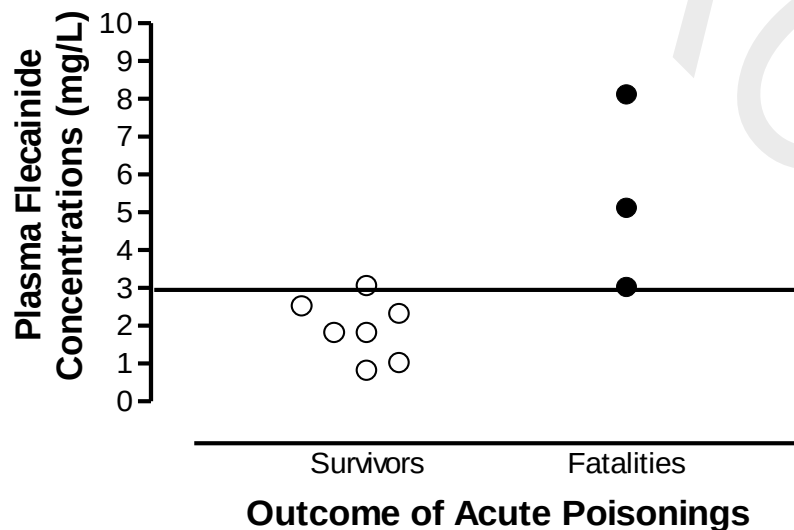


Dihydropyridines
= the commonest
CCB overdoses
with amlodipine
making up half of
the patients

More severe
toxicity occurred
with diltiazem and
verapamil

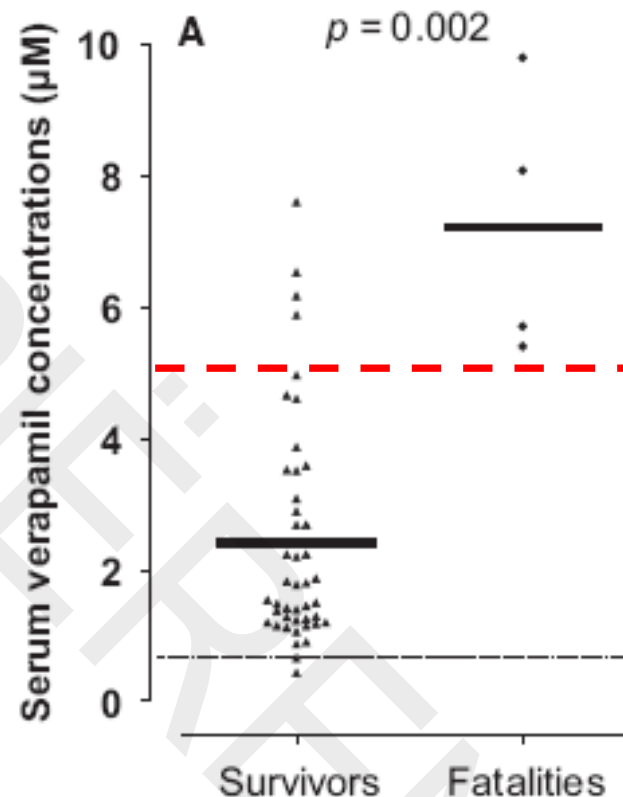
Prognostic value of plasma concentrations of the cardiotoxicant

Flecainide poisonings



Mégarbane B. *Clin Tox* 2007

Verapamil poisonings



Mégarbane B. *BCPT* 2010

Strategy of management of toxic cardiovascular failure

Diagnosis of shock



Determination of the mechanism of shock



Definition of the optimal treatment



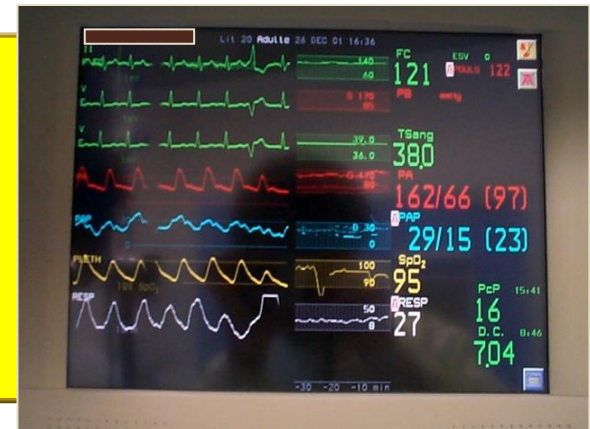
Diagnosis of the refractoriness of shock



Hemodynamic monitoring of cardiotoxicant poisonings

Macrocirculation level:

- 1- Hypotension: systolic BP < 90 mm Hg
or systolic BP decrease > 40 mmHg
or mean BP < 65 mmHg
- 2- Unresponsive to fluids
- 3- At least one sign of organ hypoperfusion

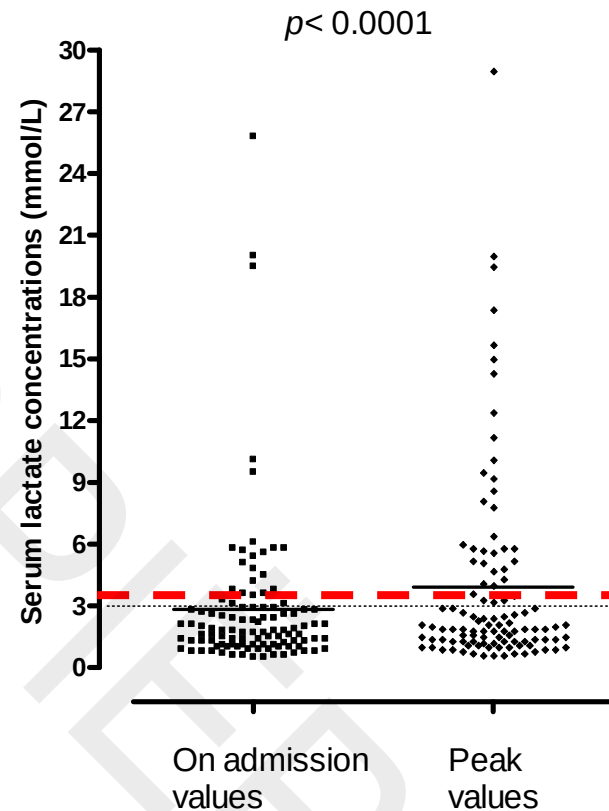
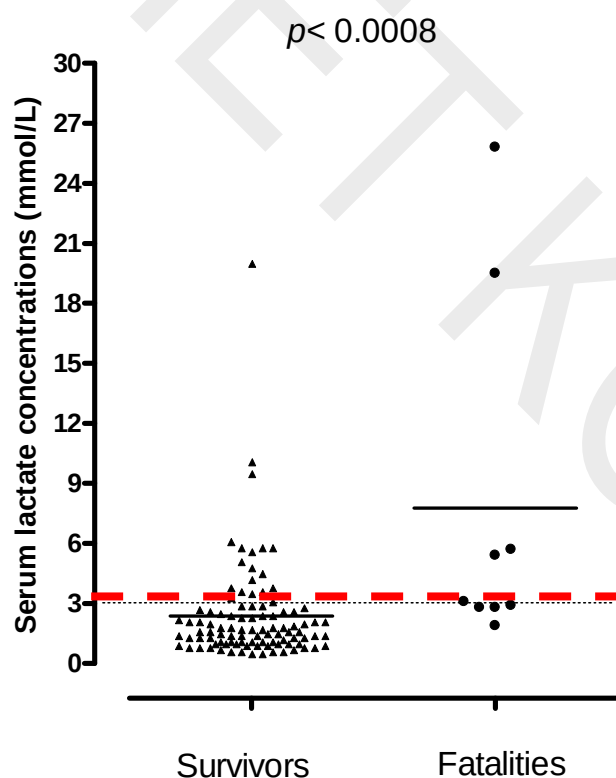


Microcirculation level:

- Simple signs: dizziness, transitory consciousness loss and collapse, skin discoloration, or even chest pain.
- More sophisticated signs requiring close and repeated assessment of changes in mental status, low urine output, and routine clinical chemistry (lactate, creatinine, and liver function tests).

Betablocker poisoning

Prognostic value of blood lactate on admission



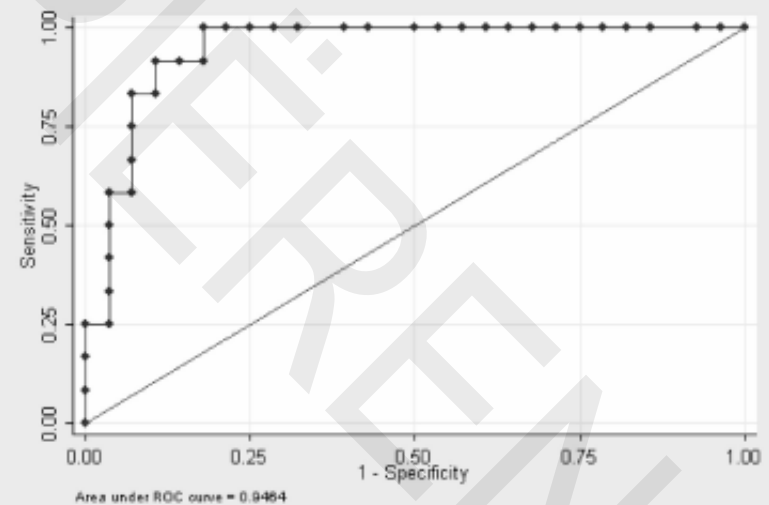
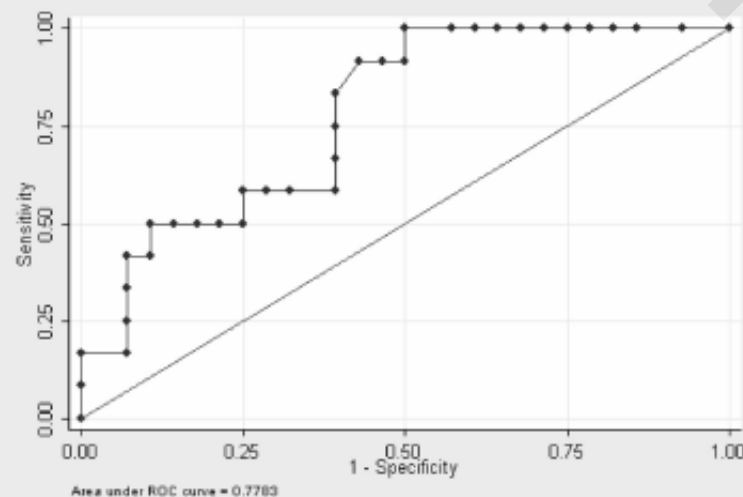
ROC-AUC of initial blood lactate to predict mortality = 0.84 (0.74-0.94).
Cutoff point maximizing the sum of sensitivity + specificity = 2.7 mmol/L.
For the selected 3.0 mmol/L lactate cutoff point: 55% sensitivity, 80% specificity.

Calcium-channel antagonist poisoning

Predictive value of hyperglycemia

	No Composite End Point	Composite End point	<i>p</i> Value
Total, n	28	12	
Initial blood glucose, mg/dL ^a	129 (98.5–156.5)	188 (143.5–270.5)	.0058
Peak blood glucose, mg/dL ^a	145 (107.5–160.5)	364 (267.5–408.5)	.0001
Initial heart rate, beats/min ^a	60 (45–87)	50.5 (40–67.5)	.18
Minimal heart rate, beats/min ^{a,b}	58 (40–68)	40 (39–45)	.0589
Initial systolic blood pressure, mm Hg ^a	129 (100–144)	89 (60–113)	.0091
Lowest systolic blood pressure, mm Hg ^{a,b}	110.5 (94–130)	72 (60–84)	.0004

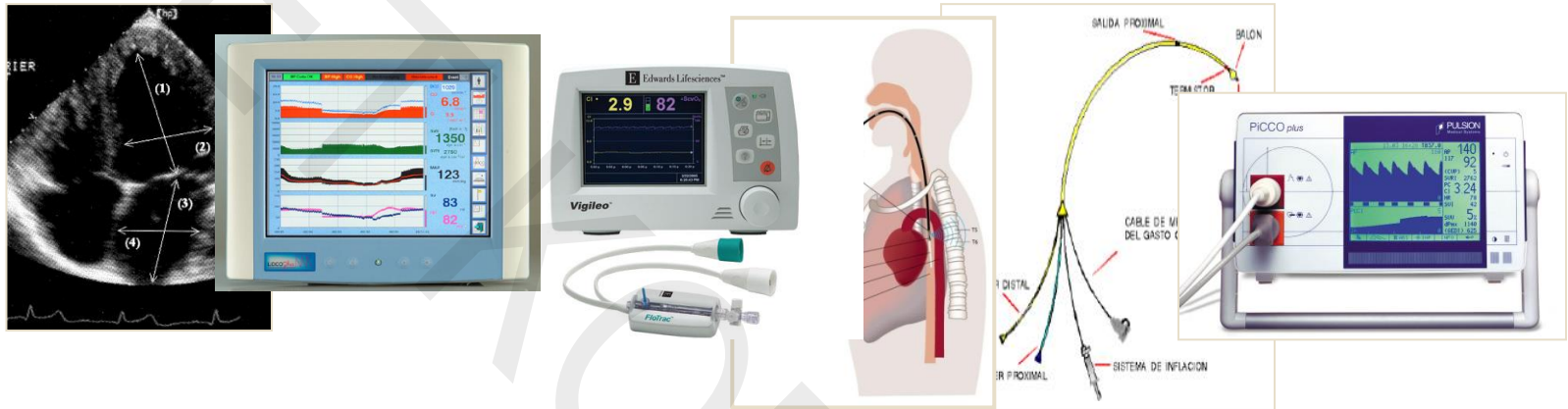
^aMedian (interquartile range); ^blowest value during the first 24 hrs of admission.



Cardiac glycoside poisoning: Predictive factors of death

	Age	AV block	K ⁺ >4.5	Death rate
Female	< 55	Yes	Yes	17
			No	4
	> 55	No	Yes	8
			No	2
		Yes	Yes	49
			No	18
Male	< 55	Yes	Yes	29
			No	9
		No	No	38
			Yes	11
	> 55	Yes	No	20
			Yes	6
		No	No	74
			Yes	35
		Yes	No	50
			Yes	23

Evaluation of the mechanisms involved in drug-induced cardiovascular failure

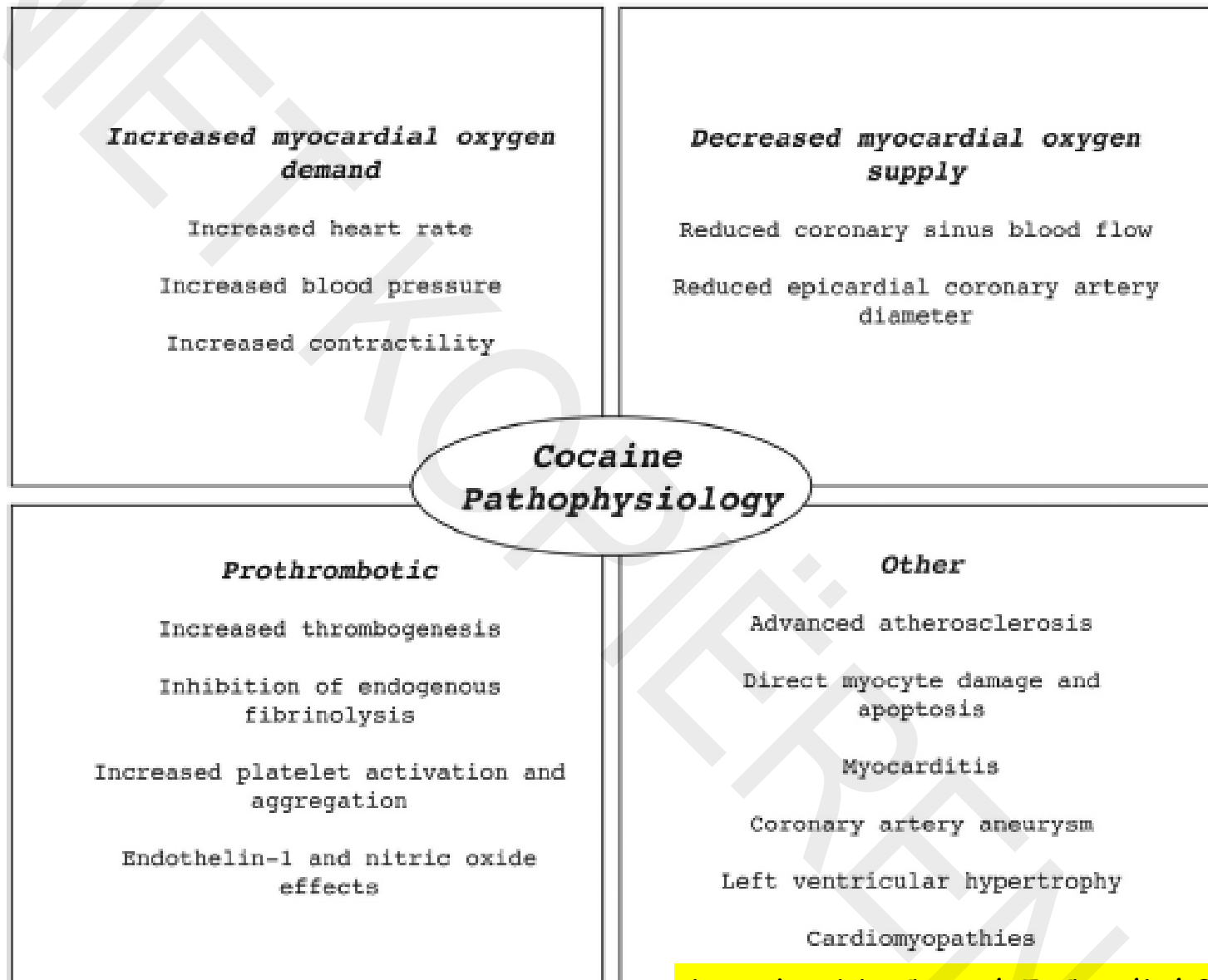


	Peripheral Shock	Cardiogenic Failure
Cardiac Index ($\text{l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$)	> 3.5	< 2.5
Systemic Resistance ($\text{d} \cdot \text{s}^{-1} \cdot \text{cm}^{-5} \cdot \text{m}^2$)	< 1500	> 2000
P_{aw} (mmHg)	< 10	> 18
LVEF (%)	> 70	< 60

Conventional supportive treatments in the ICU

- ❖ **Intubation and mechanical ventilation :**
 - Severe arrhythmias and collapse
 - Coma, convulsions, respiratory failure
- ❖ **Treatment of collapse/shock**
 - Fluids + **adequate catecholamine infusion**
- ❖ **Treatment of torsade-de-pointes**
 - Defibrillation, MgSO_4 , titrated isoproterenol, cardiac pacing
 - Correction of electrolyte imbalance (K^+ , Mg^{2+})
- ❖ **Treatment of monomorphic ventricular tachycardia**
 - Defibrillation, MgSO_4 , lidocaine infusion
- ❖ **Cardiac pacing**
 - High-degree AV block with preserved inotropism

Pathophysiology of cocaine cardiotoxicity



Recommendations for the management of life-threatening betablocker poisonings

Beta-blockers

Dobutamine 5-20 $\mu\text{g/kg/min}$
Isoprenaline 1-5 mg/h (Sotalol)



Glucagon 2-5 mg IV bolus
 2-10 mg/h continuous infusion
 Or

Insulin 1 IU/kg IV bolus
 1 IU/kg/h continuous infusion



Epinephrine 0.5-10 mg/h

± **Cardiac Pacing**

COR	LOE	Recommendations
1	B-NR	1. We recommend that high-dose insulin be administered for hypotension due to β -blocker poisoning refractory to or in conjunction with vasopressor therapy.
1	C-LD	2. We recommend that vasopressors be administered for hypotension due to β -blocker poisoning.
2a	C-LD	3. It is reasonable to use a bolus of glucagon, followed by a continuous infusion, for bradycardia or hypotension due to β -blocker poisoning.
2a	C-LD	4. It is reasonable to utilize extracorporeal life support techniques such as VA-ECMO for life-threatening β -blocker poisoning with cardiogenic shock refractory to pharmacological interventions.
2b	C-LD	5. It may be reasonable to administer atropine for β -blocker-induced bradycardia.
2b	C-LD	6. It may be reasonable to attempt electrical pacing for β -blocker-induced bradycardia.
2b	C-LD	7. It may be reasonable to use hemodialysis for life-threatening atenolol or sotalol poisoning.
3: No Benefit	C-LD	8. Intravenous lipid emulsion therapy is not likely to be beneficial for life-threatening β -blocker poisoning.

Recommendations for the management of life-threatening calcium-channel blocker poisonings

Calcium channel blockers

Calcium chloride 1 g IV bolus /15 min
4 doses, 20-50 mg/kg/h infusion



Insulin 1 IU/kg IV bolus
1-10 IU/kg/h continuous infusion



Epinephrine 0.5-10 mg/h
Norepinephrine 0.5-10 mg/h

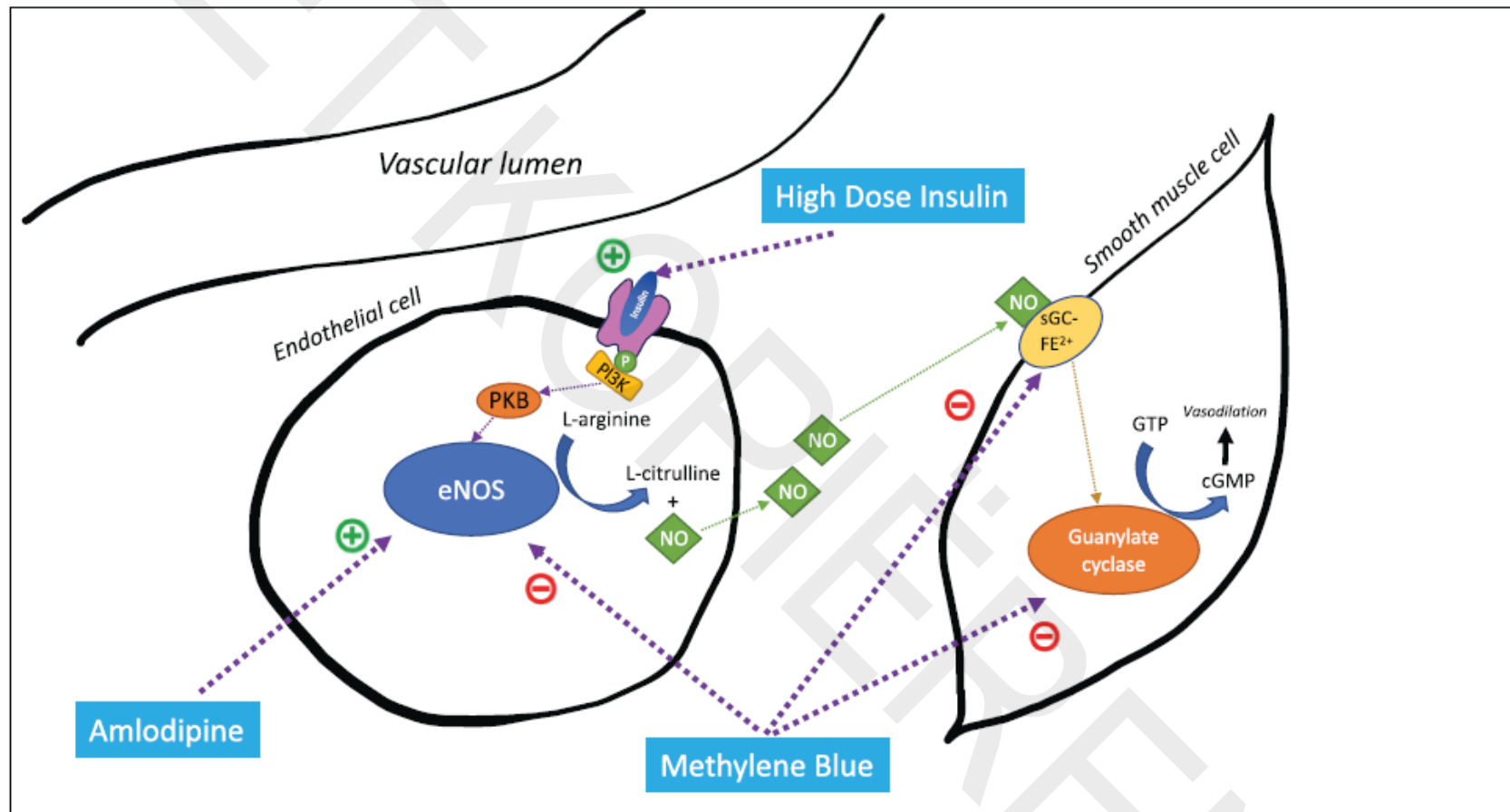


Methylene blue 2 mg/kg bolus
1 mg/kg/h infusion

COR	LOE	Recommendations
1	B-NR	1. We recommend administering vasopressors for hypotension from calcium channel blocker (CCB) poisoning.
1	B-NR	2. We recommend administering high-dose insulin for hypotension due to CCB poisoning.
2a	C-LD	3. It is reasonable to administer calcium for CCB poisoning.
2a	C-LD	4. It is reasonable to administer atropine for hemodynamically significant bradycardia from CCB poisoning.
2a	C-LD	5. It is reasonable to utilize extracorporeal life support techniques such as VA-ECMO for cardiogenic shock due to CCB poisoning that is refractory to pharmacological interventions.
2b	C-LD	6. It might be reasonable to attempt electrical pacing for CCB poisoning with refractory bradycardia.
2b	C-LD	7. The usefulness of a glucagon bolus and infusion for CCB poisoning is uncertain.
2b	C-LD	8. The usefulness of administering methylene blue for refractory vasodilatory shock due to CCB poisoning is uncertain.
3:No Benefit	C-LD	9. The routine use of intravenous lipid emulsion (ILE) therapy for CCB poisoning is not recommended.

Lavonas EJ. *Circulation* 2023

Mechanisms of synergistic vasodilation between amlodipine and high-dose insulin



Recommendations for the management of life-threatening sodium-channel blocker poisonings

Sodium channel blockers

Sodium bicarbonates 8.4%
250 ml to be repeated 3 times
+ 2g KCl / 250 ml
(cocaine: **Lidocaine IV**)



Epinephrine 0.5-10 mg/h
Norepinephrine 0.5-10 mg/h

COR	LOE	Recommendations
1	B-NR	1. We recommend using sodium bicarbonate to treat life-threatening cardiotoxicity from tricyclic and/or tetracyclic antidepressant poisoning.
2a	C-LD	2. It is reasonable to use sodium bicarbonate to treat life-threatening cardiotoxicity caused by poisoning from sodium channel blockers other than tricyclic or tetracyclic antidepressants.
2a	C-LD	3. It is reasonable to use extracorporeal life support, such as VA-ECMO, to treat refractory cardiogenic shock from sodium channel blocker poisoning.
2b	C-LD	4. It may be reasonable to use Vaughan-Williams class Ib antidysrhythmics (eg, lidocaine) to treat life-threatening cardiotoxicity from class Ia or Ic sodium channel blockers.
2b	C-LD	5. It may be reasonable to use intravenous lipid emulsion to treat life-threatening sodium channel blocker poisoning refractory to other treatment modalities.

Recommendations for the management of life-threatening cocaine & local anesthetic poisonings

Cocaine Poisoning

COR	LOE	Recommendation
1	C-LD	1. We recommend rapid external cooling for life-threatening hyperthermia from cocaine poisoning.
2a	C-LD	2. It is reasonable to administer sodium bicarbonate for wide-complex tachycardia or cardiac arrest from cocaine poisoning.
2a	C-LD	3. It is reasonable to administer lidocaine for wide-complex tachycardia from cocaine poisoning.
2a	C-LD	4. It is reasonable to administer vasodilators (eg, nitrates, phentolamine, calcium channel blockers) for patients with cocaine-induced coronary vasospasm or hypertensive emergencies.

Local anesthetic Poisoning

COR	LOE	Recommendations
1	C-LD	1. We recommend the administration of intravenous lipid emulsion for local anesthetic poisoning.
1	C-LD	2. We recommend the use of benzodiazepines to treat seizures associated with local anesthetic systemic toxicity.
2a	C-LD	3. It is reasonable to administer sodium bicarbonate for life-threatening wide-complex tachycardia associated with local anesthetic toxicity.
2a	C-EO	4. It is reasonable to administer atropine for life-threatening bradycardia associated with local anesthetic systemic toxicity.
2a	C-EO	5. It is reasonable to utilize extracorporeal life support techniques such as VA-ECMO in local anesthetic toxicity with refractory cardiogenic shock.

Recommendations for the management of life-threatening cardiac glycoside poisonings

Cardioglycosides

Atropine 0.5-1 mg to be repeated



Anti-digoxin Fab fragments
Semi-molar or molar dose
(if not available: ventricular pacing)

COR	LOE	Recommendations
1	B-NR	1. We recommend administration of digoxin-specific antibody fragments (digoxin-Fab) for digoxin or digitoxin poisoning.
2a	C-LD	2. It is reasonable to administer digoxin-Fab for poisoning due to <i>Bufo</i> toad venom and yellow oleander.
2b	C-LD	3. It may be reasonable to administer digoxin-Fab to treat poisoning from cardiac glycosides other than digoxin, digitoxin, <i>Bufo</i> toad venom, and yellow oleander.
2b	C-LD	4. It may be reasonable to administer atropine for bradycardias caused by digoxin and other cardiac glycoside poisoning.
2b	C-LD	5. It may be reasonable to attempt electrical pacing to treat bradycardias from digoxin and other cardiac glycoside poisoning.
2b	C-LD	6. It may be reasonable to administer lidocaine, phenytoin, or bretylium to treat ventricular dysrhythmias caused by digitalis and other cardiac glycoside poisoning until digoxin-Fab can be administered.
3: No Benefit	B-NR	7. We do not recommend the use of hemodialysis, hemofiltration, hemoperfusion, or plasmapheresis to treat digoxin poisoning.

Anecdotic antidotes to treat drug-induced cardiovascular toxicity

Low-level evidence:

- Animal studies with positive effects on hemodynamics but no improvement of mortality
 - Single human cases or limited series

However, variable results and limited methodologies

- ❑ Phosphodiesterase inhibitors (amrinone / milrinone)
- ❑ Vasopressin, terlipressin
- ❑ 4-aminopyridine and 3,4-diaminopyridine
- ❑ Levosimendan
- ❑ Bay K8644, CGP 28932, digoxin, cyclodextrin, liposomes, bicarbonate,
- ❑ L-carnitine, fructose 1,6-diphosphate, PK 11195, triiodothyronine

Refractoriness to catecholamines - epinephrine versus dobutamine -

F, 17 years, severe propranolol poisoning

Sedation + mechanical ventilation + FiO₂ 100%

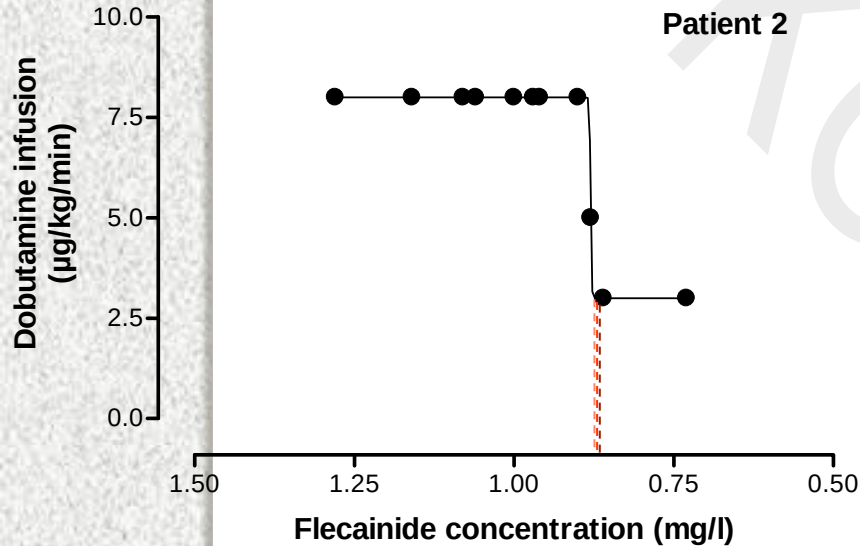
Epinephrine 1.5 mg/h			Dobutamine 15 µg/kg/min	
BP	S	93	56	mmHg
	D	64	33	mmHg
	M	75	43	mmHg
P _{RA}		7	6	cmH ₂ O
P _{AP}	S	27	19	cmH ₂ O
	D	19	11	cmH ₂ O
	M	23	15	cmH ₂ O
P _{cw}		17	13	cmH ₂ O
Cardiac Index		1.4	1.8	l/min/m ²
Systemic resistances		50.3	20.3	UI

30 min later

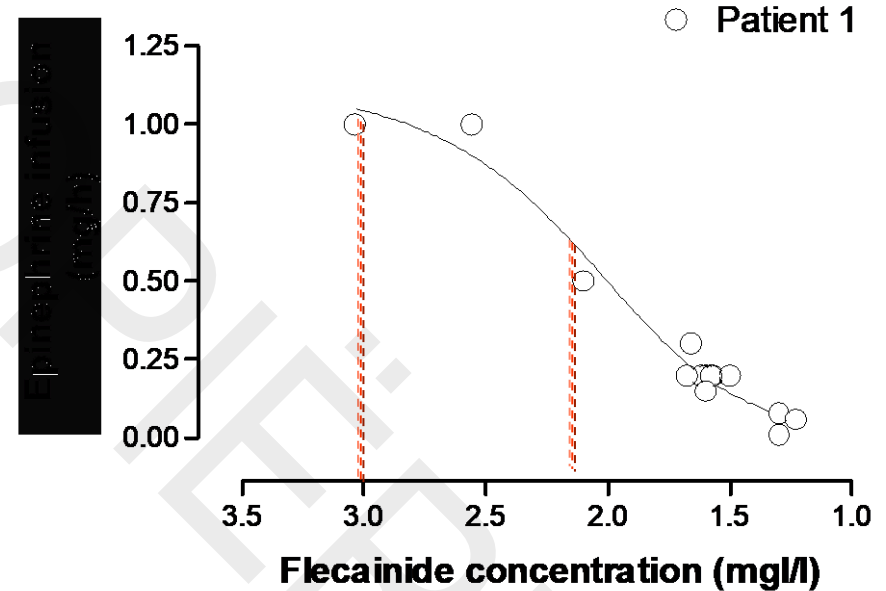
Dramatic decrease in BP

Assessment of catecholamine limits to reverse cardiac failure

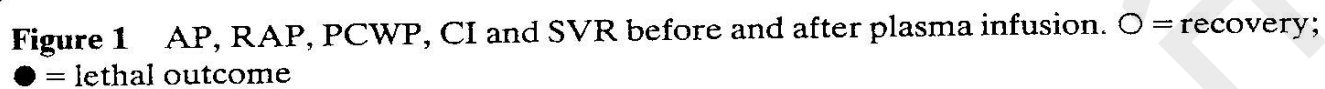
Dobutamine infusion



Epinephrine infusion



Mégarbane B. *Clin Tox* 2005

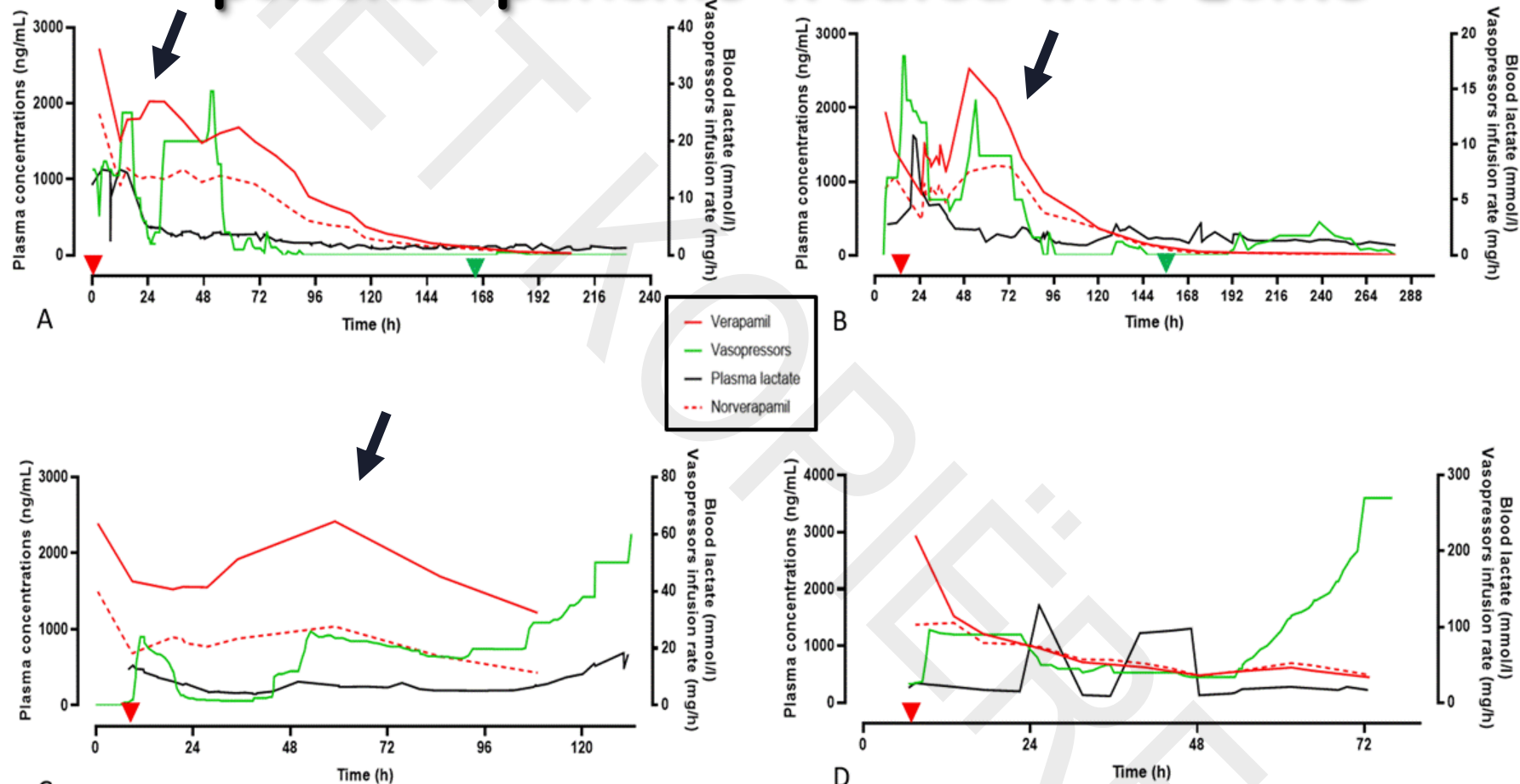




**Which interventions could improve
life-threatening poisonings with
suspicion of refractoriness?**

1

Second plasma concentration peak followed by prolonged elimination in severely CCB-poisoned patients treated with ECMO



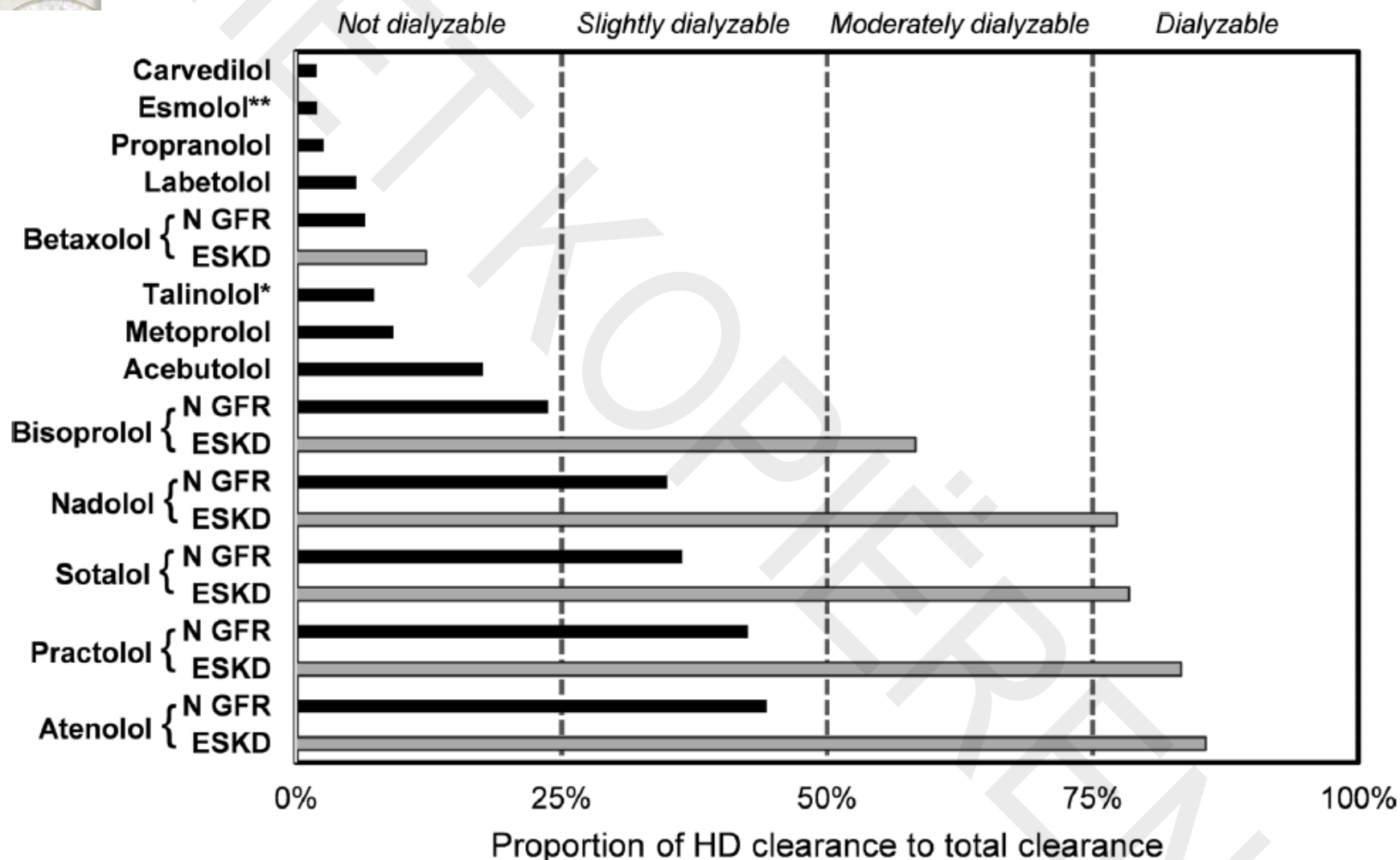
C Second plasma CCB concentration peak 49 h (41-51) post-ingestion (33%, N=40)
 Increase in vasopressors and blood lactate (60%), paralleling the 2nd peaks
 No difference in mortality

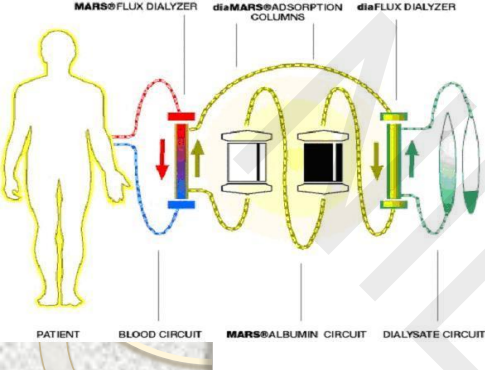
Chevillard L (submitted)

ECTR for poisoning to beta-adrenergic antagonists: recommendations from the



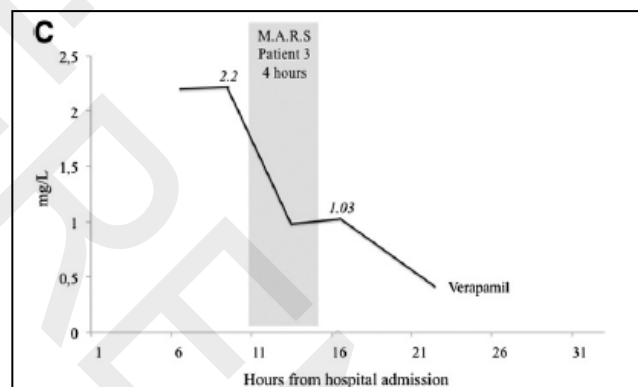
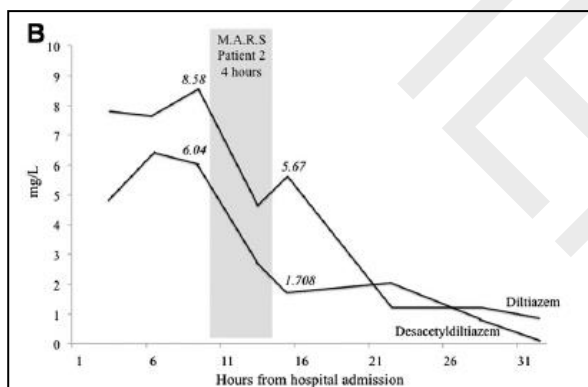
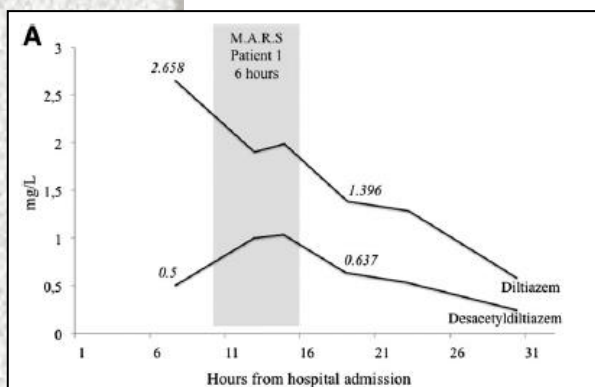
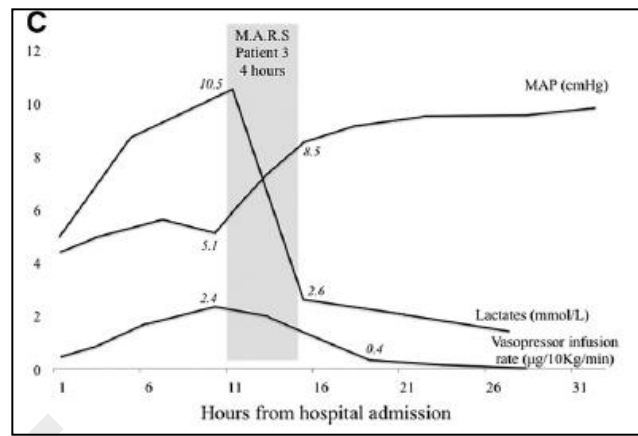
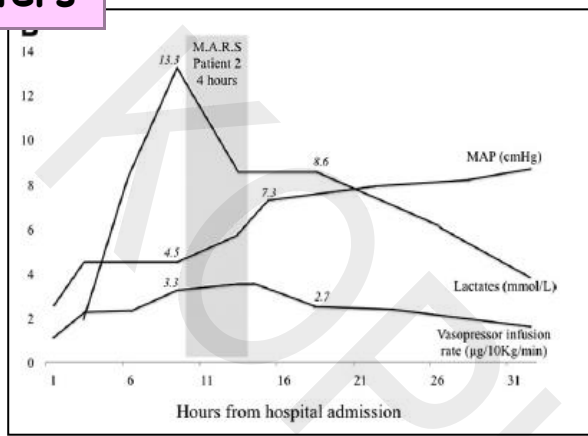
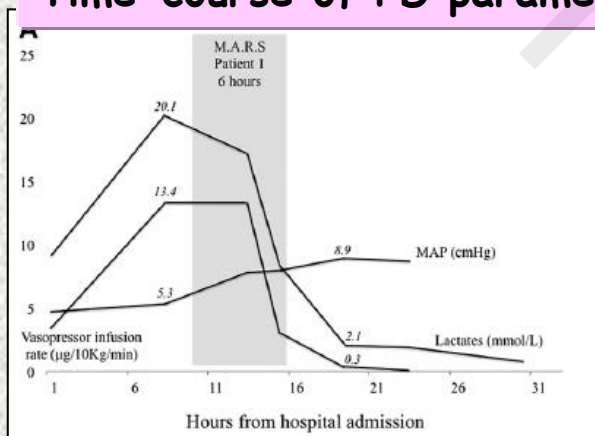
workgroup





Assessment of MARS usefulness in diltiazem and verapamil poisonings with refractory shock

Time-course of PD parameters



Time-course of PK

CCB extraction coefficients and clearance by MARS™

	Overall CCB extraction coefficients (%)	Overall CCB clearance (mL/min)	Charcoal cartridge Extraction coefficient (%)	Anion exchanger cartridge extraction coefficient (%)
Amlodipine (N=7)	5.8 [4.6-6.1]	9.4 [6.5-11.3]	41.3 [31.7-47.6]	4.5 [4.5-4.5]
Diltiazem (N=3)	10.6 [8.4-13.8]	17.8 [13.7-20.9]	58.3 [42.7-66.8]	6.9 [6.9-6.9]
Lercanidipine (N=1)	5.4	7.1	< 0.1	< 0.1
Nicardipine (N=3)	< 0.1	< 0.1	14.1 [12.8-15.4]	10.3 [7.3-13.4]
Verapamil (N=13)	5.9 [5.3-6.8]	7.7 [6.6-9.9]	51.6 [34.0-58.9]	2.0 [0.5-2.1]
Norverapamil (N=13)	5.4 [3.5-12.9]	7.1 [4.8-17.1]	37.5 [19.9-43.6]	0.4 [0.4-0.4]

Sutterlin L (in preparation)



Lipid emulsion to treat cardiotoxicant drug-related toxicity

To treat severe anesthetics side-effects in the OR as well as membrane-stabilizing agent or calcium-channel blocker poisonings.

Dose regimen: 1.5 ml/kg IV bolus then 0.25 ml/kg/min infusion

Mechanisms:

- Lipid sink / sponge: alteration of tissue distribution
- Modulator of myocardial energy, overcoming the inhibition of fatty acid-dependent metabolism
- Activator of myocardial Ca^{2+} channel increasing Ca^{2+} current
- Other toxin-specific mechanisms?

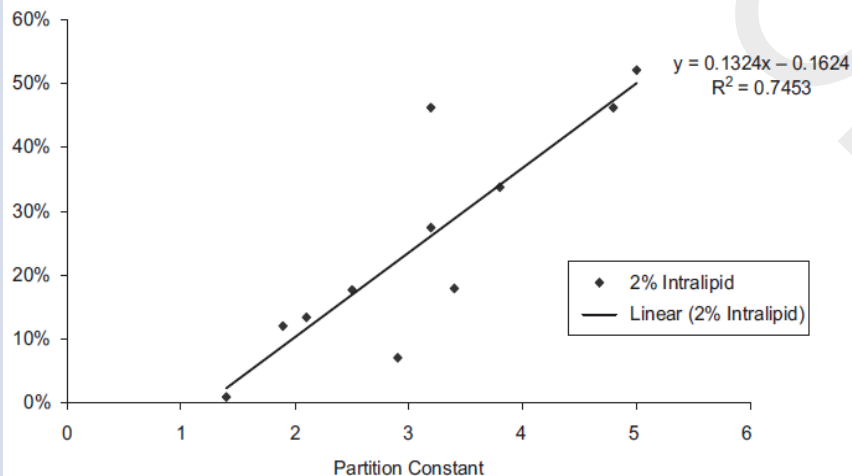


Sirianni AJ. *Ann Emerg Med* 2008
 Finn SD. *Anesthesia* 2009
 Weinberg GL. *Anesthesiology* 2009

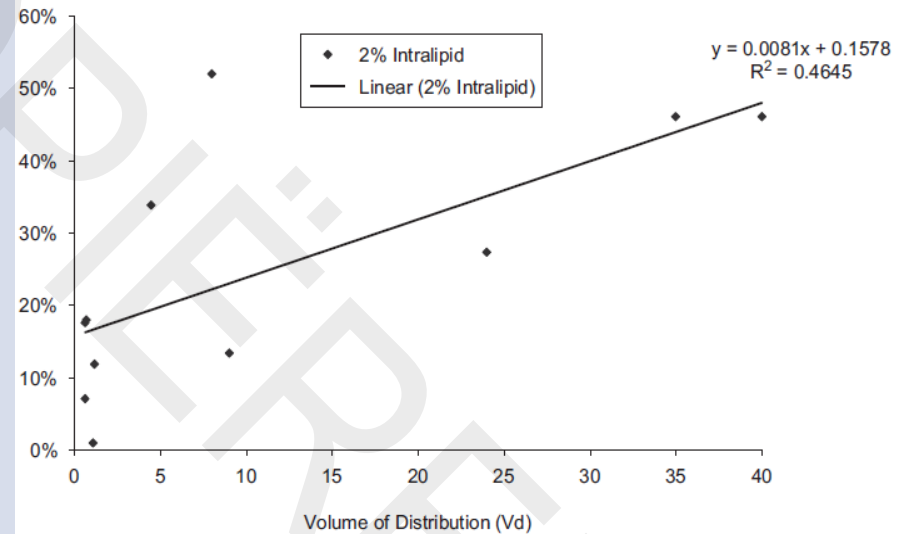
Partition constant and volume of distribution as predictors of ILE efficacy for toxicological emergencies

Serum drug concentration decrease plotted against the partition constant and the volume of distribution of eleven drugs with 20% Intralipid® added to the sample

Partition constant



Volume distribution



Agents with positive bench evidence for class effect and reported clinical use associated with a positive outcome

While the evidence base for ILE use in drug intoxication is evolving, the present evidence supports its use only in local anesthetic systemic toxicity and lipophilic cardiotoxin intoxication when there is an immediate threat to life, and other therapies have proven ineffective.

Evidence-based recommendations on the use of intravenous lipid emulsion therapy in poisoning

For the management of cardiac arrest:

We recommend using ILE with bupivacaine toxicity, while our recommendations are neutral regarding its use for all other toxins.

For the management of life-threatening toxicity:

- We suggest using ILE as a part of treatment in bupivacaine toxicity and we recommend its use if other therapies fail;
- We suggest using ILE if other therapies fail for toxicity due to other local anesthetics, amitriptyline, and bupropion;
- Our recommendations are neutral for all other toxins.

In the treatment of non-life-threatening toxicity, recommendations varied according to the balance of expected risk/benefit for each toxin

4

High-dose norepinephrine infusion (100 $\mu\text{g/kg/min}$) in a near-fatal amlodipine (200 mg) + perindopril (100 mg) poisoning: are there any limits?



Hours after admission	Norepinephrine infusion rate ($\mu\text{g/kg/min}$)	Serum creatinine concentration (mg/dL)	Serum creatinine concentration ($\mu\text{mol/L}$)	Serum lactate concentration (mmol/L)
1	6	1.24	110	4.4
12*	100	1.27	112	8.6
24	21	1.72	152	7.8
48	0.4	1.13	99	3.1
72	0.2	0.77	68	1.6

With clinical improvement, the dose of norepinephrine could be decreased 23 h after admission, and it was discontinued on day 6. The patient was discharged from the ICU on day 11 with no sequelae.

Brahmi N. *Clin Tox* 2024

Patients treated with massive catecholamine doses

Poisoned patients admitted to our ICU during a 13-year period (2003-2016) and who received massive catecholamine doses to treat cardiovascular failure:

epinephrine 1 $\mu\text{g/kg/min}$ ($> 5 \text{ mg/h}$)

norepinephrine 2 $\mu\text{g/kg/min}$ ($> 10 \text{ mg/h}$)

and/or isoprenaline 1 $\mu\text{g/kg/min}$ ($> 5 \text{ mg/h}$)

246 poisoned patients (~25% poisoned patients + catecholamines)

Sex ratio: 56% females/44% males,

Age: 47 years [36; 57]

Self- (88%) or accidental overdose (12%).

Involved toxicants: calcium-channel inhibitors (35%), beta-blockers (30%), vasodilators (15%) and sodium-channel blockers (10%)

Final outcome: 117 survivors (48%)

Patients treated with massive catecholamine doses

The maximal infusion rates associated with survival were:

50 mg/h epinephrine
140 mg/h norepinephrine
25 mg/h isoprenaline

Max infusion rate	Survivors	Non-survivors	<i>p</i>
Epinephrine	9.5 mg/h (6.0; 10.0)	10.0 mg/h (8.5; 20.0)	0.0001
Norepinephrine	20.0 mg/h (13.0; 38.0)	40.0 mg/h (20.0; 55.0)	0.0002
Isoprenaline	10.0 mg/h (7.3; 14.0)	7.0 mg/h (6.0; 9.0)	0.3

Catecholamine-attributed complications (11%) included limb (6%) and mesenteric ischemia (4%).

VA-ECMO in cardiogenic shock

The purpose of VA-ECMO is to take over heart function until recovery can occur, minimizing myocardial work, improving organ perfusion and maintaining the renal and biliary elimination of the toxicant



Two options to bring ECMO to the patient

To transfer the patient
to Cardiac Surgery
Department



To implement ECMO
by mobile TCS team



To develop an ECMO program in the ICU
in our hospital devoid of cardiac surgery



ECMO indications in acute poisonings

Which patients to treat with ECLS ?



Numerous risks



Too late : To result in anoxic brain injury or multiorgan failure

Undiscriminated use: to treat patients who would spontaneously have had favorable outcome with pharmacological treatments



Definition of refractory cardiac failure in sodium-channel blocker poisonings

N = 137

Hypotension Systolic BP $\leq$ 90 mmHg) despite :

Adequate fluids $\geq$ 1,000 ml

+ 8.4% sodium bicarbonate $\geq$ 375 ml

+ epinephrine $\geq$ 3 mg/h (glucagon $\geq$ 5 mg/h if b-blocker)

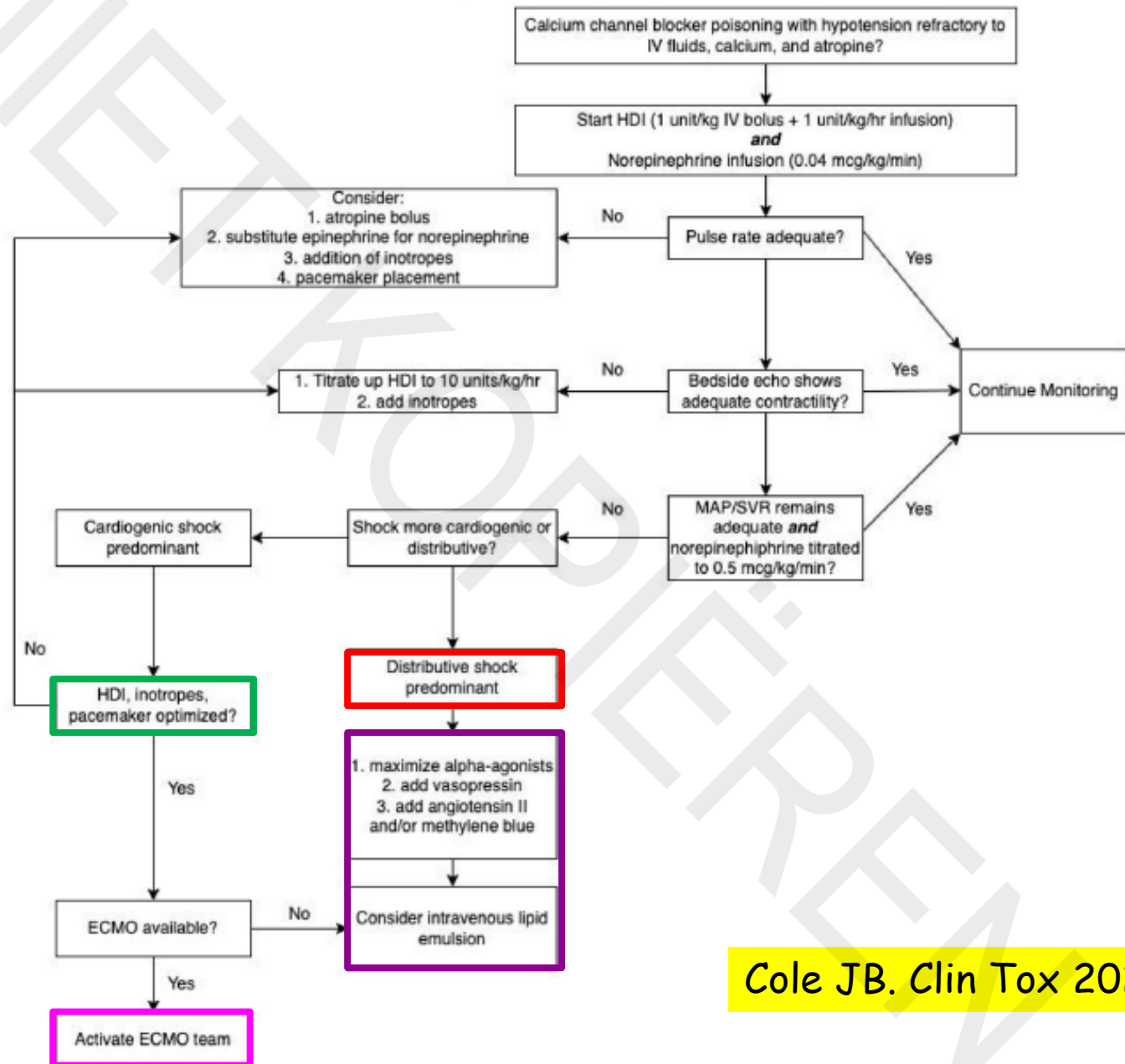
Respiratory failure : $\text{PaO}_2/\text{FiO}_2 \leq 150$ mmHg with MV + sedation

+

Renal failure : urine output $\leq$ 20 ml/h ou creatinine $\geq$ 120 μM (M) ou 90 μM (F)

The cardiac origin is supported by echocardiography (surface shortening fraction $< 30\%$) or right catheterism (cardiac index ≤ 2.5 l/min/m² + pulmonary artery occlusion pressure ≥ 18 mmHg)

Updated treatment algorithm for CCB poisoning

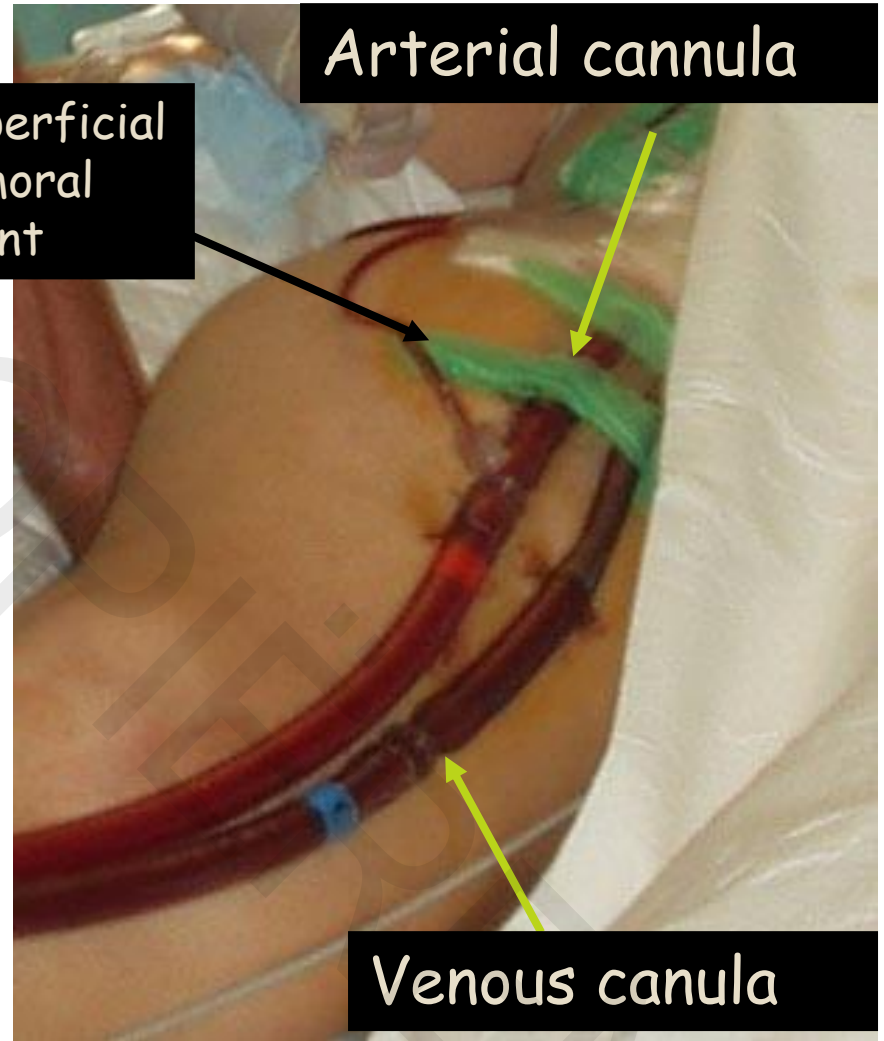


Preparation of ECMO device in the medical ICU



Superficial
femoral
shunt

Arterial cannula



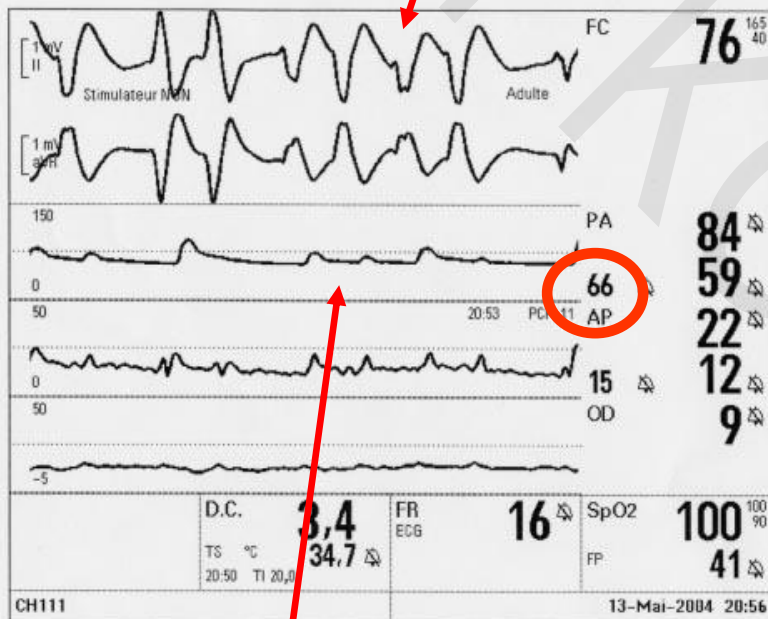
Venous cannula

7F/9F catheter connected with the
arterial cannula

ECMO monitoring in the ICU

Spontaneous cardiac rhythm

ECLS completely dependent cardiac flow (around 5-6 l/min)



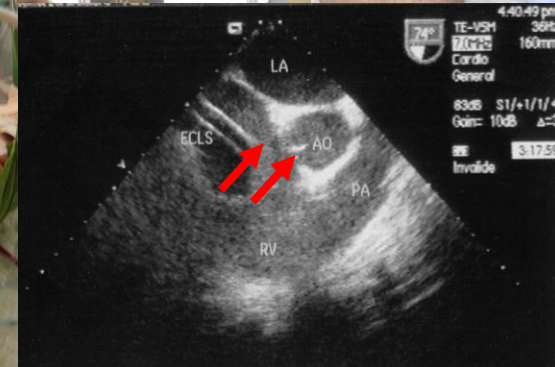
Severe hypotension despite high dose catecholamine



Spontaneous cardiac flow

Monitoring of ECMO-treated patients in the ICU

- **Efficient anticoagulation:**
heparin to obtain ACT = 2N
- **Catecholamines**
for mean BP = 60-70 mmHg +
dobutamine to facilitate LV discharge
- **Adequate transfusions**
- Adapted **Mechanical ventilation**
ABG monitoring by radial catheter
- **Temperature control**
- **Canulated lower limb monitoring**
- **Echocardiography:**
weaning criteria
- **Neurological evaluation** (EEG, clinical)
- **Care, nursing**



ECMO complications

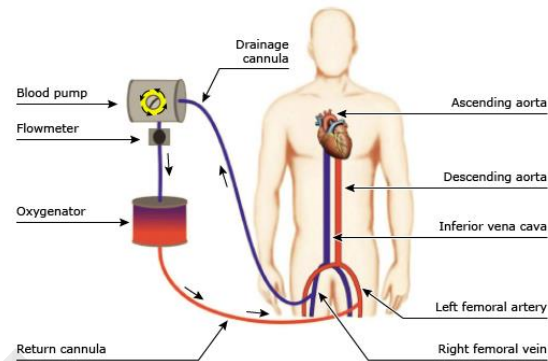
Local complications

- Acute limb ischemia 10%*
- Scarpa hemorrhage 9%
- Sub-acute ischemia 5%
- Infected lymphocele 5%
- Arterial dissection 2%



General complications: hemorrhage, thrombosis, systemic infection, pulmonary edema, thrombocytopenia

* 50% (Pozzi M. J Thorac Dis 2017)



Is ECMO efficient to improve outcome in the poisoned patient?



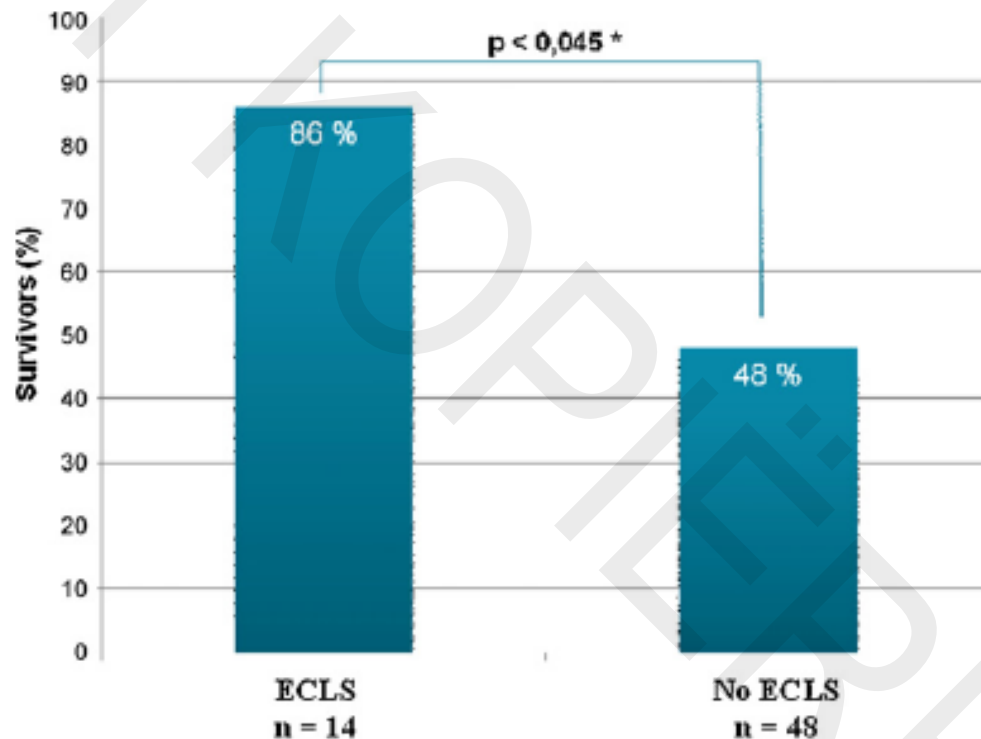
The level of evidence still limited !

Published cases of VA-ECMO- treated acute poisonings:

- Beta-blockers
- CCB
- Sodium channel blockers

Agent	References
Acebutalol	29,37
Amiodarone	38
Antidepressants (tricyclic)	15,29,39–41
Arsenic	42
Atenolol	29
Bisoprolol	29
Bupropion	43
Calcium Channel Blockers	1,44–49
Carbamazepine	29,50
Carbon monoxide	51
Chloroquine	15,52
Cibenzoline	29,53
Citalopram	29
Cocaine	54
Disopyramide	29,55
Diltiazem	29
Flecainide	29,56–58
Hydrocarbon products	59–63
Ibuprofen	64
Lidocaine	65
Mepivacaine	66
Methadone	67
Metoprolol	29
Opioids	67–69
Organophosphates	70
Paraquat	31,32
Paroxetine	29
Phosphine	71
Propafenone	15,29
Propranolol	29,72–74
Quetiapine	75
Quinidine	76
Radiocontrast material (intravenous)	77
Sotalol	29,78
Taxus	79
Venlafaxine	29
Verapamil	29
Zinc chloride	80
Zotepine	81

Comparison of survival with and without ECMO support in severe poisonings



* Adjusted on IGS II and beta-blockers intoxication

Clinical utility of VA-ECMO in patients with drug-induced cardiogenic shock - The ELSO case registry (N=104)

55 Survivors (53%)

VA-ECMO duration: 68 h [48-113]

Significant improvement of hemodynamics (MAP, BP), acidosis (pH, HCO₃) and ventilatory parameters (PaO₂, SpO₂, and SvO₂).

Univariate tests of association with in-hospital mortality

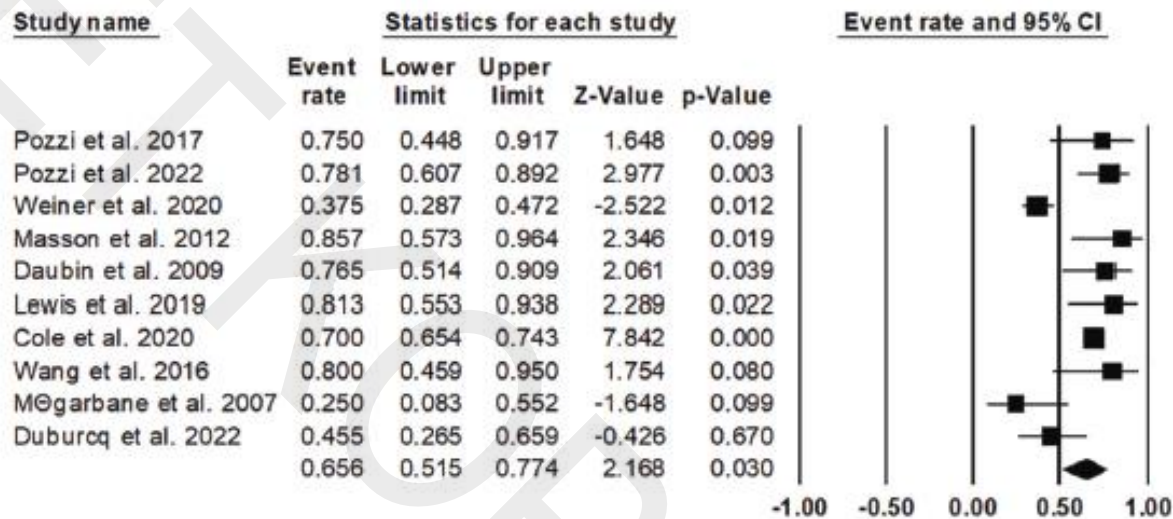
Variables	OR [95% CI]
Demographic	
Age	1.02 [0.99–1.05]
Male gender	1.96 [0.88–4.33]
Pre-ECMO variables	
CV agent vs. non-CV agent	0.64 [0.29–1.40]
pH at cannulation	0.38 [0.03–5.44]
HCO ₃ at cannulation	1.01 [0.97–1.05]
MAP at cannulation	0.99 [0.96–1.02]
Pre-ECMO arrest	1.47 [0.64–3.34]
Intra-aortic balloon pump	13.72 [0.74–254.84]
Pacemaker insertion	3.01 [0.56–16.29]
Organ failures during ECMO	
Renal replacement therapy	0.57 [0.24–1.37]
Hyperbilirubinemia	3.92 [0.43–35.71]

ECMO in cardiovascular drug poisoning - A German-wide retrospective study

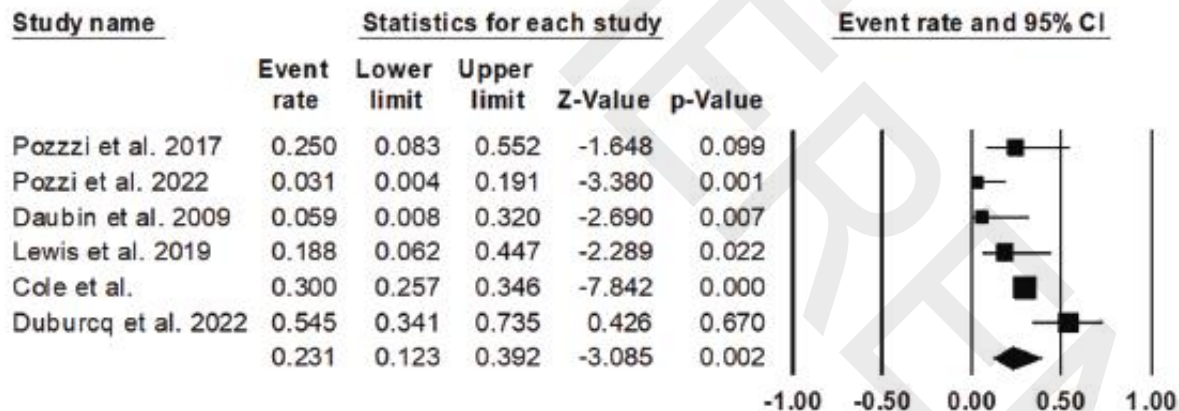
	Total	Survivors	Non-survivors	p value
Total patients, n	49	31	18	
Female, n (%)	28 (57.1%)	16 (51.6%)	12 (66.7%)	0.30
Age (year), median (Q1; Q3)	54 (38; 61)	53 (32; 61)	56.5 (45; 61)	0.25
Elixhauser score, median (Q1; Q3)	13 (5; 20)	13 (5; 21)	14 (9; 20)	0.55
Hospital stay (d), median (Q1; Q3)	11.5 (5.1; 25.6)	14.6 (10.5; 42.2)	3.1 (1.4; 6.2)	<0.01
Ventilated patients, n (%)	46 (93.9%)	28 (90.3%)	18 (100.0%)	0.17
Comorbidities, n (%)				
Depression	28 (57.1%)	19 (61.3%)	9 (50.0%)	0.44
Congestive heart failure	21 (42.9%)	14 (45.2%)	7 (38.9%)	0.67
Hypertension	19 (38.8%)	12 (38.7%)	7 (38.9%)	0.99
Complications, n (%)				
CPR after hospitalisation	13 (26.5%)	4 (12.9%)	9 (50.0%)	<0.01
Asystole	12 (24.5%)	3 (9.7%)	9 (50.0%)	<0.01
Anoxic brain damage	4 (8.2%)	*	*	0.10
Dialysis requirement	27 (55.1%)	14 (45.2%)	13 (72.2%)	0.07
ECMO duration (h), n (%)				
< 48	18 (36.7%)	*	*	
48–96	12 (24.5%)	*	*	
96–144	9 (18.4%)	*	*	
144–192	3 (6.1%)	*	*	
> 192	7 (14.3%)	*	*	
Discharge destination, n (%)				
Regular discharge	7 (22.6%)			
Rehabilitation facility	5 (16.1%)			
Transfer to another hospital	19 (61.3%)			

Meta-analysis unveiling the pivotal role of ECMO in drug overdose

Survival to discharge rate



Adverse event rate



Outcome of patients supported by ECMO for aluminum phosphide poisoning: An observational study

Comparison according to ECMO

Parameters	Conventional group (n = 30)	ECMO group (n = 15)	p Value
Average hospital stay (in days)	6.8 ± 10	16.1 ± 12.9	<0.0001
pH <7.0	8 (26.7%)	15 (100%)	–
LVEF (%)	27.2 ± 4.0	27.1 ± 2.9	0.7
Systolic blood pressure (<90 mmHg)	22	15 (100%)	–
In-hospital mortality	86.7% (26)	33.3% (5)	0.001

Comparison according to survival

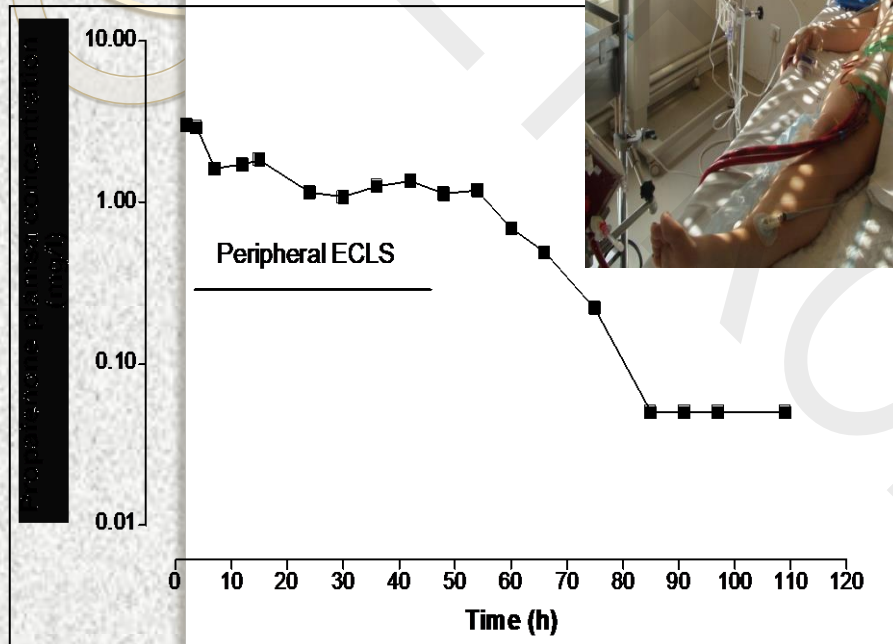
	Survivors (n = 10)	Non-survivors (n = 5)	p Value
LVEF at admission (%)	26.2 ± 4.8	19.6 ± 1.7	0.01
Delay in presentation (hours)	7.3 ± 2.6	12.0 ± 2.6	0.01
Hospital stay (days)	22.8 ± 10.3	2.6 ± 0.5	0.002
Poison exposure to ECMO (hours)	10.8 ± 4.2	15.8 ± 3.1	0.01
Admission to ECMO (hours)	3.5 ± 3.2	3.8 ± 0.8	0.2
Duration of ECMO (hours)	60 ± 35	62.4 ± 13.1	0.1

Recommendations for the use of VA-ECMO in patients with life-threatening poisoning

COR	LOE	Recommendations
2a	C-LD	1. It is reasonable to use VA-ECMO for persistent cardiogenic shock or cardiac arrest due to poisoning that is not responsive to maximal treatment measures.
2a	C-LD	2. It is reasonable to use VA-ECMO for persistent dysrhythmias due to poisoning when other treatment measures fail.
2b	C-EO	3. The effectiveness of VA-ECMO for poisoned patients with cardiovascular collapse from causes other than cardiogenic shock has not been established.

Toxicokinetics in severe poisonings requiring ECMO

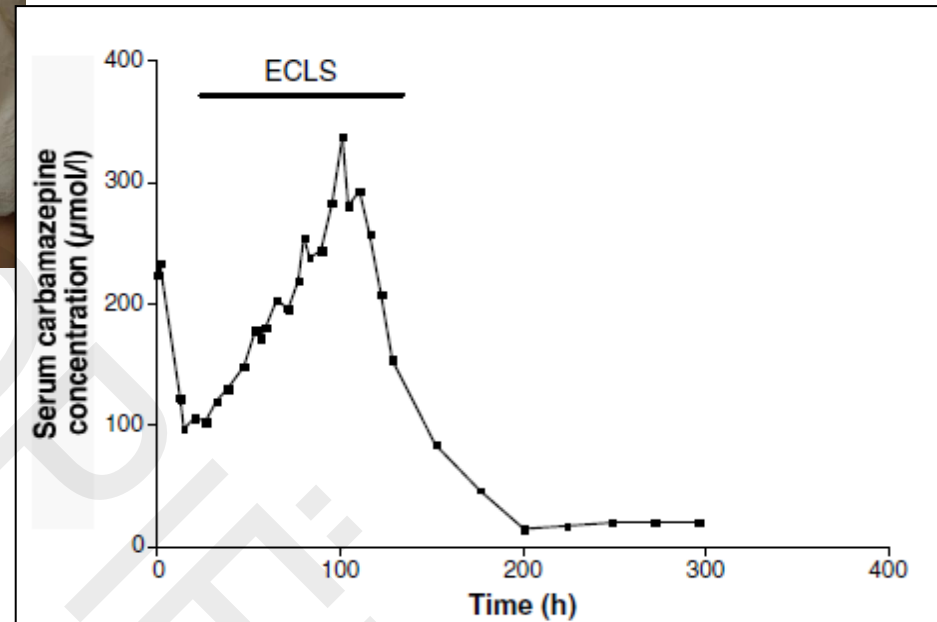
Propafenone poisoning



- $T_{1/2}$: 30 h (pharmacology: 4 h)
- V_d : 151 l/kg
- Clearance: 262 l/h



Carbamazepine poisoning

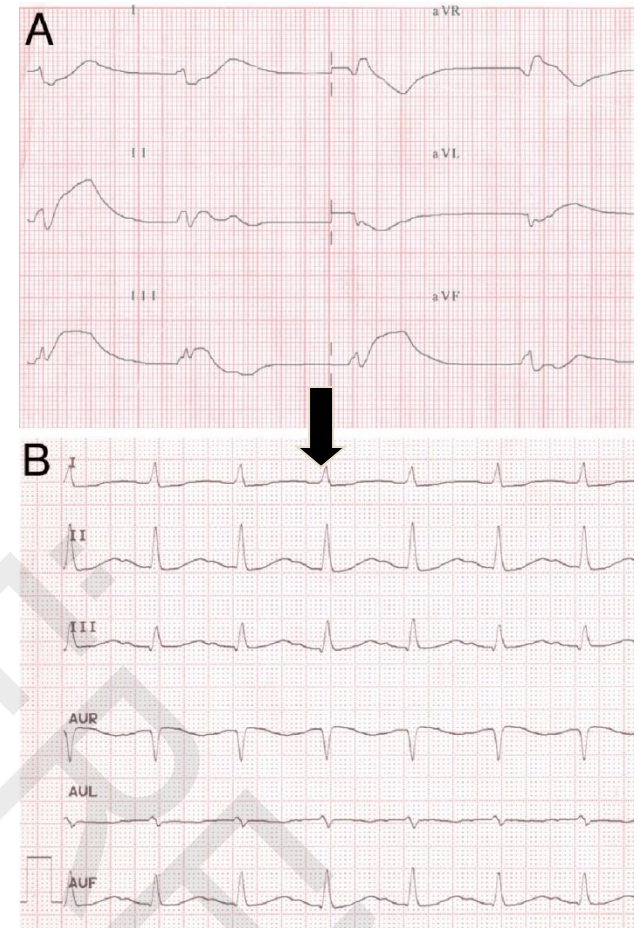


Mégarbane B. *Intensive Care Med* 2006

- Concentration on admission: 224 $\mu\text{mol/l}$
- Peak concentration: 338 $\mu\text{mol/l}$ at 101 h
- Prolonged absorption despite MDAC
- $T_{1/2}$: 22.6 h (pharmacology: 12-20 h)

Death of ECMO-treated poisoned patient

- **Death** resulted from multiorgan failure, anoxic encephalopathy or capillary leak syndrome if ECLS was performed under cardiac massage.
- Four patients presented **documented brain death**, allowing organ donation in 2 cases.
- **The heart** of one flecainide-poisoned patient was successfully transplanted, after normalization of ECG and myocardial function as well as toxicant elimination under ECLS.



Take home messages

- Shock and arrhythmias following poisonings with cardiotoxicants (especially with digitalis, sodium-channel, and calcium channel blockers) may lead to life-threatening symptoms and death.
- Adequate monitoring of severity and assessment of prognostic criteria are mandatory to improve patient management.
- Treatment is mainly supportive. Despite the absence of high-level of evidence, administration of antidotes is life-saving.
- Lipid emulsion and ECMO (cardiogenic shock) should be considered in refractory cardiovascular failure although their definitive benefit still needs to be evaluated.