Cardiopulmonary resuscitation
Drugs and drug administration routes

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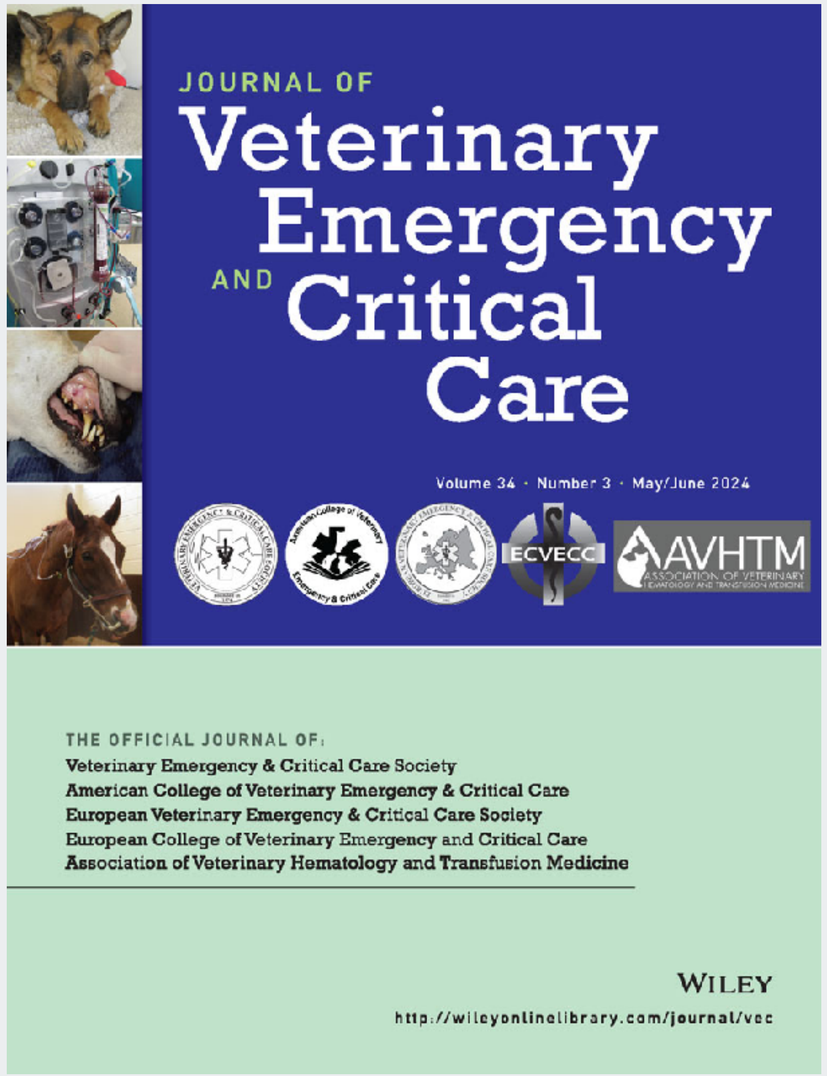
Learning objectives

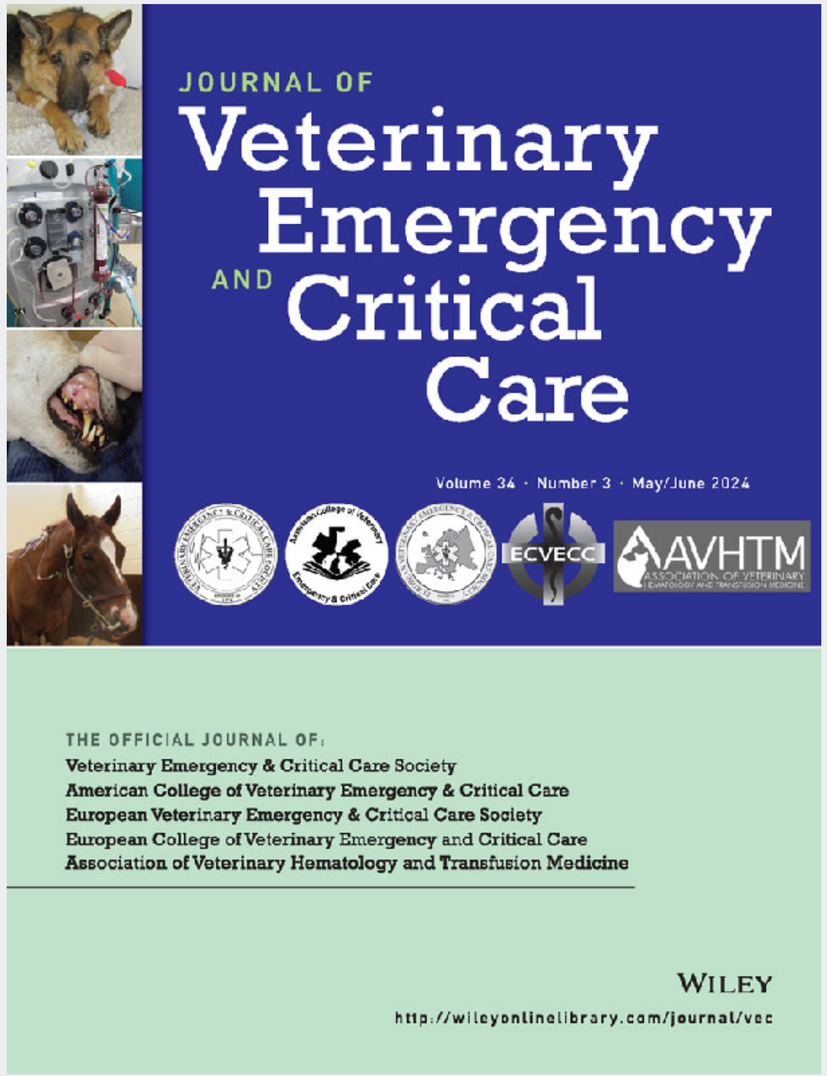
- To understand the evidence-based recommendations for CPR drug use and administration routes
- To assess the advantage and limitations of different drug administration routes in CPR
- To determine the appropriate drug selection for managing shockable and non-shockable rhythms in CPR



RECOVER
(Reassessment Campaign On Veterinary Resuscitation)

1. Evidence analysis and consensus process
2. Basic life support
3. Advanced life support
4. Monitoring
5. Updated treatment recommendations

RECOVER Journal of Veterinary Emergency and Critical Care, June 2024



We are translating into some languages

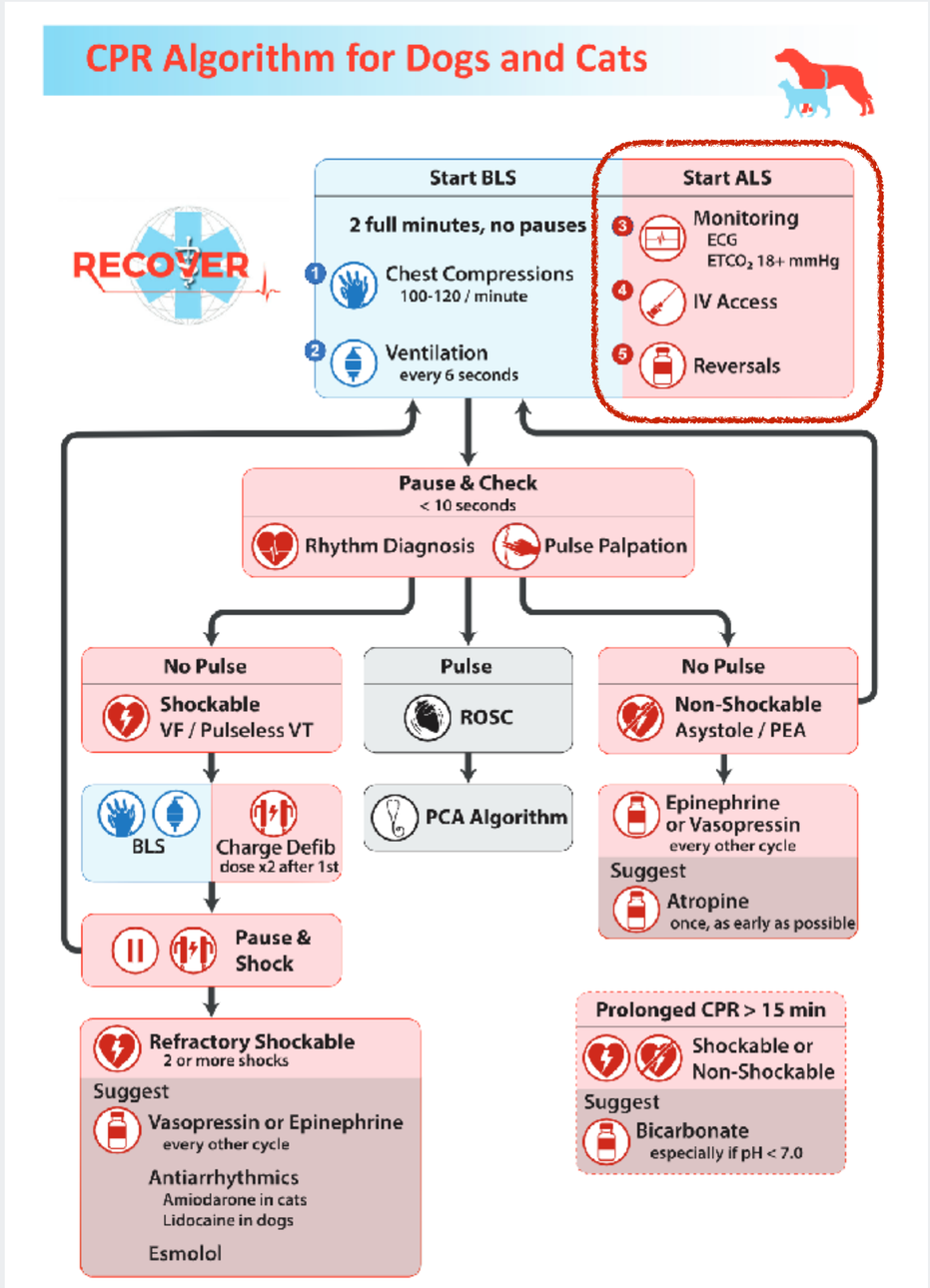
Korean

Chinese - Simplified

Chinese - Traditional

Malyasian

Japanese


CPR Algorithm for Dogs and Cats
RECOVER
Start BLS
2 full minutes, no pauses
1 Chest Compressions
100-120 / minute
2 Ventilation
every 6 seconds
Start ALS
3 Monitoring
ECG
ETCO2 18+ mmHg
4 IV Access
5 Reversals
Pause & Check
< 10 seconds
Rhythm Diagnosis
Pulse Palpation
No Pulse
Shockable
VF / Pulseless VT
BLS
Charge Defib
dose x2 after 1st
Pause & Shock
Refractory Shockable
2 or more shocks
Suggest
Vasopressin or Epinephrine
every other cycle
Antiarrhythmics
Amiodarone in cats
Lidocaine in dogs
Esmolol
Pulse
ROSC
PCA Algorithm
No Pulse
Non-Shockable
Asystole / PEA
Epinephrine
or Vasopressin
every other cycle
Suggest
Atropine
once, as early as possible
Prolonged CPR > 15 min
Shockable or
Non-Shockable
Suggest
Bicarbonate
especially if pH < 7.0

Why this drug and why this route?

- Route of drug administraiton
  - Intravenous (IV)
  - Intraosseous (IO)
  - Endotreacheal (ET)

CPR Dosing Chart for Dogs and Cats

RECOVER

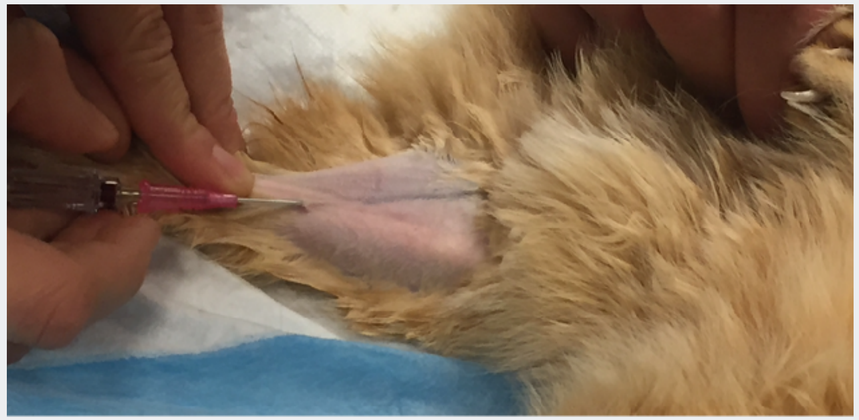
	DRUG	DOSE	Weight (kg)	2.5	5	10	15	20	25	30	35	40	45	50
			mL	mL	mL	mL	mL	mL	mL	mL	mL	mL	mL	mL
Arrest	Epinephrine (1:1000; 1mg/mL)	0.01 mg/kg		0.03	0.05	0.1	0.15	0.2	0.25	0.3	0.35	0.4	0.45	0.5
Arrest	Vasopressin (20 U/mL)	0.8 U/kg		0.1	0.2	0.4	0.6	0.8	1	1.2	1.4	1.6	1.8	2
Arrest	Atropine (0.4 - 0.54 mg/mL)	~ 0.05 mg/kg		0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Anti-Arrhythmic	Amiodarone (50 mg/mL)	5 mg/kg		0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Anti-Arrhythmic	Lidocaine (20 mg/mL)	2 mg/kg		0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Anti-Arrhythmic	Esmolol* (10 mg/mL)	0.5 mg/kg		0.13	0.25	0.5	0.75	1	1.3	1.5	1.8	2	2.3	2.5
Reversal	Naloxone (0.4 mg/mL)	0.04 mg/kg		0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Flumazenil (0.1 mg/mL)	0.01 mg/kg		0.25	0.5	1	1.5	2	2.5	3	3.5	4	4.5	5
Reversal	Atipamezole (5 mg/mL)	100 µg/kg		0.06	0.1	0.2	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1
Monophasic Defibrillation	External Defib (J)	4 - 6 J/kg		10 J	20 J	40 J	60 J	80 J	100 J	120 J	140 J	160 J	180 J	200 J
Monophasic Defibrillation	Internal Defib (J)	0.5 - 1 J/kg		2 J	3 J	5 J	8 J	10 J	15 J	15 J	20 J	20	20 J	25 J
			Weight (kg)	2.5	5	10	15	20	25	30	35	40	45	50

*Administer esmolol 0.5 mg/kg IV or IO over 3-5 minutes followed by a CRI at 50 mcg/kg/min

Venous access - IV catheter

- IV administration provides rapid and predictable drug delivery
  - Achieve higher drug concentration compared to IO or ET route

- Place an IV catheter close to the heart
  - Cephalic vein
  - Jugular vein
  - Saphenous vein



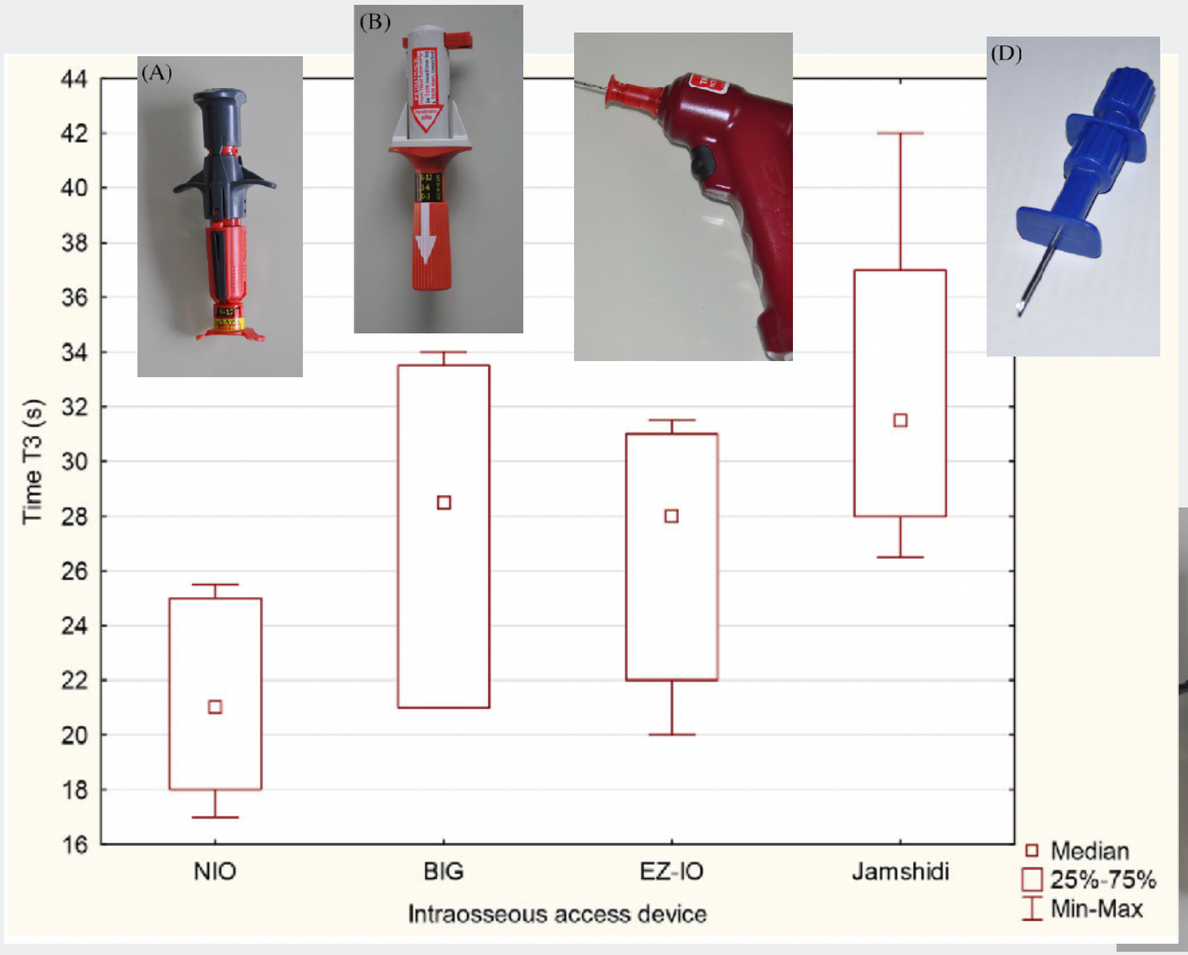
Venous access - IO catheter

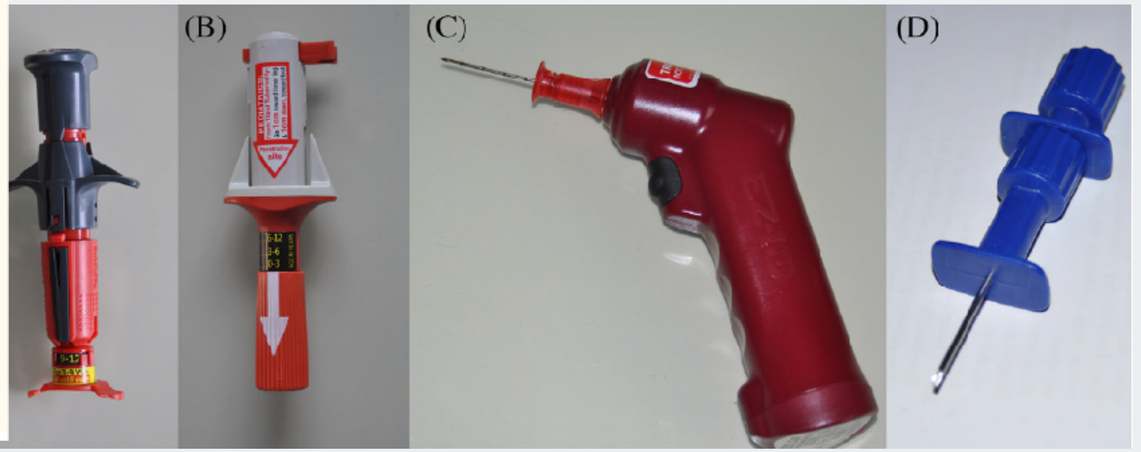
- IO catheter placement

Courtesy of Dr. Bernie Hansen

IO access using different devices

- Faster to achieve IO access using automated devices





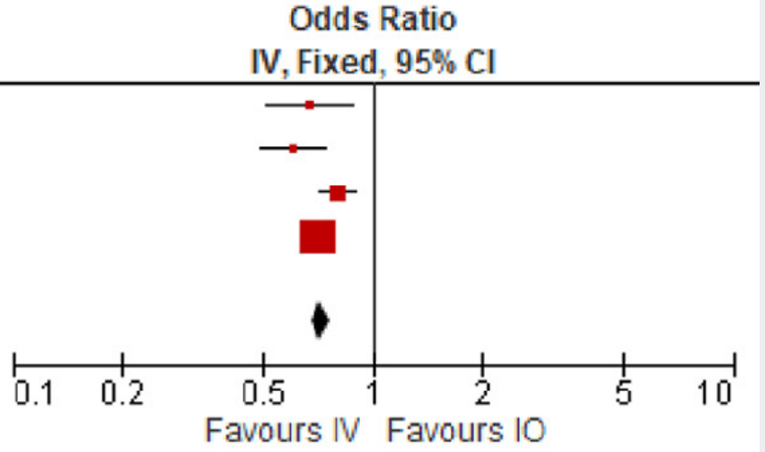
IV vs IO administration?

- ROSC, survival to discharge, and neurological outcome
  - IV administration is slightly superior to IO
  - Depends on types of drugs (reduced efficacy of certain drugs)
  - Depends on the IO site (humerus > Tibia)

ROSC

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Fixed, 95% CI
Feinstein 2017	-0.405	0.143	3.9%	0.67 [0.50, 0.88]
Kawano 2017	-0.5108	0.1043	7.3%	0.60 [0.49, 0.74]
Mody 2019	-0.225	0.057	24.4%	0.80 [0.71, 0.89]
Zhang 2020	-0.3481	0.0351	64.4%	0.71 [0.66, 0.76]
Total (95% CI)			**100.0%**	**0.72 [0.68, 0.76]**

Heterogeneity: Chi² = 6.93, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 11.79 (P < 0.00001)



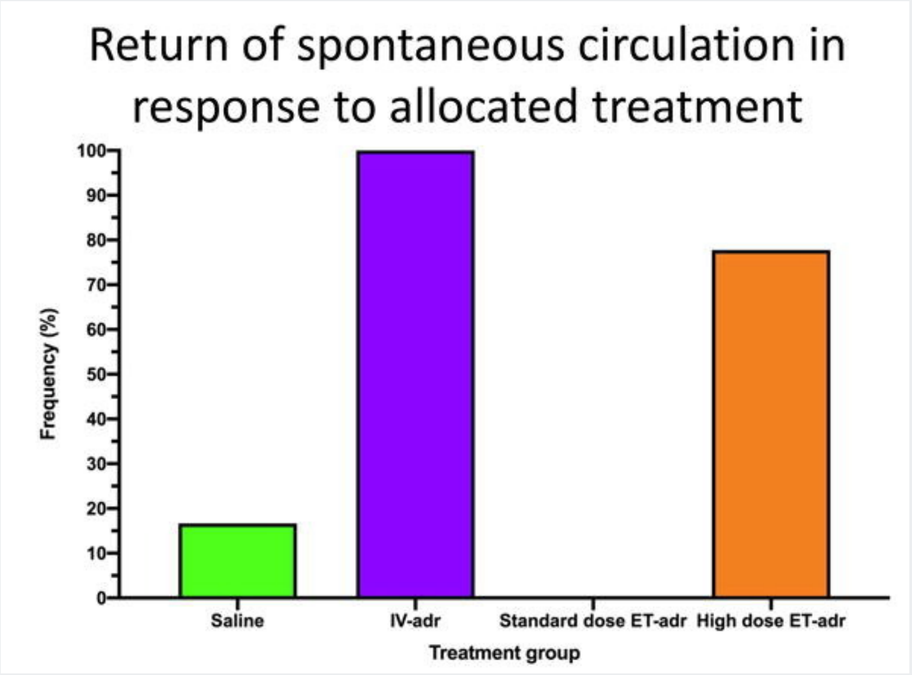
Grandfeldt A et al.

IV vs IO administration?

- Recommend IO if IV access is not obtained within 2 minutes
- If both IV and IO are available, IV administration is preferred
- This may also depend on types of drugs
  - Certain drugs (e.g., amiodarone, lidocaine) may have reduced efficacy when given IO compared to IV

Endotracheal administration

- Used only as a last resort when IV and IO access are not available
  - Unpredictable absorption
    - Prolonged time to achieve effective drug concentration
    - Need drug dose adjustment
    - Limited drug suitability
      - NAVEL:
        - Naloxone
        - Atropine
        - Vasopressin
        - Epinephrine
        - Lidocaine



Polglase GR et al. Resuscitation 2024

Endotracheal administration - procedure

1. Give at 2 - 3 times the standard IV dose

2. Dilute the drug in 3 - 10 mL of saline or sterile water
    - Improve absorption and spread within the lungs

3. Inject the solution through red rubber tube inserted into trachea

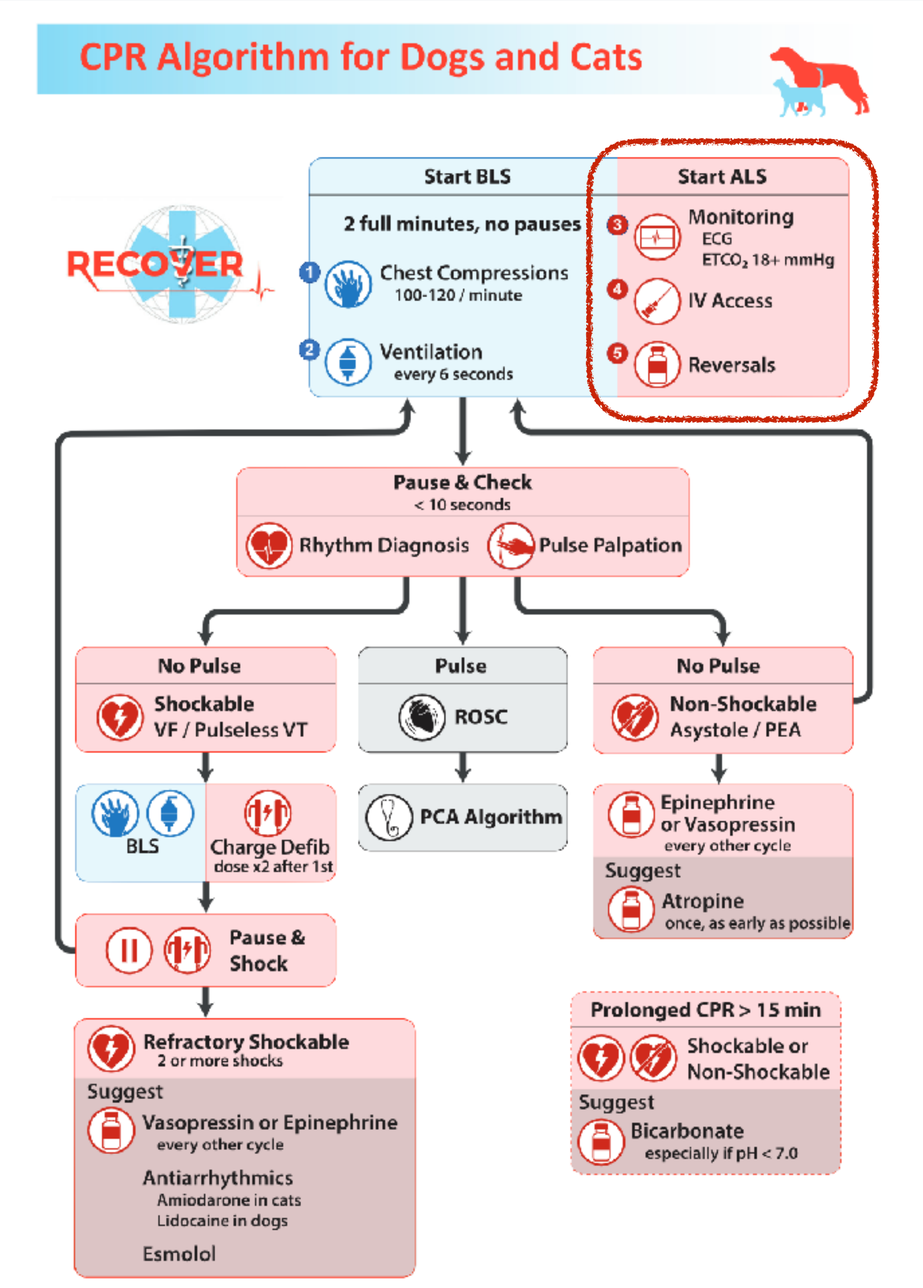
4. Follow with several positive pressure ventilations to disperse the drug into the lungs

Route for drug administration - Summary

- IV access is considered the gold standard
- IO administration is recommended alternative
  - If IV access is not successful within 2 minutes
- Endotracheal (ET) administration is an option
  - Less effective compared to IV and IO administration

Which drug? Why this drug?

- Reversals
- IV fluids
- Others
  - Calcium gluconate
  - NaHCO3
  - Dextrose



CPR drugs - reversals

Naloxone
0.04 mg/kg IV, IO

Opioid
Reversal

Flumazenil
0.01 mg/kg IV, IO

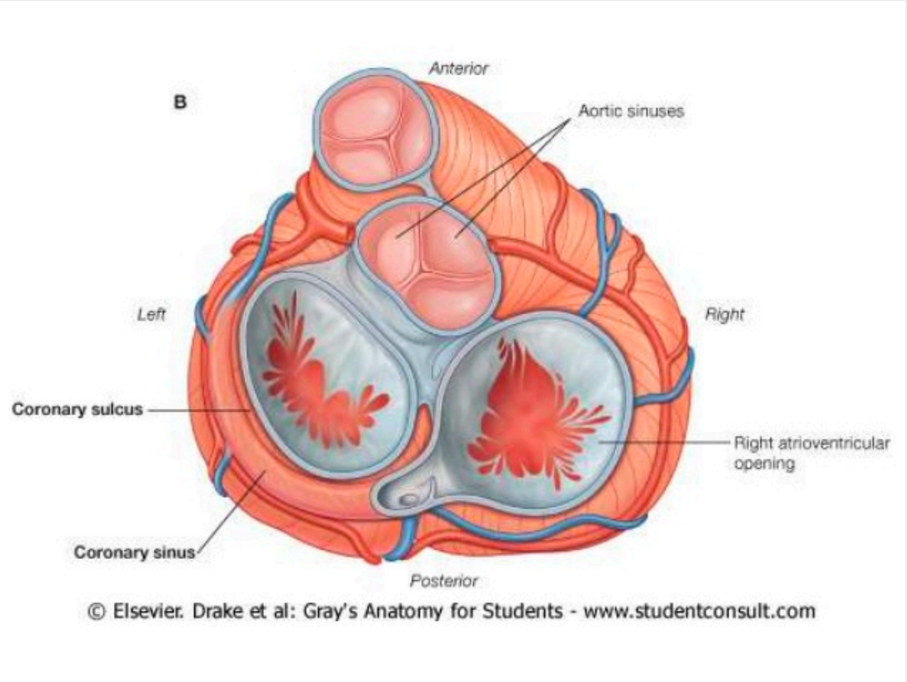
Benzodiazepine
Reversal

Atipamezole
0.1 mg/kg IV, IO

Alpha-2 agonist
Reversal

CPR drugs - IV fluids

- Coronary perfusion = Aortic pressure during diastole - right atrial pressure
  - Decreased coronary perfusion
    - Hypovolemia (↓Aortic pressure during diastole)
    - Hypervolemia (↑right atrial pressure)



CPR drugs - IV fluids

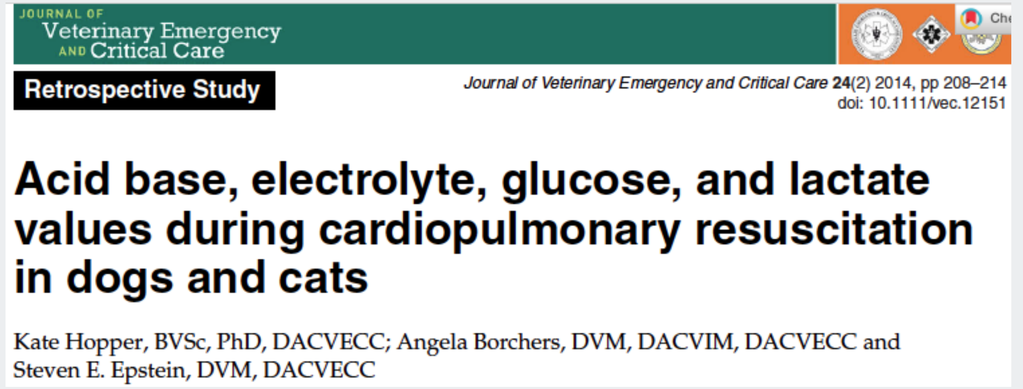
- Fluid administration to animals with:
  - Hypovolemia
  - Out-of-hospital CPA

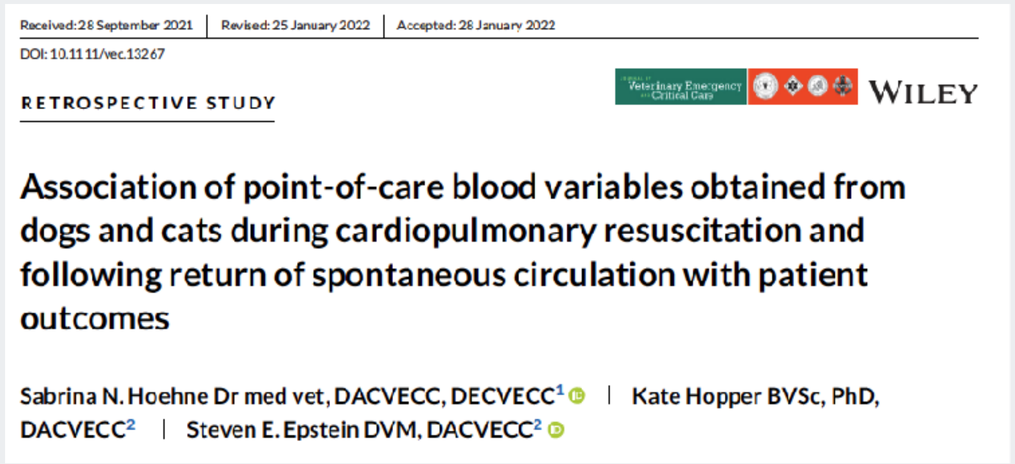
- No fluid administration to animals with
  - Normovolemia/hypervolemia
  - In-hospital CPA

CPR drugs - others

- **Common abnormalities in blood tests during CPR**
  - Metabolic acidosis (100%)
  - Hyperkalemia (65%)
  - Hyperglycemia (62%)
  - Hypoglycemia (21%)
  - Ionized hypocalcemia (18%)

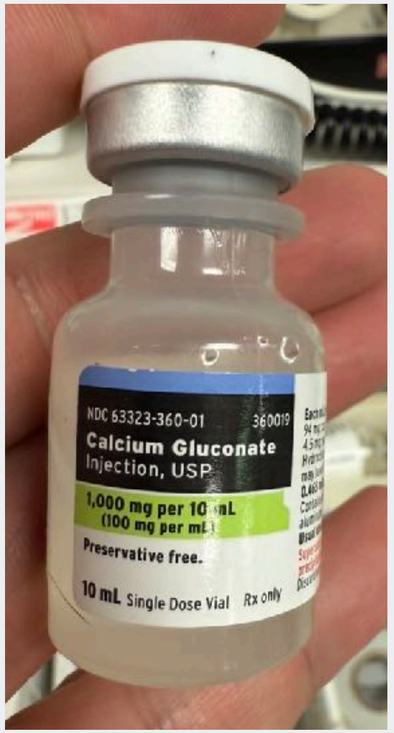
- **Abnormalities associated with outcomes**
  - PvO2 (ROSC)
  - Standard BE (ROSC)
  - Potassium (survival to discharge)
  - Chloride concentration (survival to discharge)

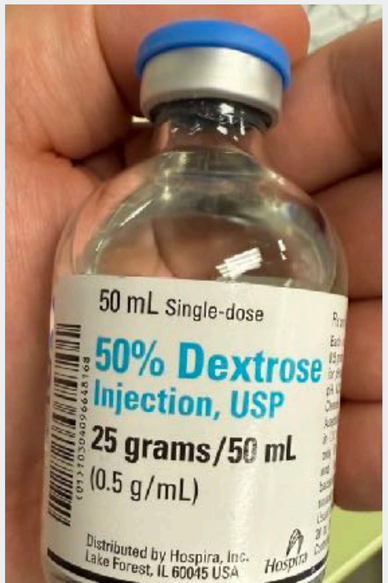




CPR drugs - others

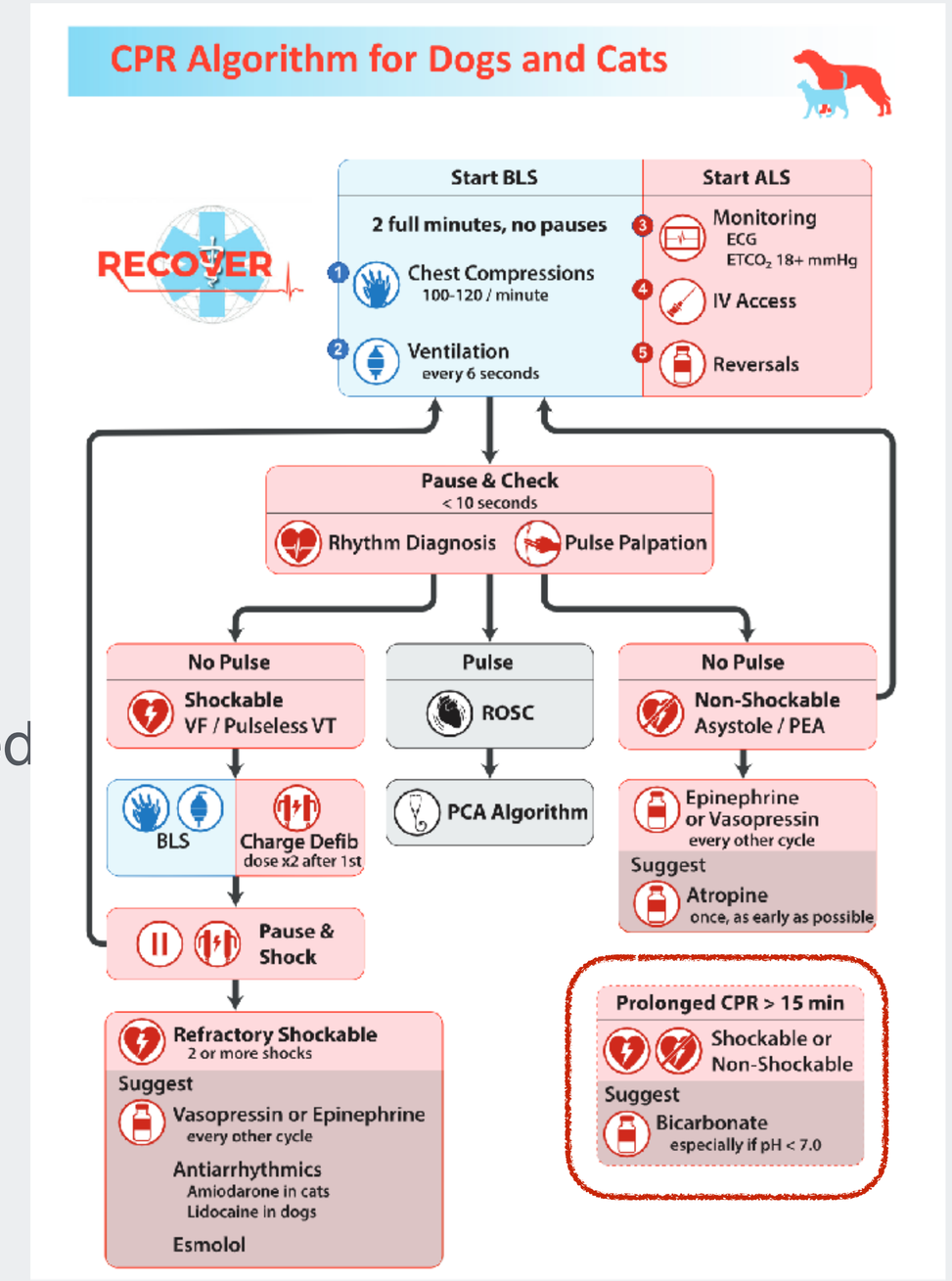
- **Hypocalcemia (venous iCa2+ < 0.8 mmol/L)**
  - Calcium gluconate: 50 mg/kg IV or IO over 2 - 5 minutes
- **Hyperkalemia (confirmed or suspected) (venous K+ > 7.5 mEq/L)**
  - Calcium gluconate: 50 mg/kg IV or IO over 2 - 5 minutes
  - NaHCO3: 1 mEq/kg IV or IO if (K+ > 7.5 mEq/L and pH < 7.2)
- **Hypoglycemia (confirmed or suspected)**
  - 50% Dextrose: 0.5 ml/kg IV or IO





CPR drugs - others

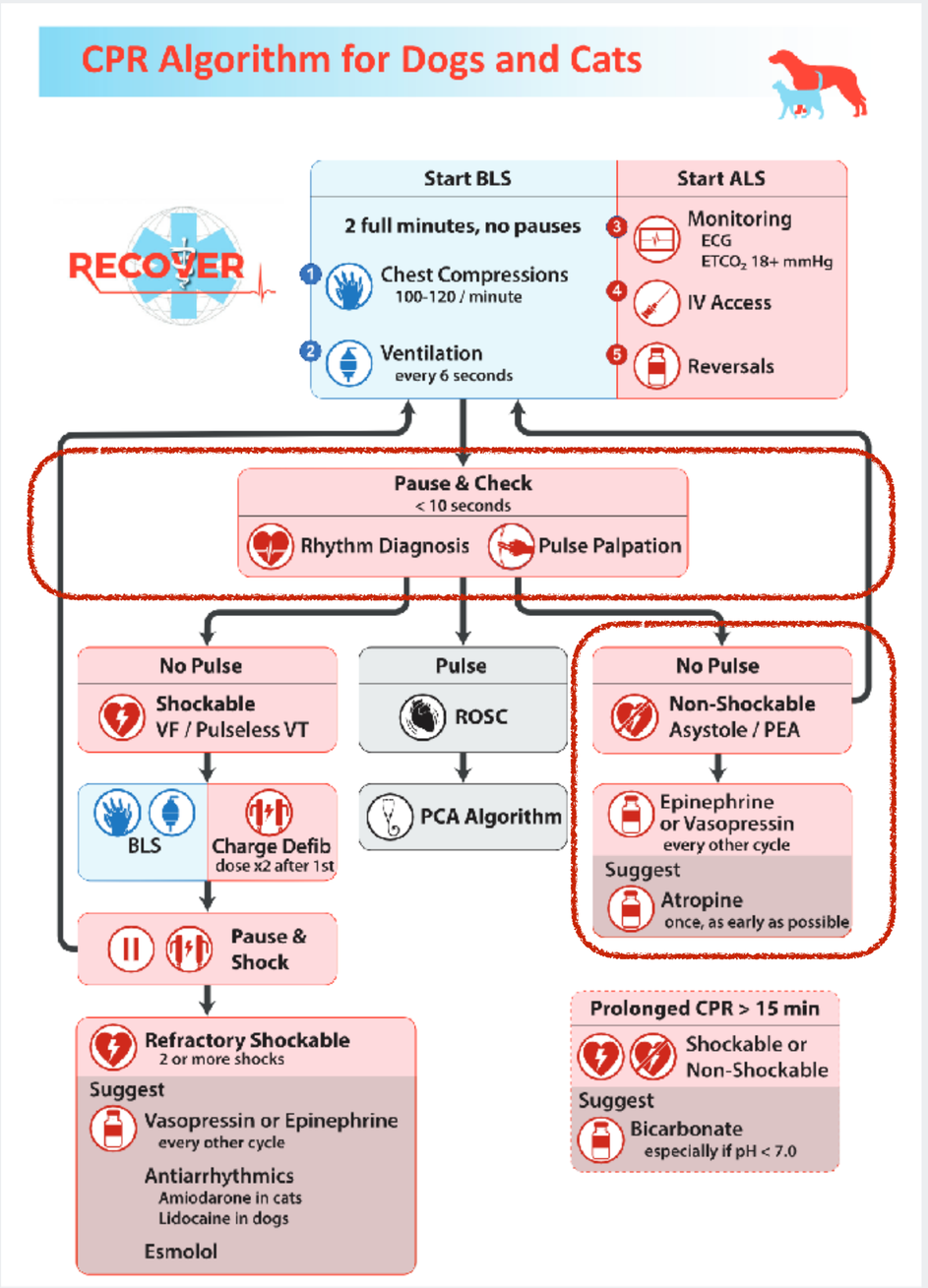
- **Prolonged CPR (longer than 10 - 15 minutes)**
  - Sodium bicarbonate (if pH < 7.0)
    - Corrects metabolic acidosis
  - Potential side effects: routine use not recommended
    - Hypernatremia
    - Hyperosmolality
    - Paradoxical intracellular acidosis
    - Increased CO2 production
    - Reduced tissue oxygen release



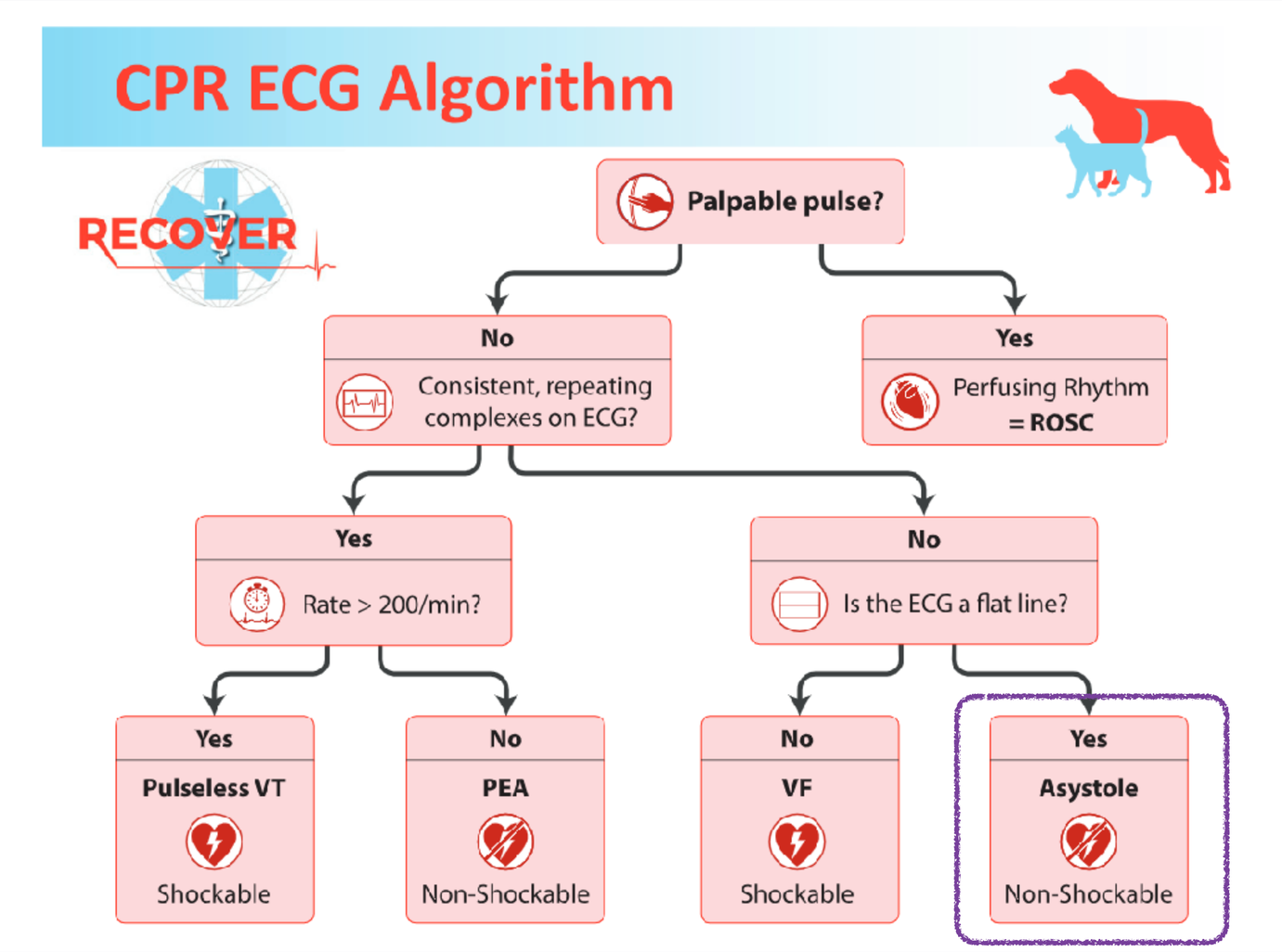
Which drug? Why this drug?

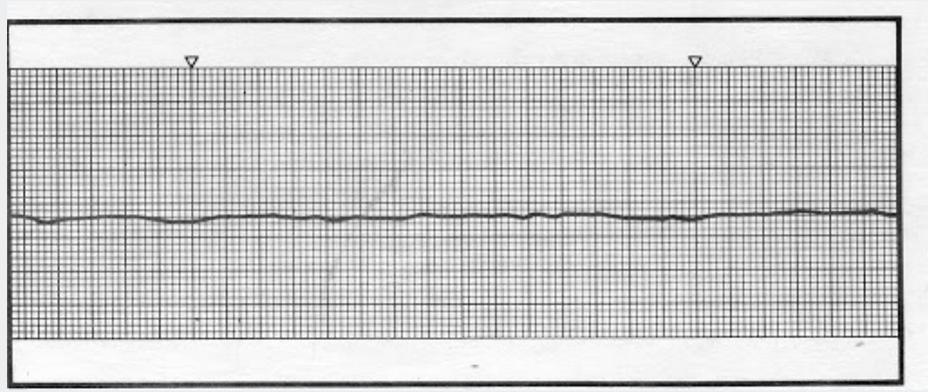
- Non-shockable rhythm
  - Low or high dose of epinephrine
  - Epinephrine vs vasopressin
  - Atropine
  - Corticosteroids

- Shockable rhythm?
  - Epinephrine or vasopressin?
  - Esmolol?
  - Lidocaine or amiodarone?



Simple CPR ECG Algorithm





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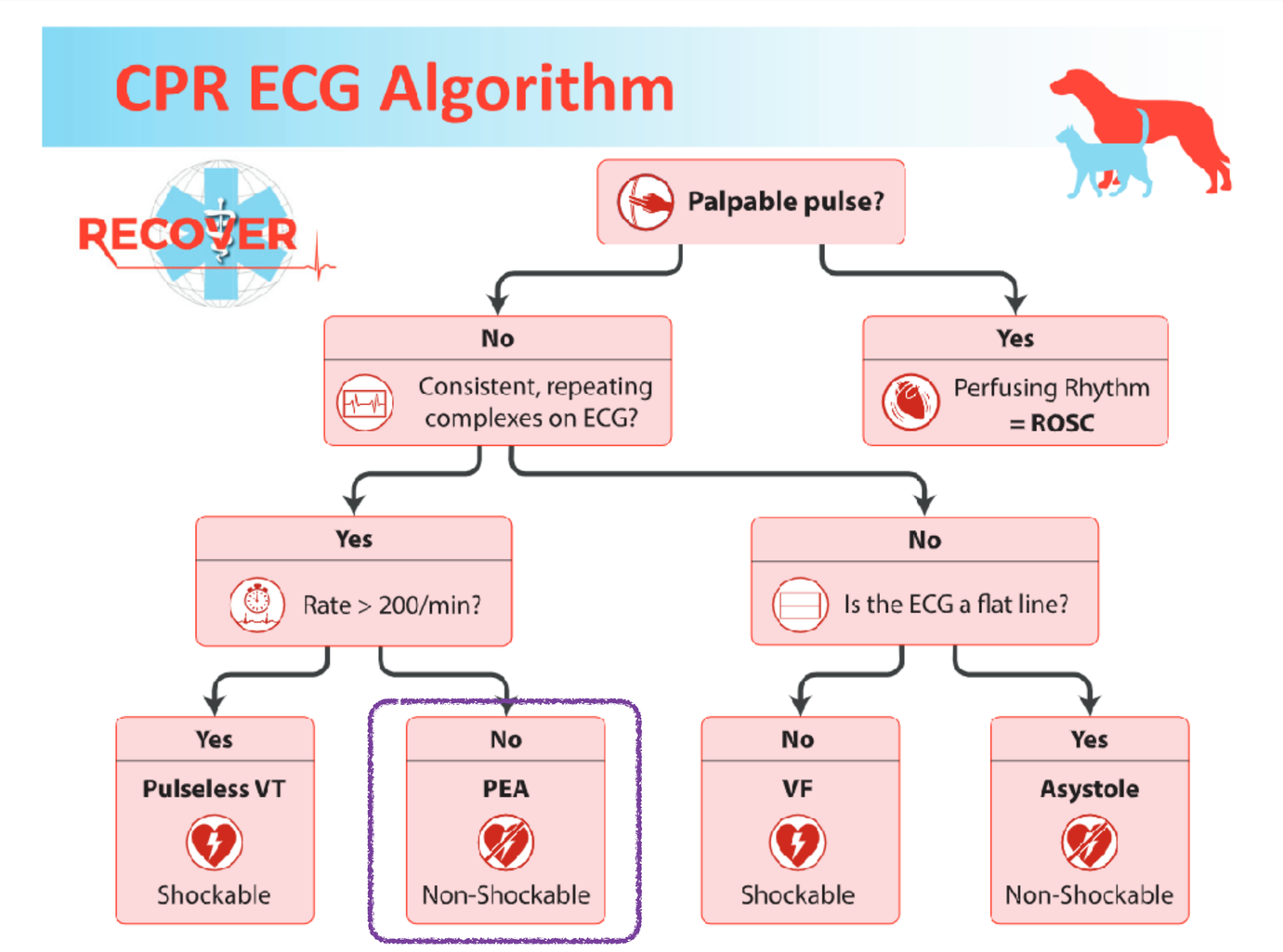
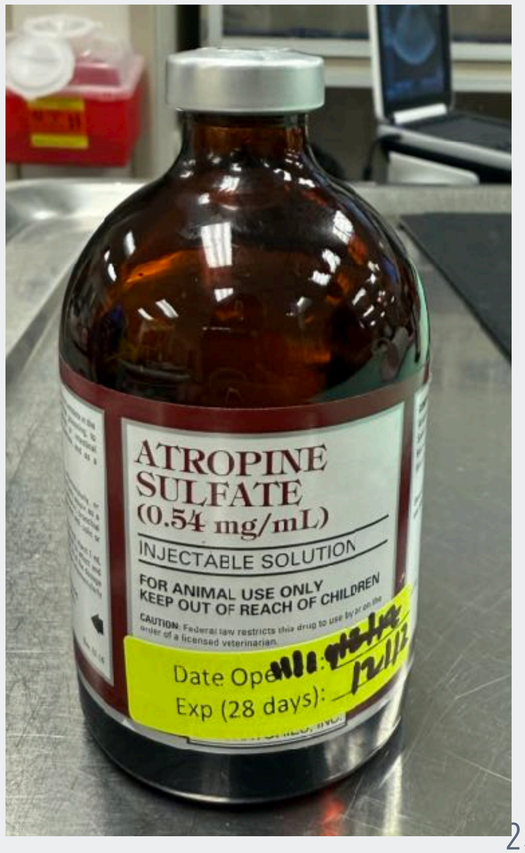
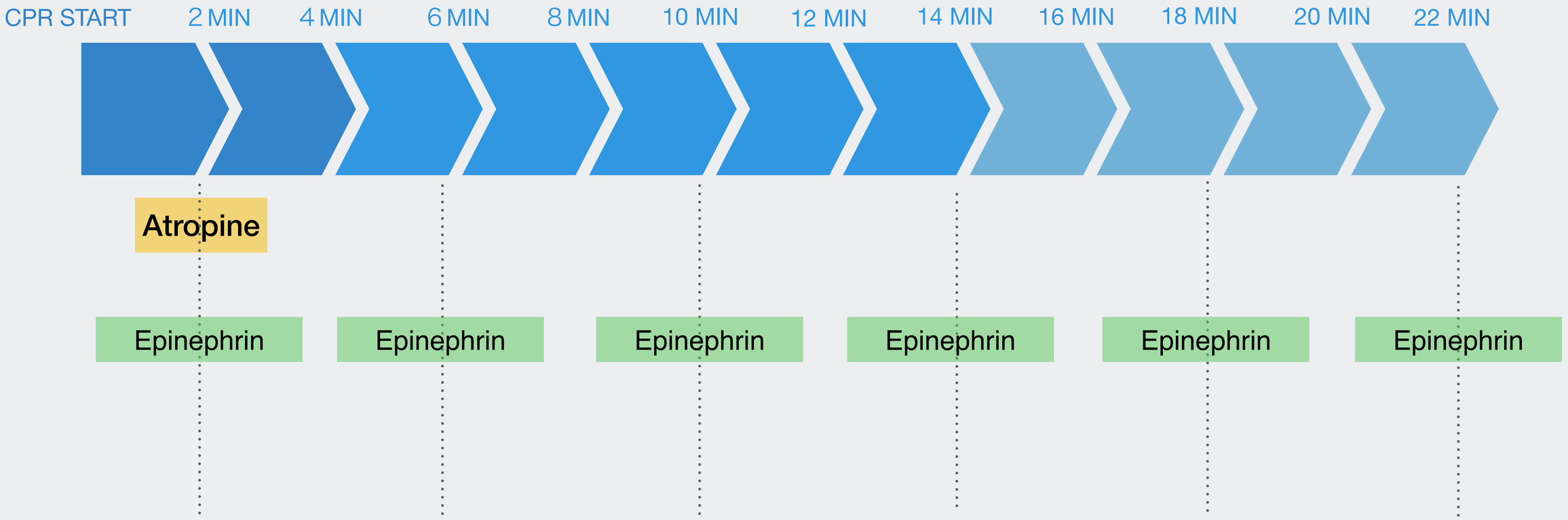


Rate = 40 /min

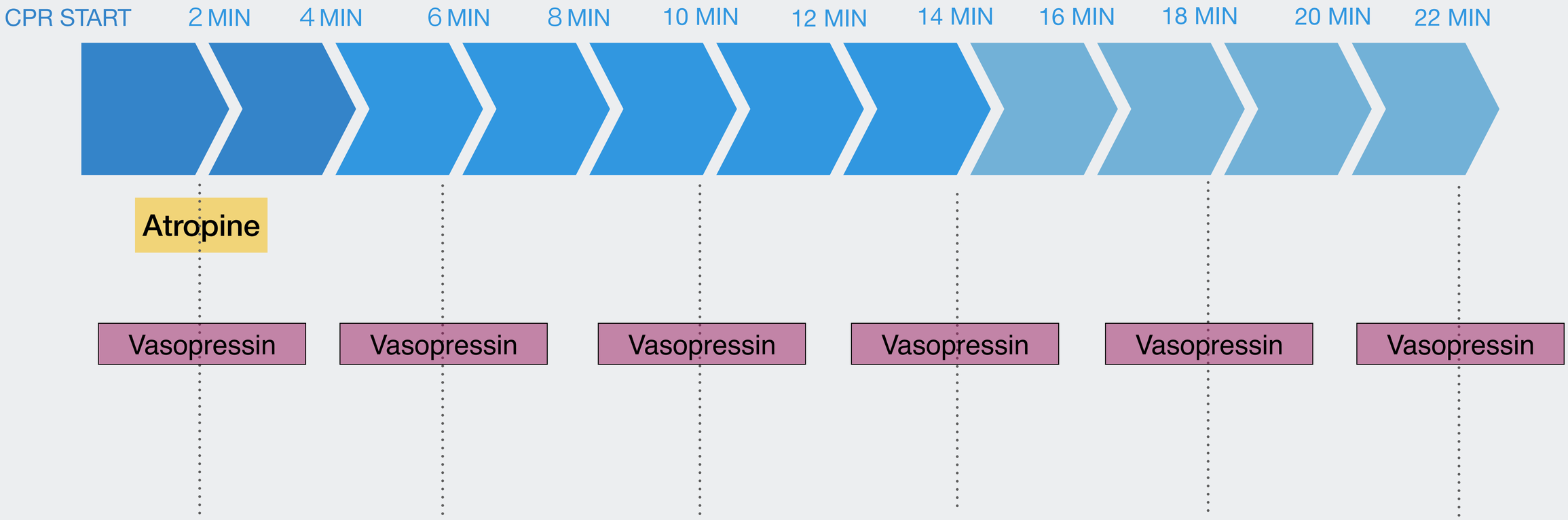
Non-shockable rhythm - drugs

- Drugs for non-shockable rhythm
  - **Epinephrine (or vasopressin)**
    - Low dose (0.01 mg/kg)
    - Every 3 - 5 min (every other cycle)
  - **Atropine**
    - Once
    - Reasonable with high vagal tone





Atropine	Epinephrine	Vasopressin
0.04 mg/kg IV, IO 0.08～0.4 mg/kg IT	0.01 mg/kg IV, IO 0.02～0.1 mg/kg IT	0.8 U/kg IV, IO 1.6 - 8 U/kg IT



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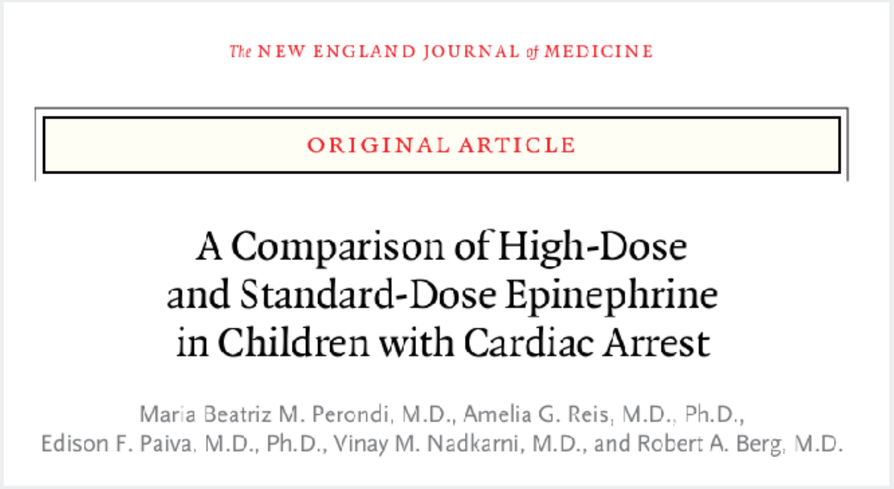
Epinephrine for non-shockable rhythm

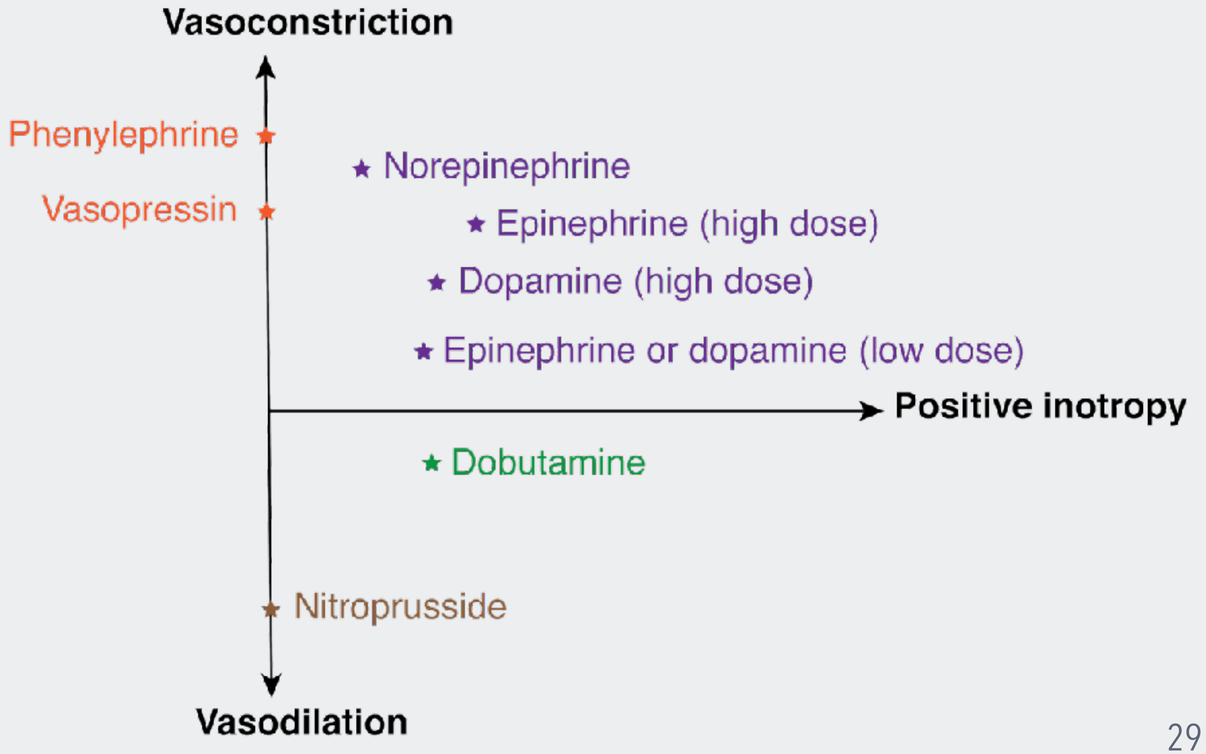
- **Alpha-1 adrenergic effects**
  - Increases aortic diastolic pressure and coronary perfusion pressure
- **Beta-1 adrenergic effects**
  - Increases the risk of recurrent arrhythmias
  - May worsen post-resuscitation myocardial dysfunction

Study	Year	ROSC	Survival to discharge	Neurology outcome
Stiell IG et al	2004	+	+/-	
Ong ME et al.	2007		+/-	
Olasveengen TM et al.	2009	+	+/-	
Jacobs IG et al.	2011	+	+/-	
Hagihara A te al.	2012	+	+/-	
Nakahara S et al.	2013			+/-
Sanghavi P et al.	2015		-	
PARAMEDIC-2	2018	+	+	-

High vs low dose epinephrine

- **High dose epinephrine (beta 1 > alpha 1): Not recommended anymore**
  - Increases the risk of recurrent arrhythmias
  - May worsen post-CPA myocardial dysfunction
  - May improve initial ROSC
  - May worsen neurological outcome

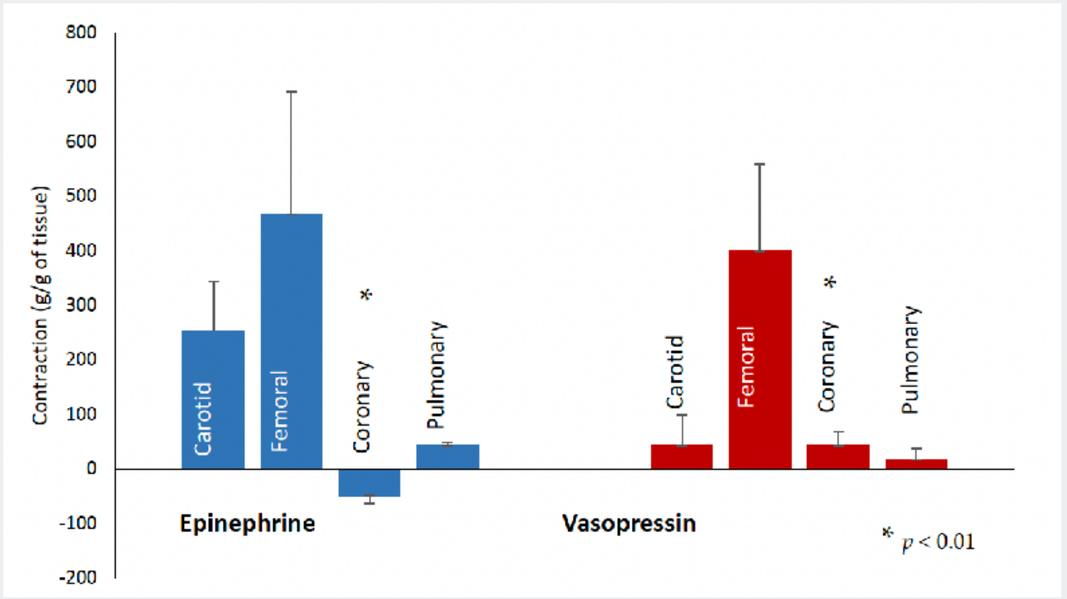




Epinephrine vs vasopressin

- Vasopressin is a vasopressin (V1) receptor agonist that causes non-adrenergic vasoconstriction

- Higher ROSC and survival with epinephrine than vasopressin
  - Vasodilation of coronary artery with epinephrine

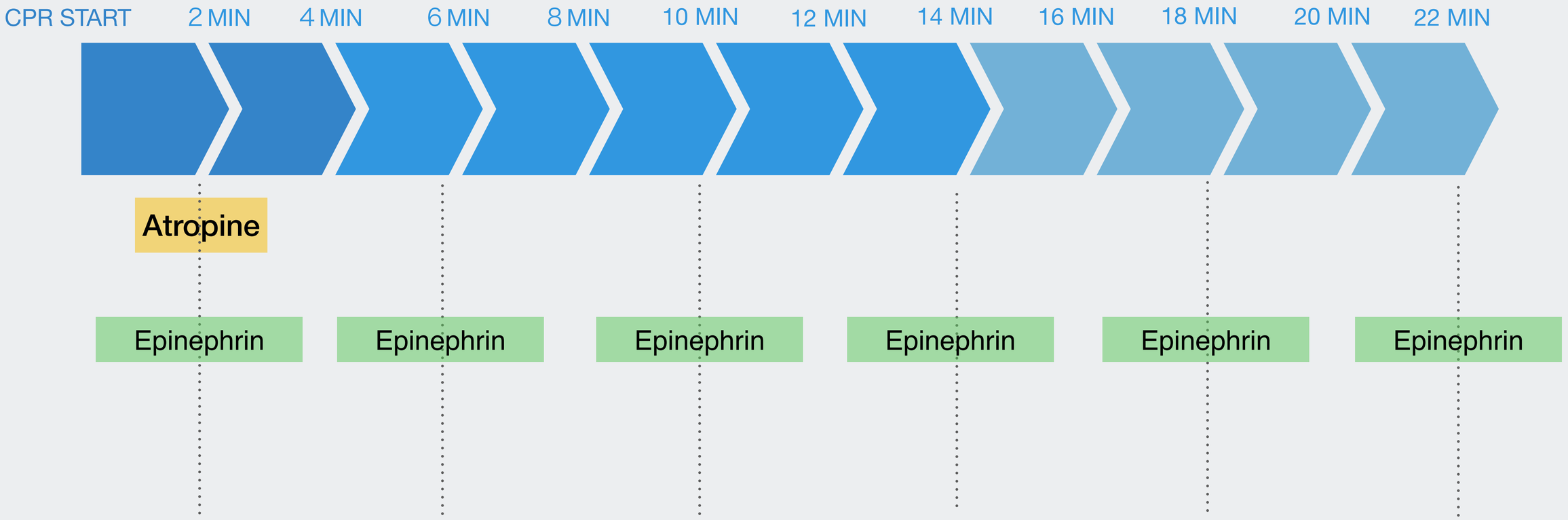


Rawat M et al. Children

Vasopressors - Summary

- Epinephrine is still the first-line drug for non-shockable rhythms
  - Low dose (standard dose) of epinephrine
  - No high dose epinephrine

- Vasopressin may be preferable in some cases
  - Low pH
  - Refractory shockable rhythm



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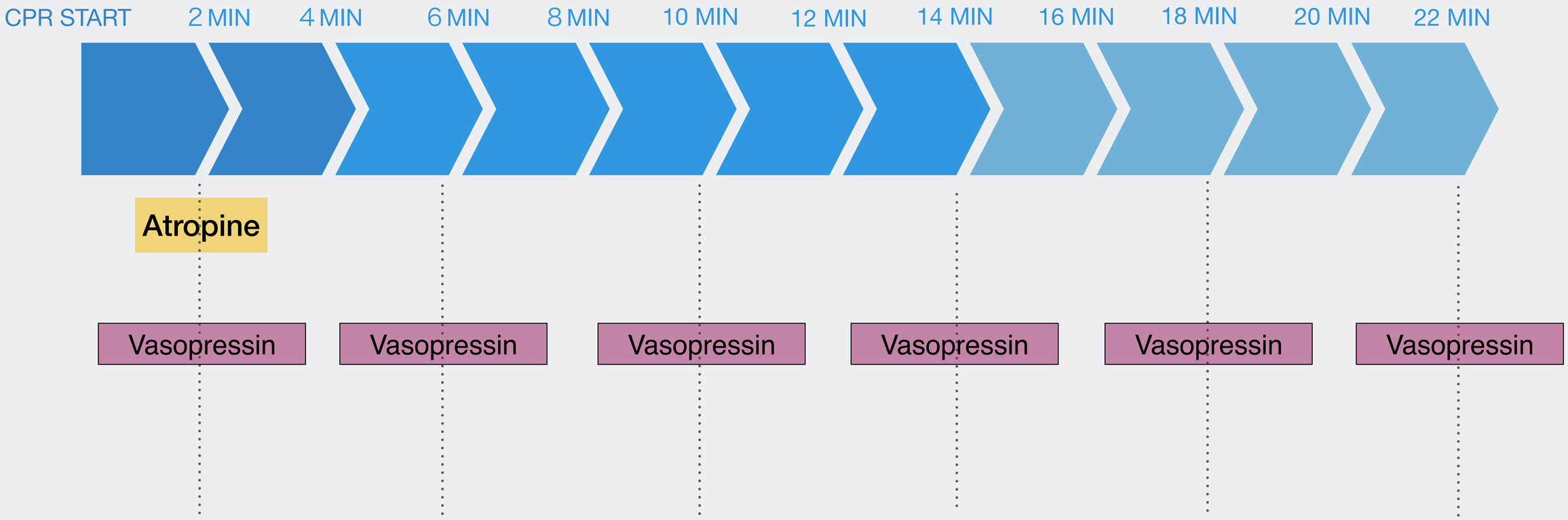

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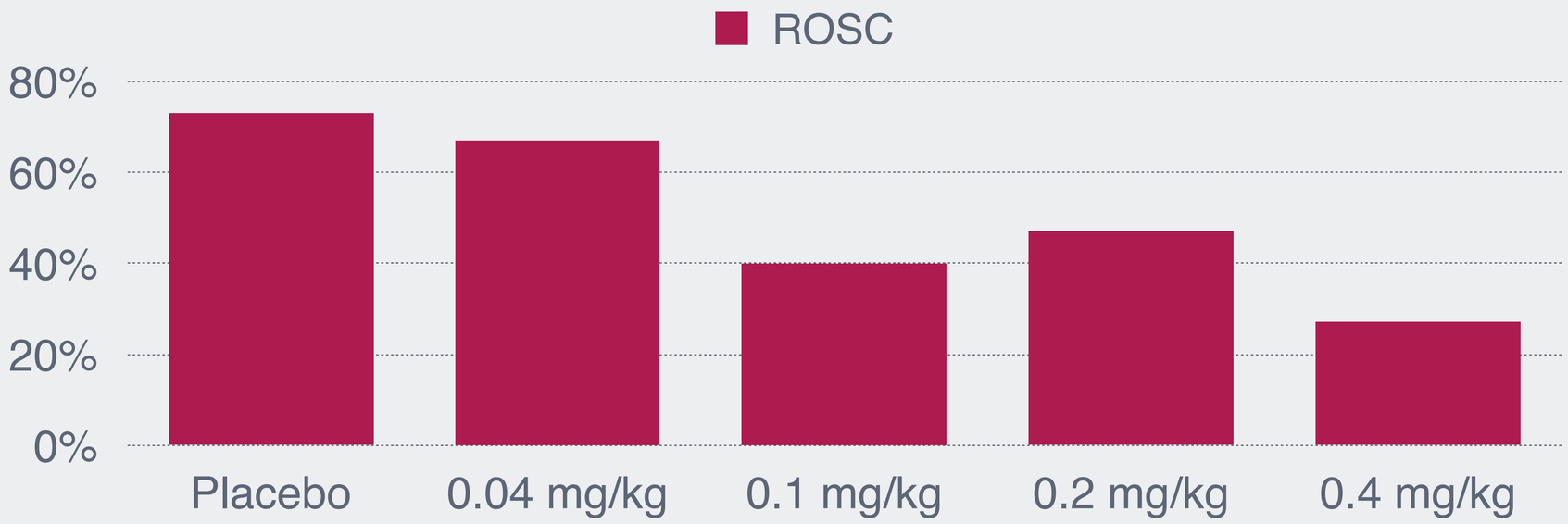
Atropine

- **Parasympatholytic agent (muscarinic receptor antagonist)**
  - Reduce vagal-mediated bradycardia
  - Increased heart rate
  - Enhanced AV node conduction
- Given for animals with asystole and PEA
  - To treat high vagal tone-induced cardiac arrest

Atropine

- Lack of evidence of benefit in non-shockable rhythms in human patients
  - No ROSC rate difference in dogs with asphyxial canine cardiac arrest model

- High atropine have been associated with worse outcomes during CPR in dogs



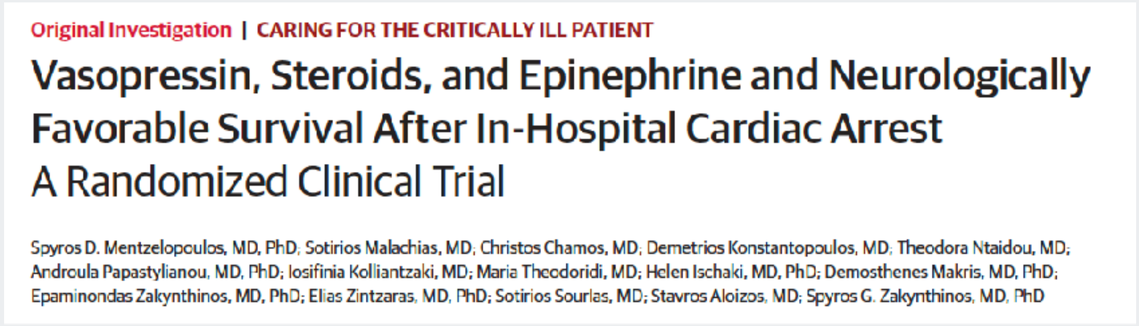
DeBehnke DJ et al. Academic Emergency Medicine 1995

Glucocorticoids in CPR

- Routine administration of glucocorticoids during CPR is NOT recommended

- May be considered in animals with
  - Vasopressor-resistant hypotension
  - Suspected hypoadrenocorticism

- Vasopressin-Steroids-Epinephrine (VSE) therapy for in-hospital CPR?
  - Improved survival and neurological outcome



Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

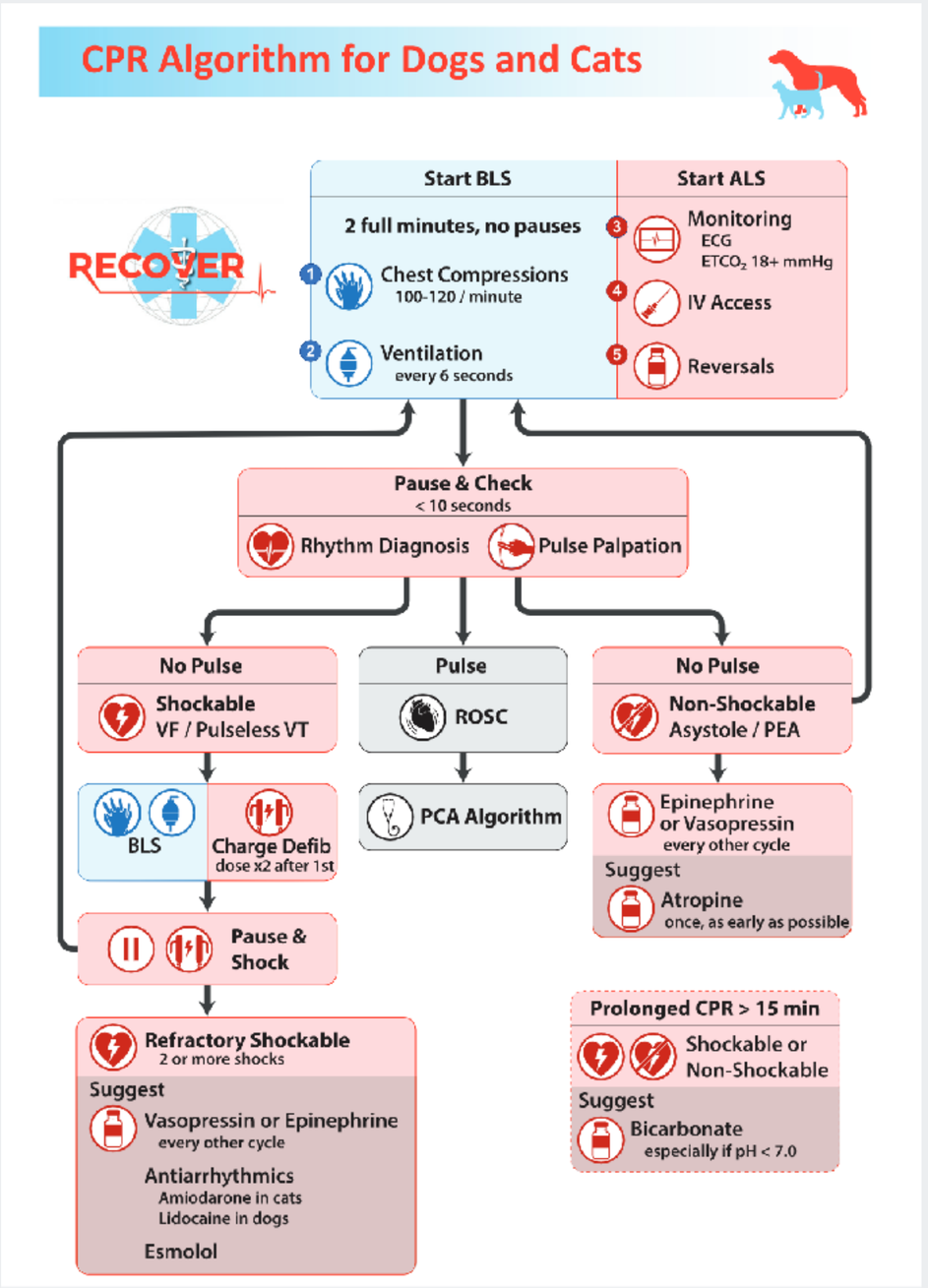
Vasopressin, Steroids, and Epinephrine and Neurologically Favorable Survival After In-Hospital Cardiac Arrest
A Randomized Clinical Trial

Spyros D. Mentzelopoulos, MD, PhD; Sotirios Malachias, MD; Christos Chamos, MD; Demetrios Konstantopoulos, MD; Theodora Ntaidou, MD; Androula Papastylianou, MD, PhD; Iosifinia Kolliantzaki, MD; Maria Theodoridi, MD; Helen Ischaki, MD, PhD; Demosthenes Makris, MD, PhD; Epaminondas Zakynthinos, MD, PhD; Elias Zintzaras, MD, PhD; Sotirios Sourlas, MD; Stavros Aloizos, MD; Spyros G. Zakynthinos, MD, PhD

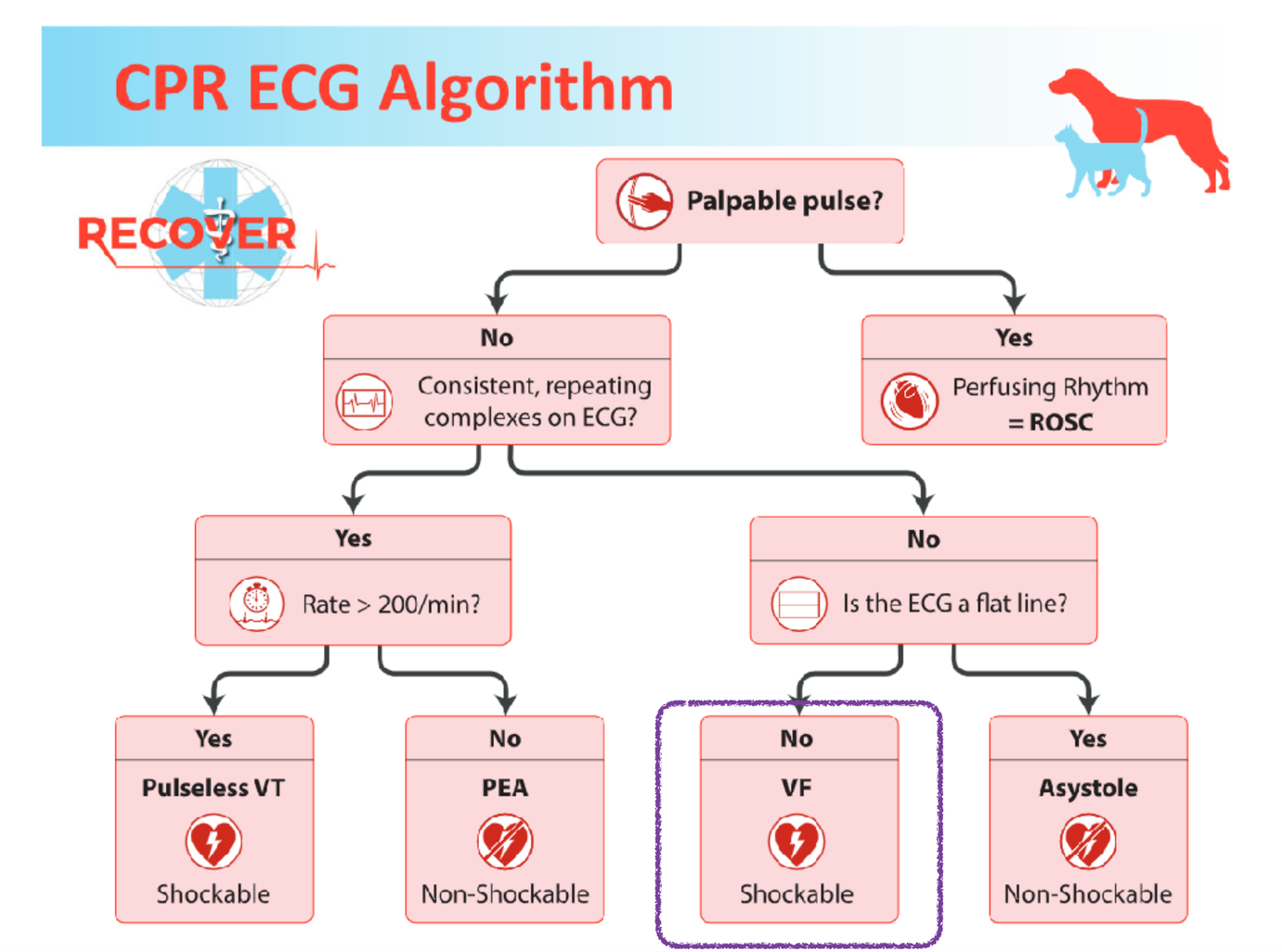
Why this drug?

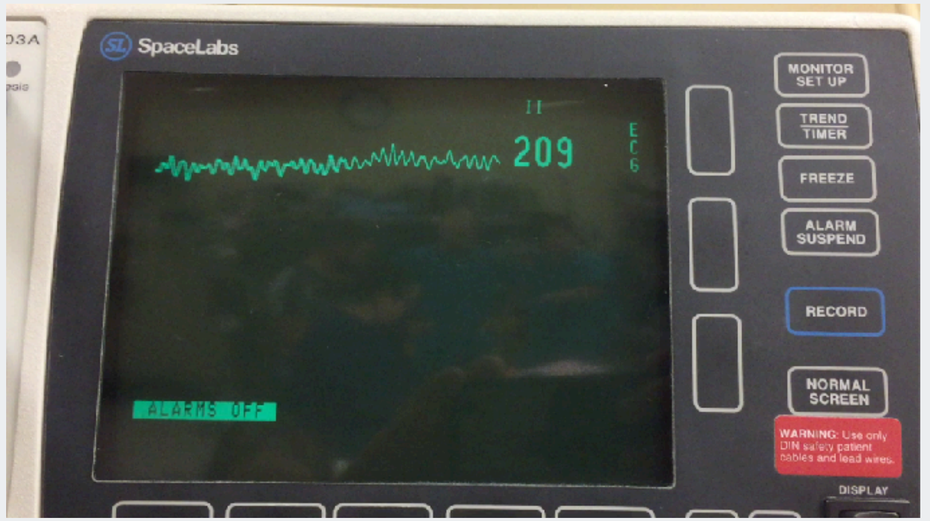
- Non shockable rhythm
  - Low or high dose of epinephrine
  - Epinephrine vs vasopressin
  - Atropine
  - Corticosteroids

- Shockable rhythm?
  - Epinephrine or vasopressin?
  - Esmolol?
  - Lidocaine or amiodarone?

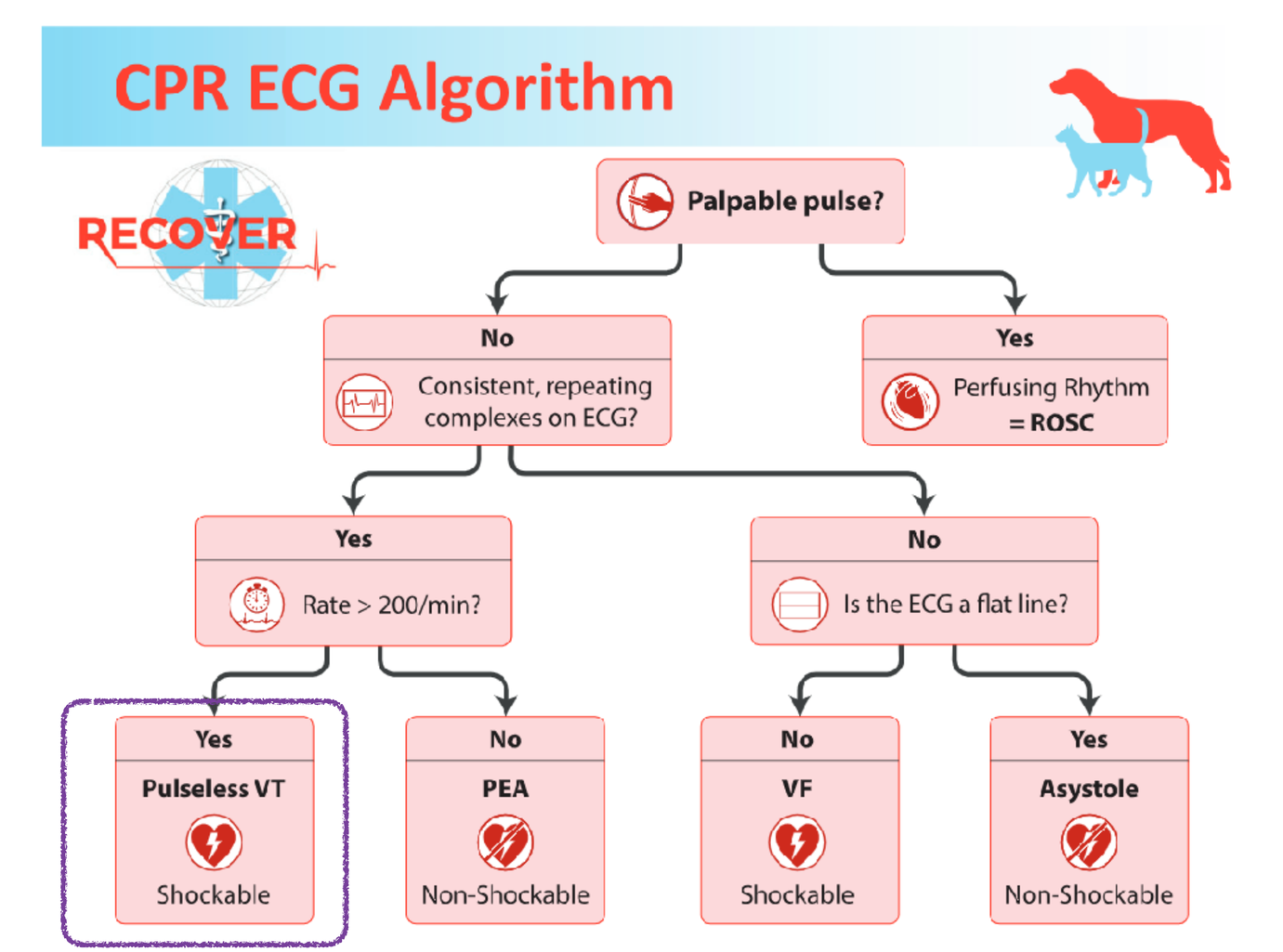


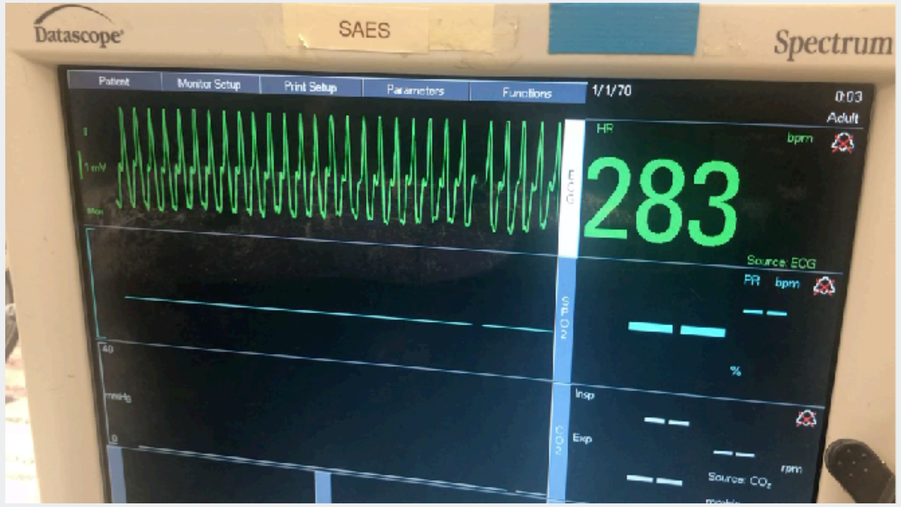
Simple CPR ECG Algorithm





Simple CPR ECG Algorithm





Shockable rhythm - defibrillation

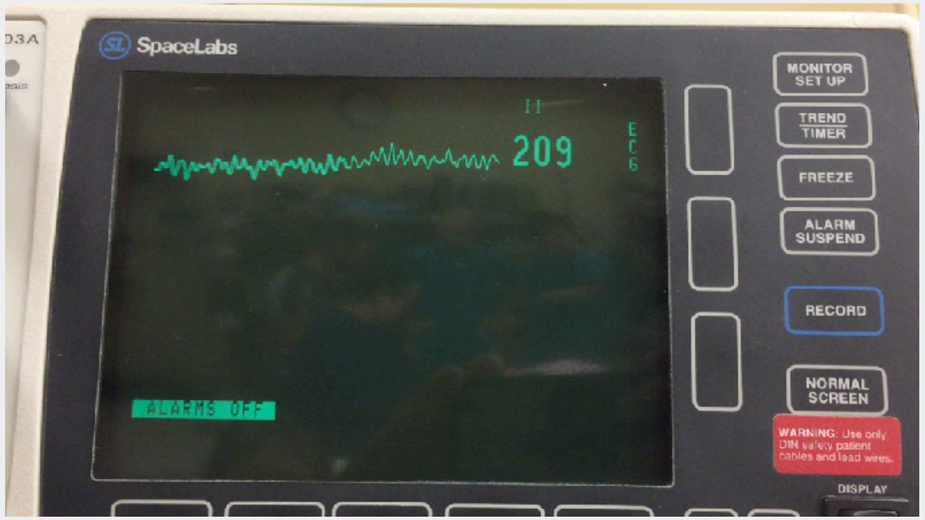
- Defibrillate once diagnose shockable rhythm
  - Chest compression until ready to defibrillate
- Resume chest compression after defibrillation
  - Full cycle (2 min) of chest compression before ECG check

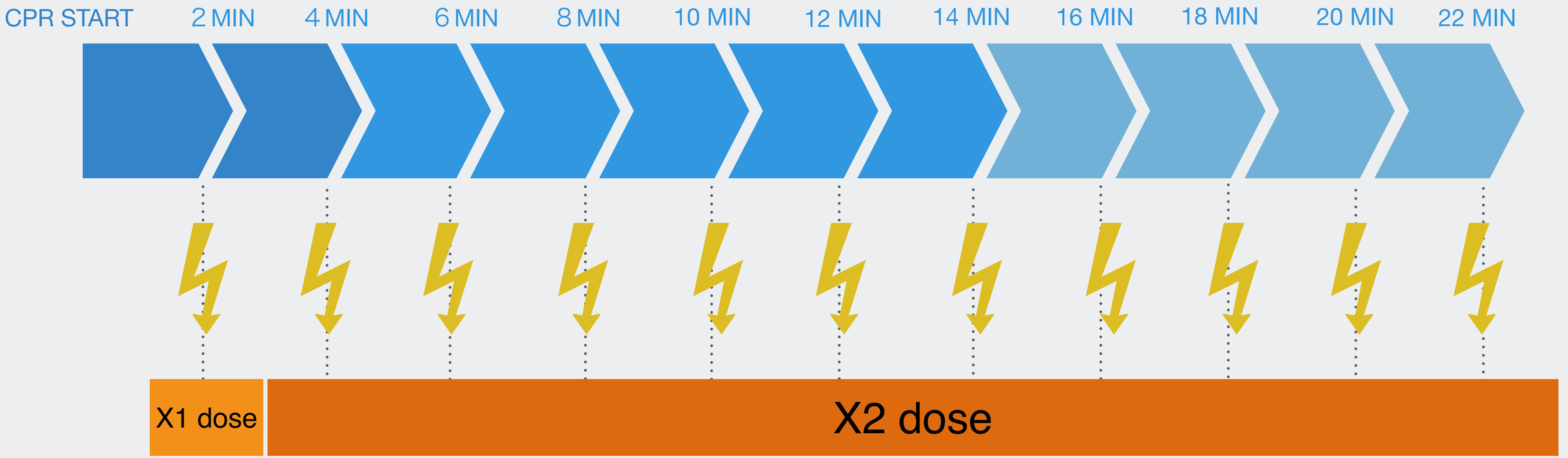
Initial shockable rhythms

- Human patients:
  - 61 - 98% of people with shockable arrest rhythms convert after the first electrical defibrillation attempt

- Dogs and cats:
  - We don’t know the conversion rate

  - Suarez LV et al. JVECC 2023
    - 4% - initial shockable rhythm
    - 12% - Animals with initial non-shockable rhythm developed subsequent shockable rhythms





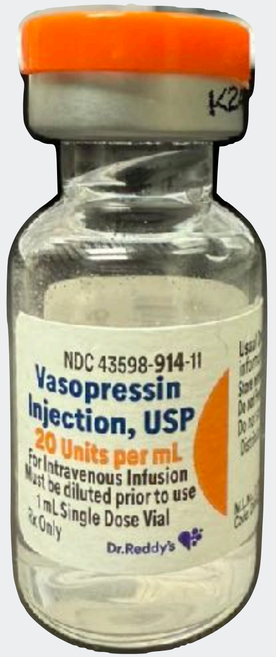
1. Low dose vasopressin (or epinephrien) every other cycle
2. Esmolol (0.5 mg/kg over 3-5 min followed by 50 μ/kg/min)
3. 1-2 doses of lidocaine (2 mg/kg) in dogs or amiodarone (5 mg/kg) in cats

Refractory shockable rhythm

❖ Refractory shockable rhythm - one that fails to convert after the first defibrillation attempt

Refractory shockable rhythm

- Vasopressors for initial shockable rhythm?
  - Do not use vasopressors (epinephrine, vasopressin) before the first defibrillation attempt in animals with shockable rhythms
- In animals with refractory shockable rhythm
  - Suggested to give vasopressin (0.8 U/kg) as the first-line vasopressor
  - Give epinephrine if no vasopressin

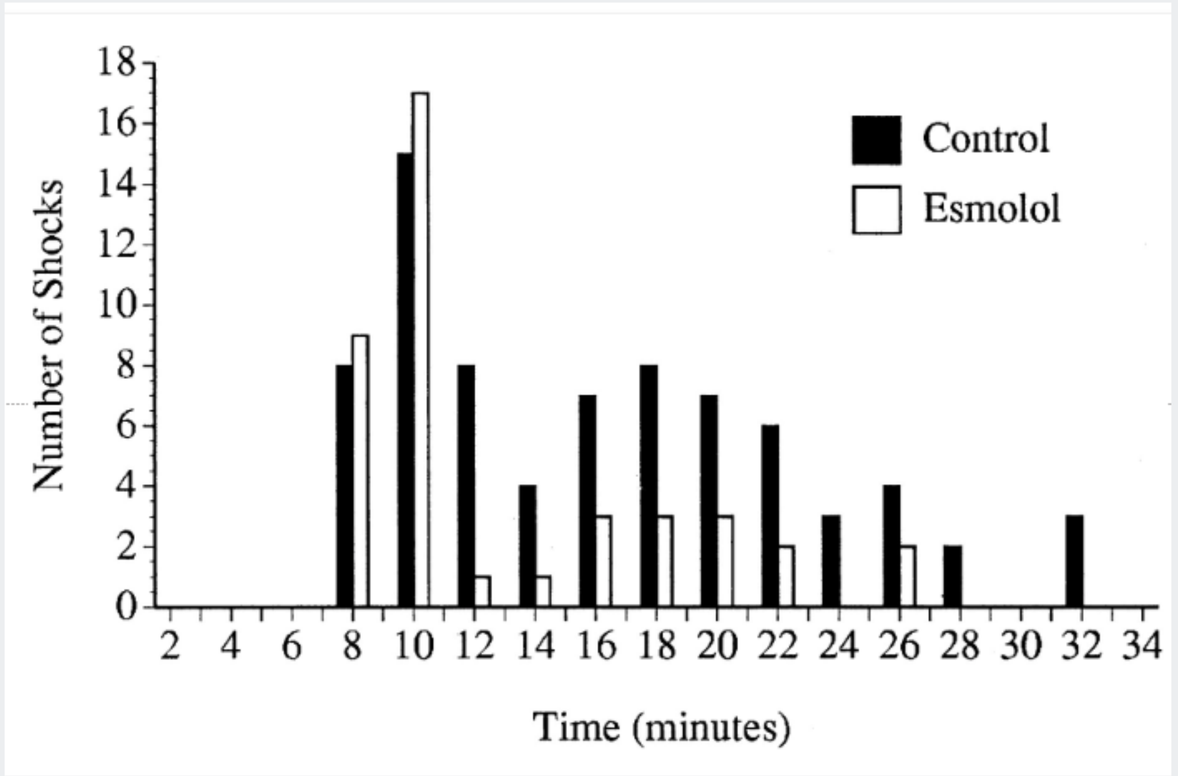


Refractory shockable rhythm

- Esmolol (beta-blocker)
  - Reduces beta-1 mediated myocardial stress
  - Improves defibrillation success by attenuating refractory IVF
  - May improve post-resuscitation myocardial function

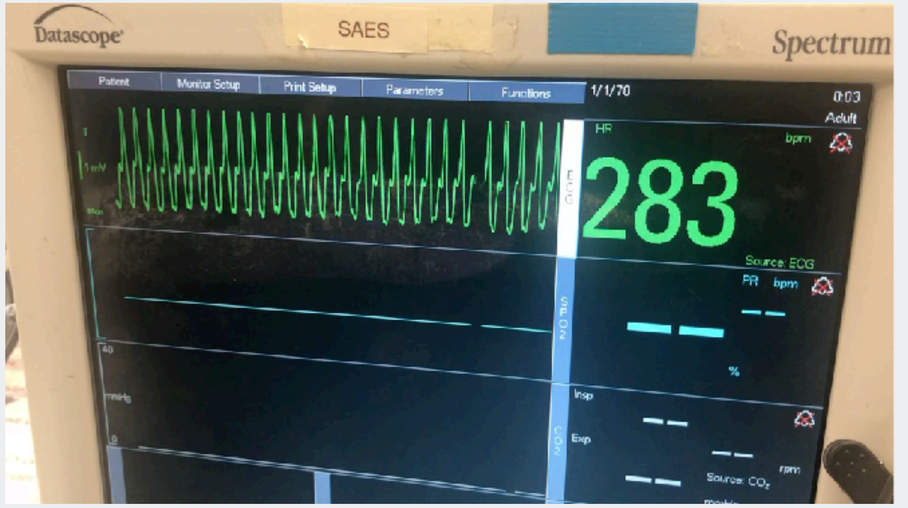
Short-Acting β-Adrenergic Antagonist Esmolol Given at Reperfusion Improves Survival After Prolonged Ventricular Fibrillation

Cheryl R. Killingsworth, DVM, PhD; Chih-Chang Wei, PhD; Louis J. Dell'Italia, MD; Jeffrey L. Ardell, PhD; Melody A. Kingsley; William M. Smith, PhD; Raymond E. Ideker, MD, PhD; Gregory P. Walcott, MD



Refractory shockable rhythm

- Lidocaine for dogs with refractory shockable rhythms
  - Class 1b antiarrhythmic blocks fast sodium channels
  - Adjunctive therapy for refractory shockable rhythms in dogs - suggestion
    - Not recommended for cats due to their increased sensitivity to lidocaine toxicity
  - May reduce defibrillation threshold, potentially enhancing the success of defibrillation
    - Only for refractory shockable rhythms



Refractory shockable rhythm

- Why should antiarrhythmics not be given before the first defibrillation?
  - Potential increase in defibrillation threshold
  - Immediate defibrilallation without pre-treatment is more effective

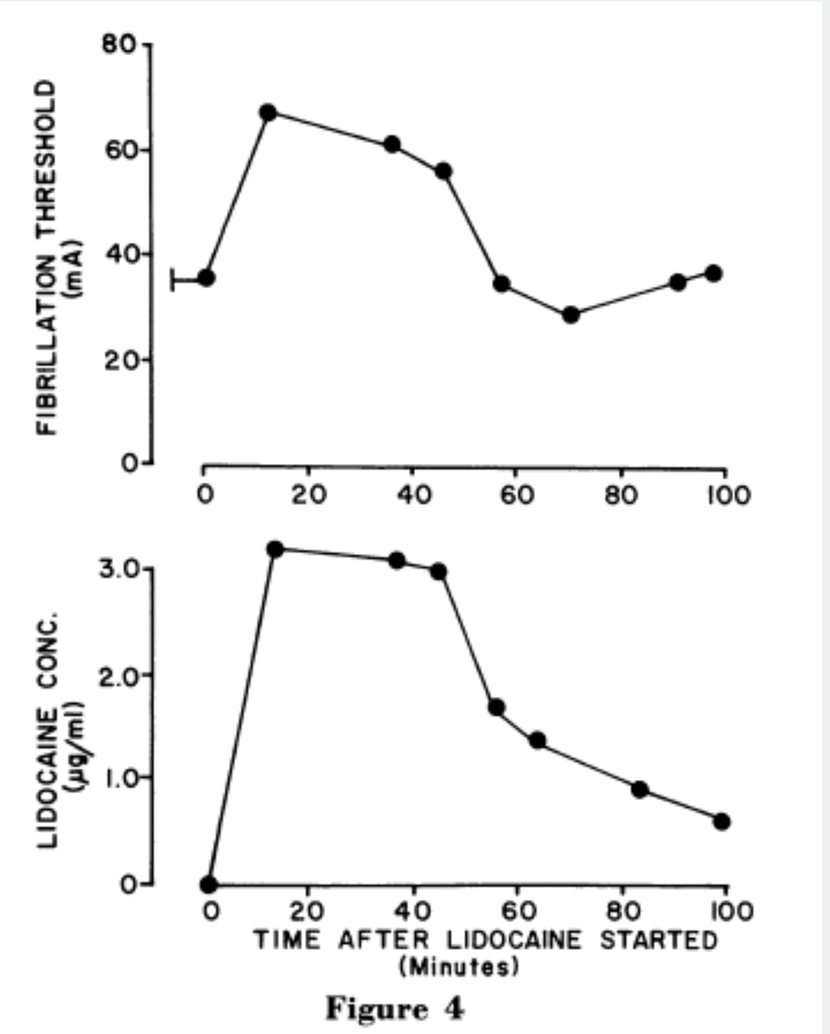
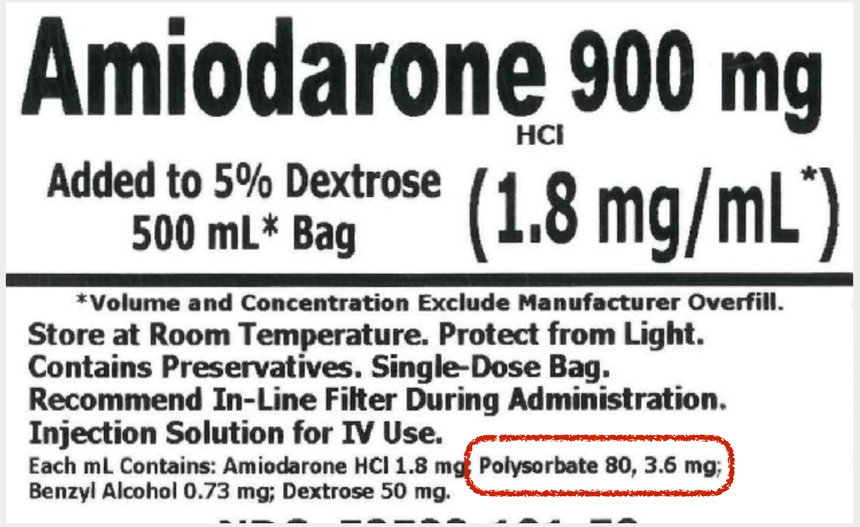


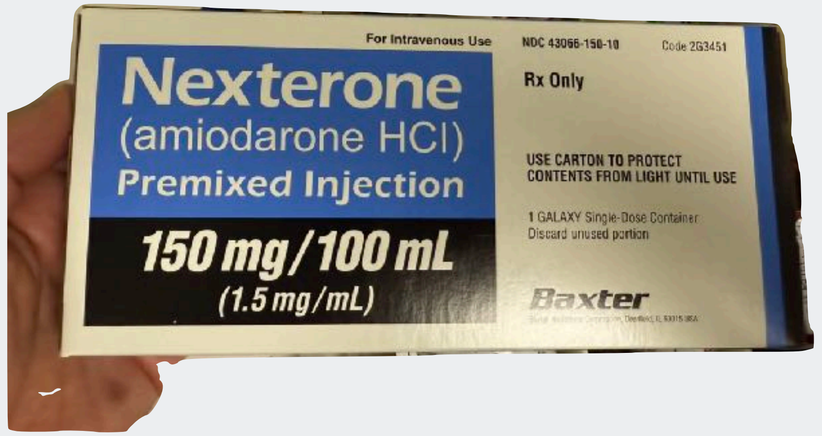
Figure 4

Spear JF et al.

Refractory shockable rhythm

- Amiodarone for cats with refractory shockable rhythms
  - Class III antiarrhythmic drug - Block K, Na, Ca channels
    - Used for patients with refractory ventricular tachycardia
    - No to limited evidence in cats with refractory shockable rhythm
    - Has vasodilatory effects - may need to administer with epinephrine/vasopressin





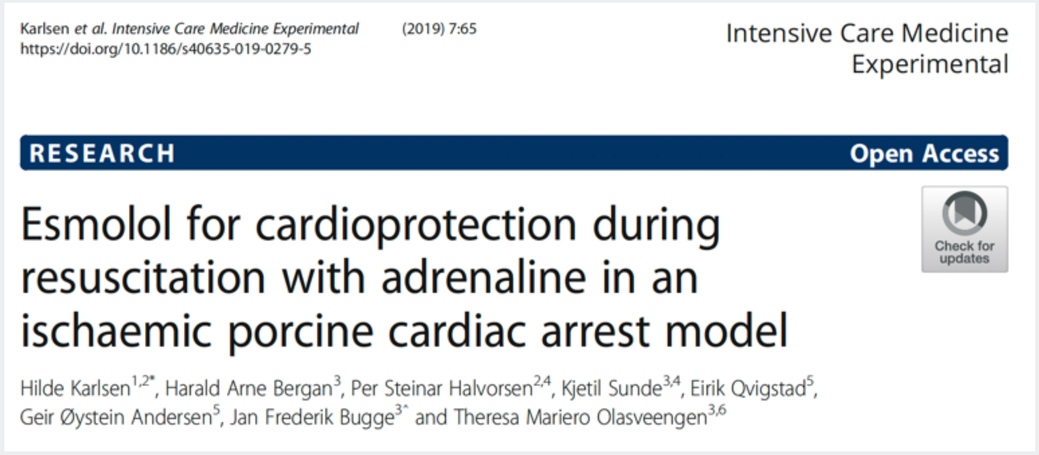
Summary

- IV access is the gold standard for drug administration in CPR
- IO administration allows for rapid drug delivery when IV access is difficult
- ET drug administration is a last resort, requiring 2-3 times the IV dose
- Low dose epinephrine remains the first-line vasopressor for non-shockable rhythms
- Vasopressin may be an alternative to epinephrine
- Atropine is suggested for suspected high vagal tone-induced cardiac arrest, but its routine use in non-shockable rhythms has limited evidence of benefit
- Defibrillation is the first-line treatment for shockable rhythms
- Vasopressors and antiarrhythmics are reserved for refractory shockable rhythms
- Lidocaine is suggested for dogs with refractory shockable rhythms, while amiodarone is suggested for cats
- Sodium bicarbonate is only suggested in prolonged CPR with severe metabolic acidoiss
- Fluid administration should be individualized- should be avoided in normovolemic patients

Questions?

Refractory shockable rhythm

- Esmolol (beta-blocker)
  - Reduces beta-1 mediated myocardial stress
  - Improves defibrillation success by attenuating refractory IVF
  - May improve post-resuscitation myocardial function



Karlsen *et al. Intensive Care Medicine Experimental* (2019) 7:65
https://doi.org/10.1186/s40635-019-0279-5

Intensive Care Medicine Experimental

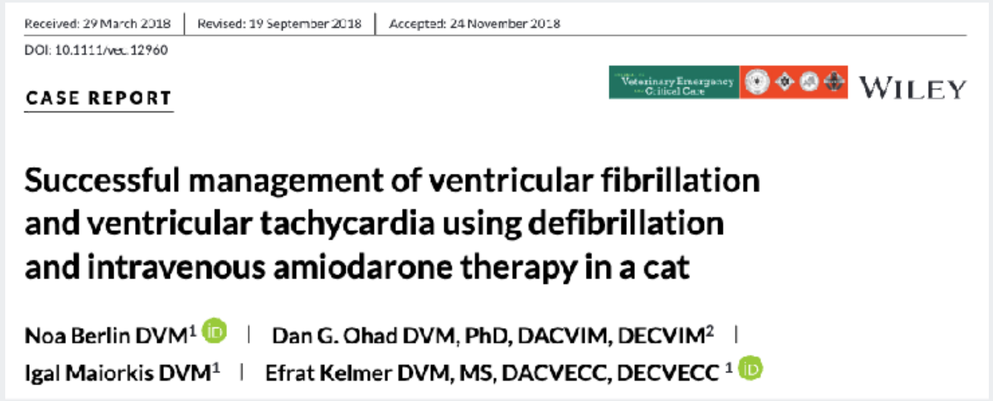
RESEARCH Open Access

Esmolol for cardioprotection during resuscitation with adrenaline in an ischaemic porcine cardiac arrest model

Hilde Karlsen[1,2*], Harald Arne Bergan[3], Per Steinar Halvorsen[2,4], Kjetil Sunde[3,4], Eirik Qvigstad[5], Geir Øystein Andersen[5], Jan Frederik Bugge[3*] and Theresa Mariero Olasveengen[3,6]

Refractory shockable rhythm

- Amiodarone for cats with refractory shockable rhythms

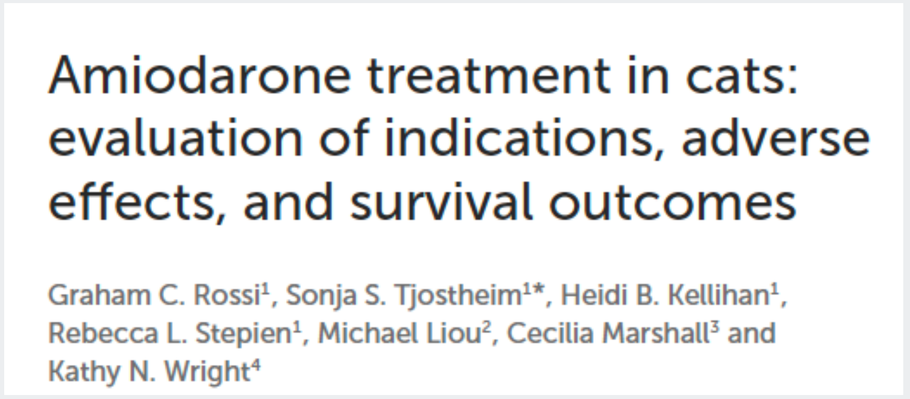


Received: 29 March 2018 | Revised: 19 September 2018 | Accepted: 24 November 2018
DOI: 10.1111/vec.12960

CASE REPORT

Successful management of ventricular fibrillation and ventricular tachycardia using defibrillation and intravenous amiodarone therapy in a cat

Noa Berlin DVM[1] | Dan G. Ohad DVM, PhD, DACVIM, DECVIM[2] | Igal Maiorkis DVM[1] | Efrat Kelmer DVM, MS, DACVECC, DECVECC [1]

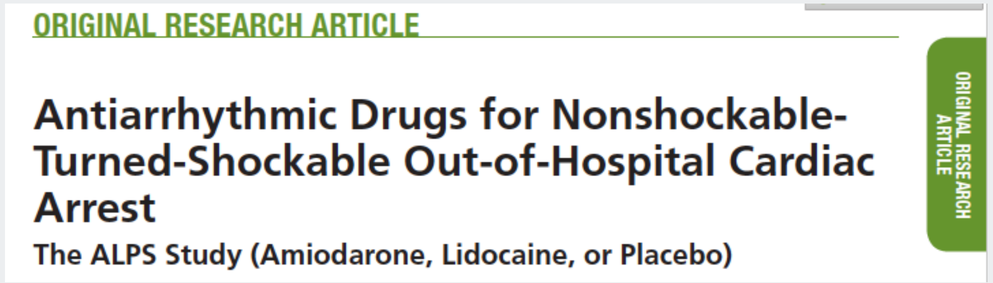


Amiodarone treatment in cats: evaluation of indications, adverse effects, and survival outcomes

Graham C. Rossi[1], Sonja S. Tjostheim[1]*, Heidi B. Kellihan[1], Rebecca L. Stepien[1], Michael Liou[2], Cecilia Marshall[3] and Kathy N. Wright[4]

CPR drugs - IV fluids

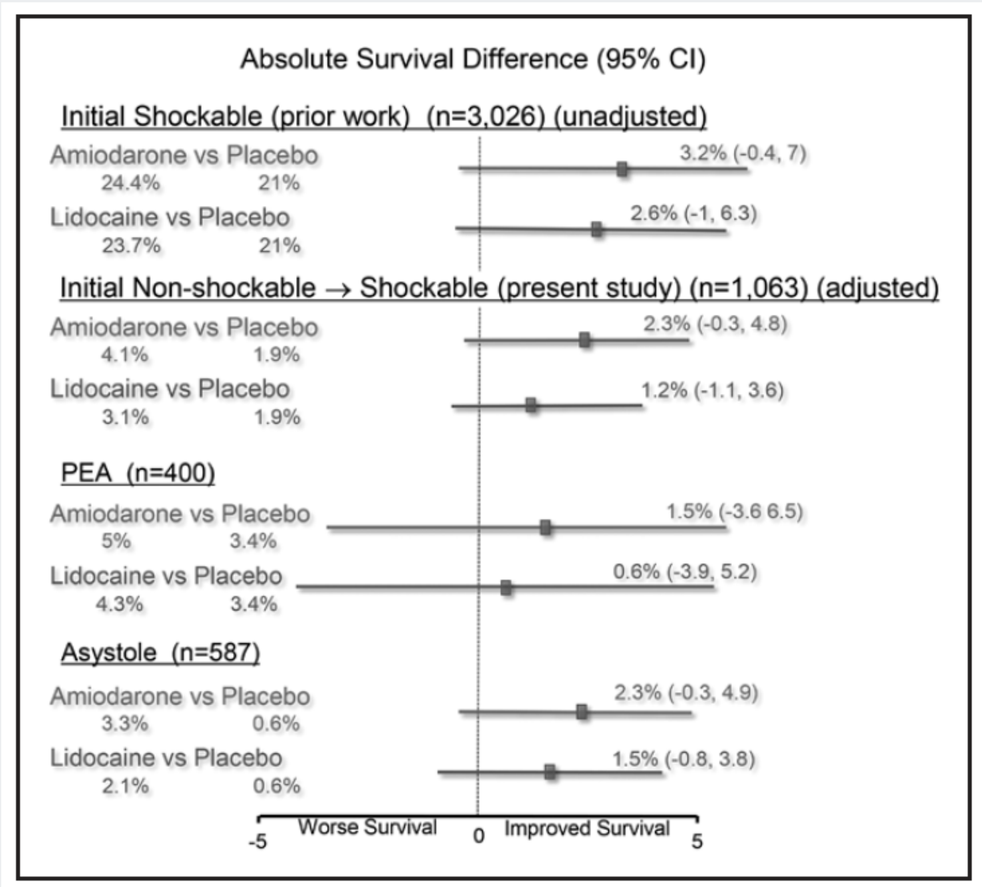
- Antiarrhythmic drugs for nonshockable-turned-shockable out of hospital cardiac arrest
  - Better survival after amiodarone or lidocaine than placebo

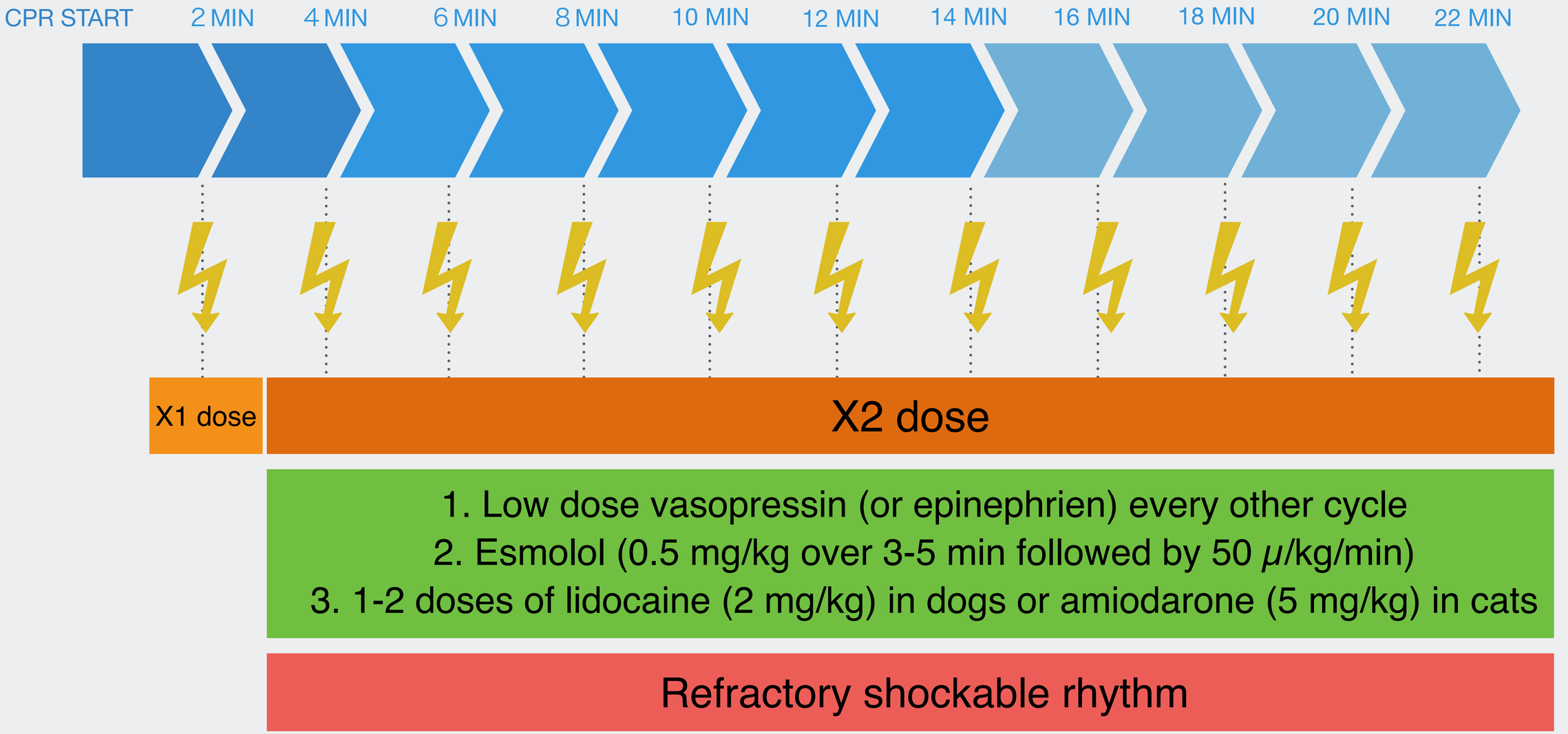

ORIGINAL RESEARCH ARTICLE

Antiarrhythmic Drugs for Nonshockable-Turned-Shockable Out-of-Hospital Cardiac Arrest

The ALPS Study (Amiodarone, Lidocaine, or Placebo)

ORIGINAL RESEARCH ARTICLE

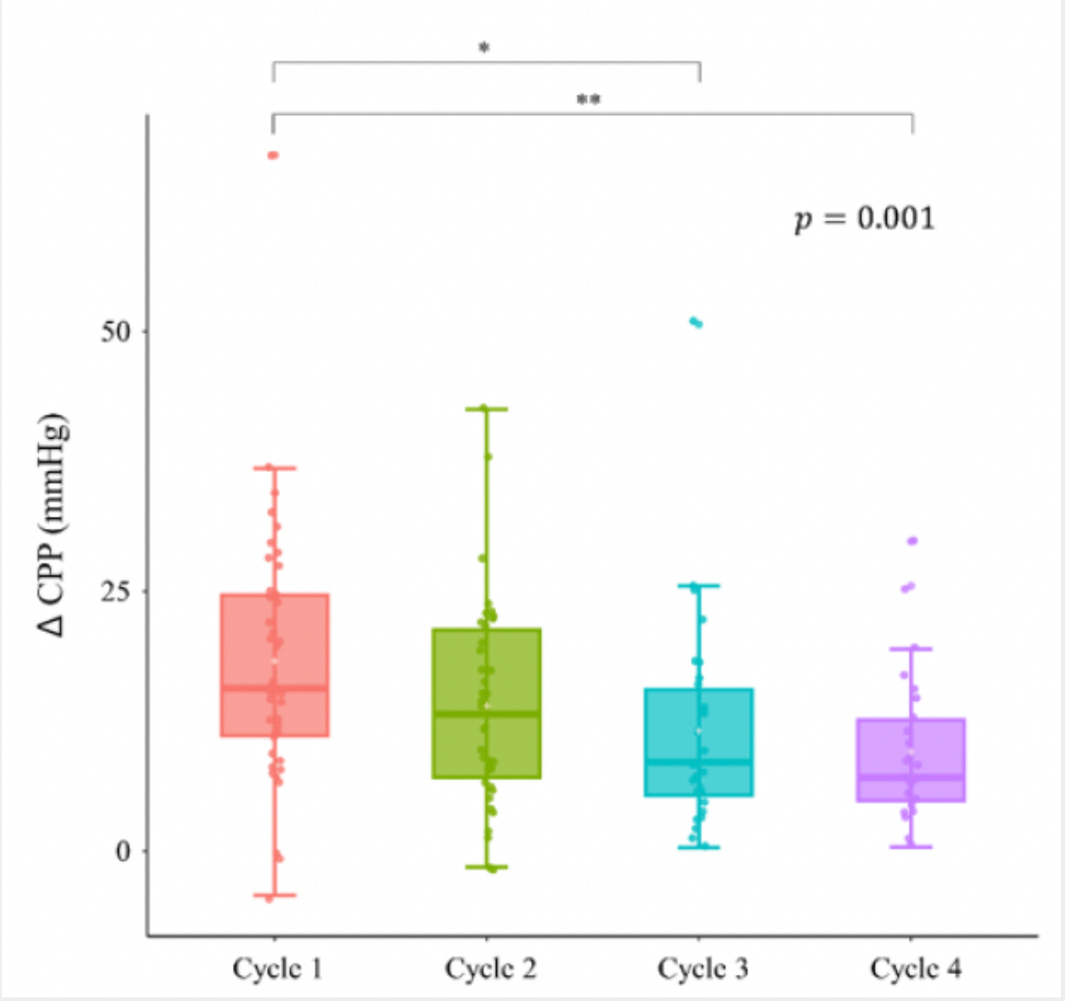




- Refractory shockable rhythm - one that fails to convert after the first defibrillation attempt

Frequency of epinephrine administration

- The duration of hemodynamic effect caused by epinephrine was shorter
  - The BP augmented by epinephrine decreased as the CPR cycle repeated
    - Higher dose of epinephrine? - no outcome benefit
    - More frequent epinephrine? - maybe…



Journal of the American Heart Association

ORIGINAL RESEARCH

Hemodynamic Effect of Repeated Epinephrine Doses Decreases With Cardiopulmonary Resuscitation Cycle Progression

Young-Il Koh, MD, PhD*; Gyo Jin Ahn, MD*; Jung Hun Lee, PhD; Woo Jin Jung, MD; Soyeong Kim, MS; Hyeon Young Im; Yujin Lee; Dahye Im; Jihye Lim; Sung Oh Hwang, MD, PhD; Kyoung-Chul Cha, MD, PhD

Refractory shockable rhythm

- Esmolol
  - Reduces beta-1 mediated myocardial stress
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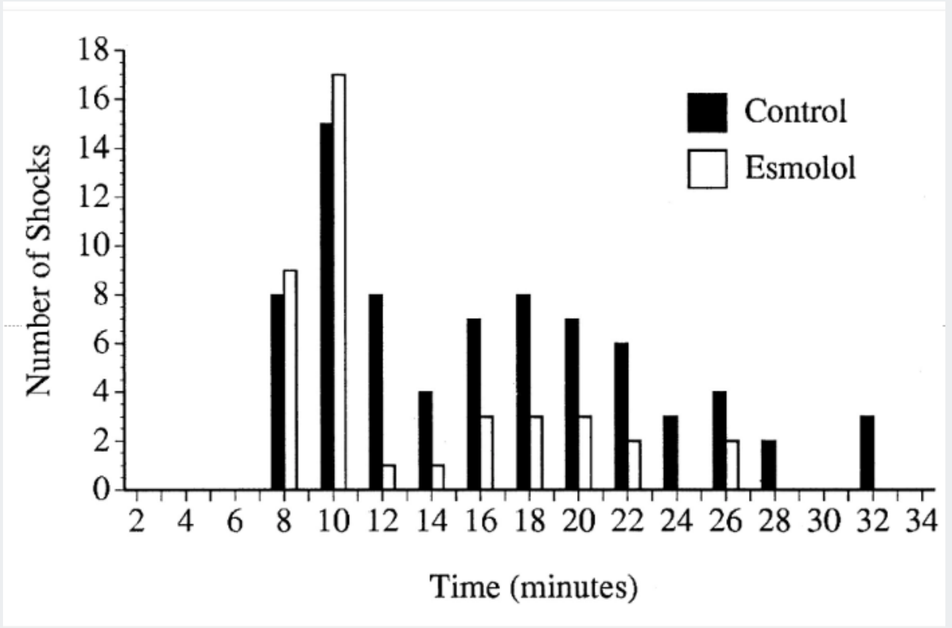


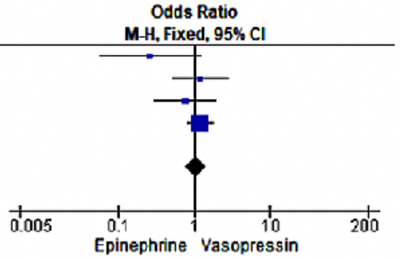
Epinephrine vs vasopressin

- Out-of-hospital CPR
  - No differences on outcomes
- In-hospital CPR
  - No difference on outcomes

Epinephrine Vs Vasopressin (*Survival to hospital discharge*)

Study or Subgroup	Epinephrine Events	Epinephrine Total	Vasopressin Events	Vasopressin Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Lindner 1997	3	20	8	20	9.2%	0.26 [0.06, 1.21]
Stiell 2001	13	96	12	104	13.5%	1.20 [0.52, 2.78]
Ong 2012	8	353	11	374	14.1%	0.77 [0.30, 1.93]
Wenzel 2004	58	500	57	578	63.2%	1.20 [0.81, 1.77]
Total (95% CI)		**969**		**1076**	**100.0%**	**1.05 [0.77, 1.45]**
Total events	82		88			

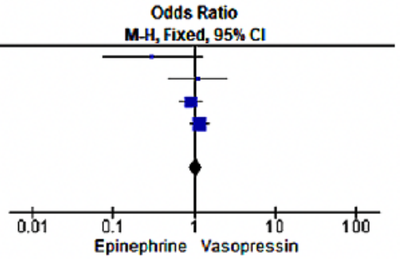
Heterogeneity: Chi² = 4.16, df = 3 (P = 0.24); I² = 28%
Test for overall effect: Z = 0.31 (P = 0.75)



Epinephrine Vs Vasopressin (*Achieving ROSC*).

Study or Subgroup	Epinephrine Events	Epinephrine Total	Vasopressin Events	Vasopressin Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Lindner 1997	11	20	16	20	3.5%	0.31 [0.07, 1.25]
Stiell 2001	13	96	13	104	5.3%	1.10 [0.48, 2.50]
Ong 2012	106	353	119	374	39.6%	0.92 [0.67, 1.26]
Wenzel 2004	167	597	145	589	51.5%	1.19 [0.92, 1.54]
Total (95% CI)		**1066**		**1087**	**100.0%**	**1.05 [0.86, 1.27]**
Total events	297		293			

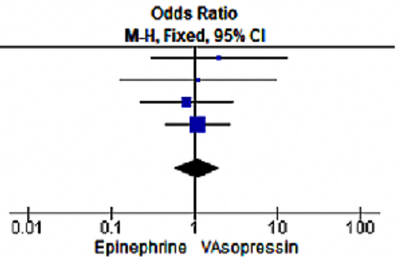
Heterogeneity: Chi² = 4.54, df = 3 (P = 0.21); I² = 34%
Test for overall effect: Z = 0.46 (P = 0.64)



Epinephrine Vs Vasopressin (*Neurologic function*).

Study or Subgroup	Epinephrine Events	Epinephrine Total	Vasopressin Events	Vasopressin Total	Weight	Odds Ratio M-H, Fixed, 95% CI
Ong 2012	5	8	5	11	8.6%	2.00 [0.31, 12.84]
Stiell 2001	11	13	10	12	8.7%	1.10 [0.13, 9.34]
Lindner 1997	11	20	12	20	29.4%	0.81 [0.23, 2.86]
Wenzel 2004	16	46	15	46	53.3%	1.10 [0.46, 2.62]
Total (95% CI)		**87**		**89**	**100.0%**	**1.09 [0.58, 2.06]**
Total events	43		42			

Heterogeneity: Chi² = 0.62, df = 3 (P = 0.89); I² = 0%
Test for overall effect: Z = 0.28 (P = 0.78)



Intramuscular administration of epinephrine

- First epinephrine given IM compared to IV/IM
  - Improved survival rate
- Not a replacement for IV/IM epinephrine

RESUSCITATION 201 (2024) 110266

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Resuscitation

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EUROPEAN RESUSCITATION COUNCIL

Clinical paper

Early intramuscular adrenaline administration is associated with improved survival from out-of-hospital cardiac arrest ☆

Helen N. Palatinus[a,], M. Austin Johnson[a], Henry E. Wang[b], Guillaume L. Hoareau[a,d], Scott T. Youngquist[a,c]*

Table 2 – Outcomes of Patients Treated with an Initial Adrenaline Dose Administered through the IV/IO Route Compared to the IM Route.

Outcome	IV/IO Cohort No. (%) (n = 985)	IM Cohort No. (%) (n = 420)	Absolute Difference (%)	Odds Ratio (95% CI) * Unadjusted	Adjusted
Survival to Hospital Admission	311 (31.6)	156 (37.1)	5.6	1.28 (1.01–1.63)	1.37 (1.06–1.77)
Survival to Hospital Discharge	69 (7.0)	46 (11.0)	4.0	1.63 (1.10–2.42)	1.73 (1.10–2.71)
Favorable Neurologic Outcome	61 (6.2)	41 (9.8)	3.6	1.64 (1.08–2.48)	1.72 (1.07–2.76)

* Multivariate logistic regression model adjusted for age, sex, witnessed arrest, bystander CPR, public location of arrest, initial cardiac rhythm, EMS response time.

Frequency of epinephrine administration

- OHCA - a shorter average epinephrine dosing interval was associated with improved survival with favorable neurological outcome

-

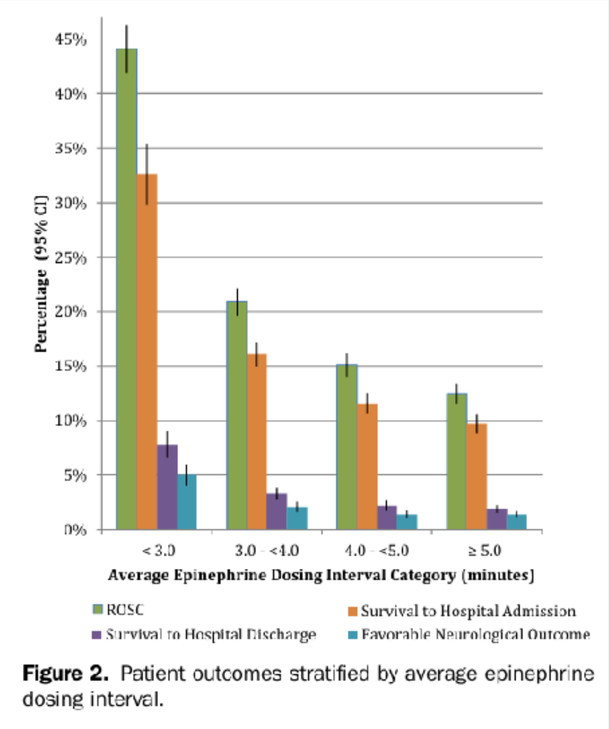
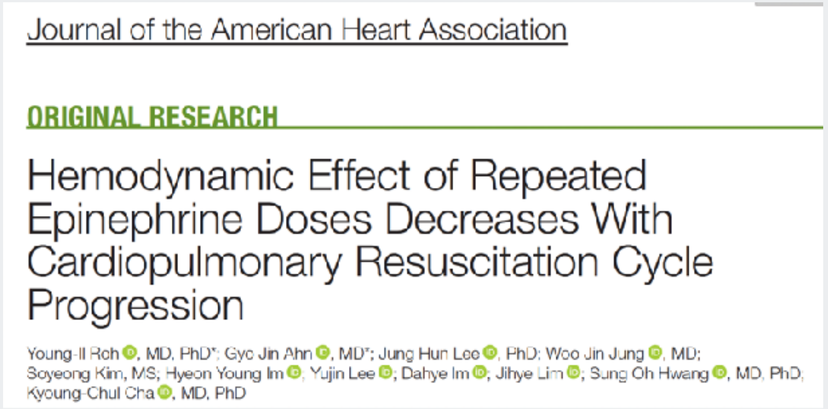


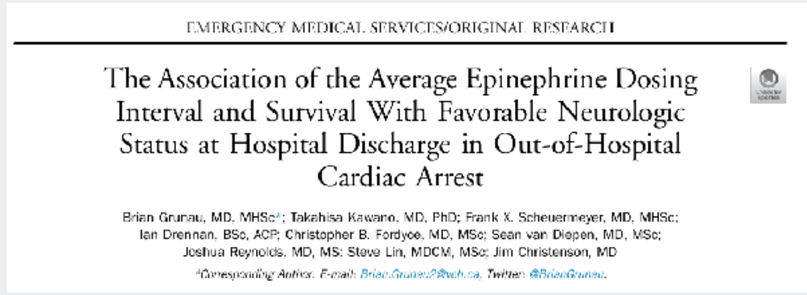
Figure 2. Patient outcomes stratified by average epinephrine dosing interval.


Journal of the American Heart Association

ORIGINAL RESEARCH

Hemodynamic Effect of Repeated Epinephrine Doses Decreases With Cardiopulmonary Resuscitation Cycle Progression

Young-Il Roh, MD, PhD*; Gyc Jin Ahn, MD*; Jung Hun Lee, PhD; Woo Jin Jung, MD; Soyeong Kim, MS; Hyeon Young Im, Yujin Lee; Dahye Im, Jihye Lim; Sung Oh Hwang, MD, PhD; Kyoung-Chul Cha, MD, PhD


EMERGENCY MEDICAL SERVICES/ORIGINAL RESEARCH

The Association of the Average Epinephrine Dosing Interval and Survival With Favorable Neurologic Status at Hospital Discharge in Out-of-Hospital Cardiac Arrest

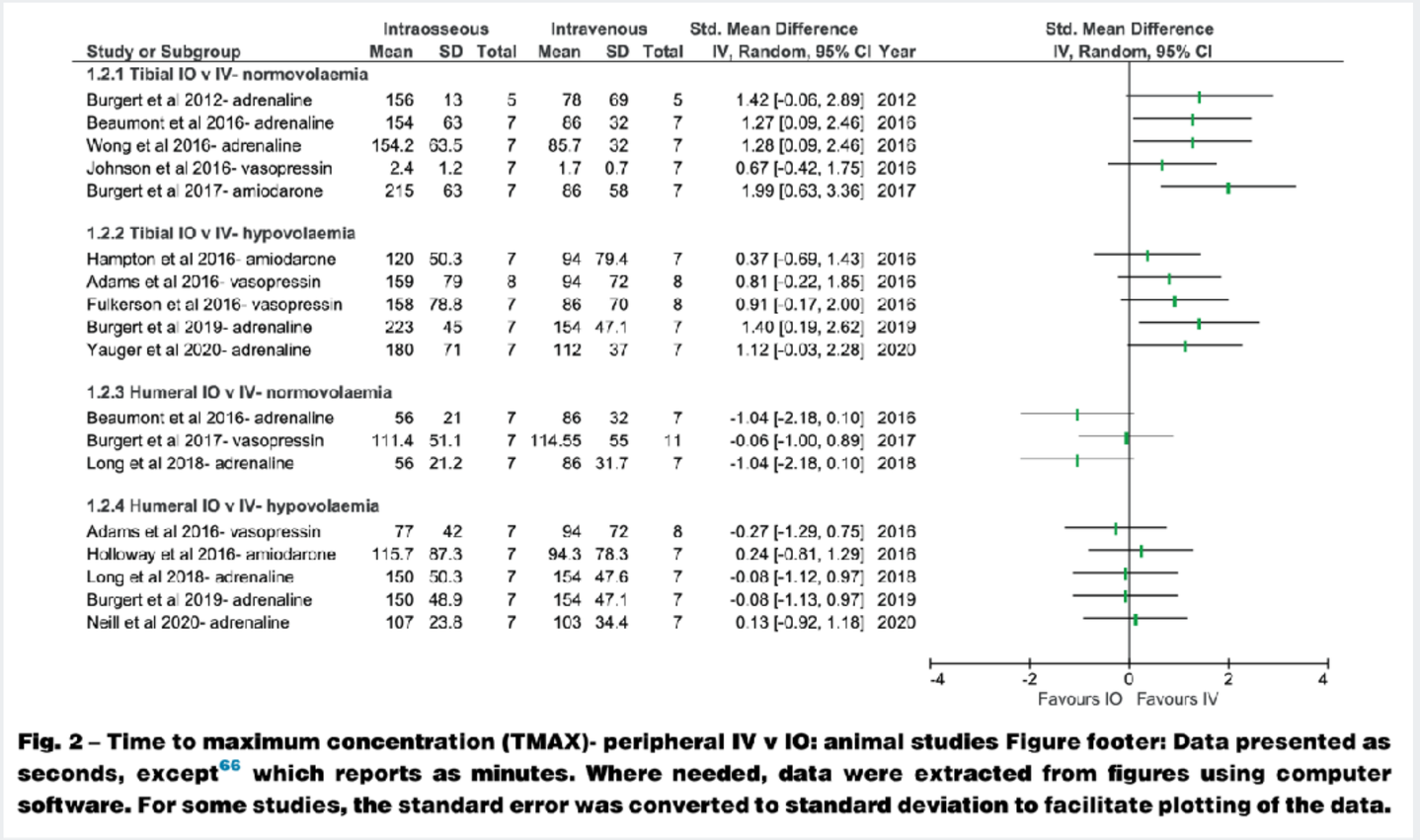
Brian Grunau, MD, MHSc*; Takahisa Kawano, MD, PhD; Frank X. Scheuermeyer, MD, MHSc; Ian Drennan, BSc, ACP; Christopher B. Fordyce, MD, MSc; Sean van Diepen, MD, MSc; Joshua Reynolds, MD, MS; Steve Lin, MDCM, MSc; Jim Christenson, MD

*Corresponding Author. E-mail: Brian.Grunau@hsch.ca, Twitter: @BrianGrunau.

Epinephrine CRI?

IO access in different location?

- Tibia: IV is better than IO
- Humerus: IO = IV



Study or Subgroup	Intraosseous Mean	SD	Total	Intravenous Mean	SD	Total	Std. Mean Difference IV, Random, 95% CI	Year
1.2.1 Tibial IO v IV- normovolaemia								
Burgert et al 2012- adrenaline	156	13	5	78	69	5	1.42 [-0.06, 2.89]	2012
Beaumont et al 2016- adrenaline	154	63	7	86	32	7	1.27 [0.09, 2.46]	2016
Wong et al 2016- adrenaline	154.2	63.5	7	85.7	32	7	1.28 [0.09, 2.46]	2016
Johnson et al 2016- vasopressin	2.4	1.2	7	1.7	0.7	7	0.67 [-0.42, 1.75]	2016
Burgert et al 2017- amiodarone	215	63	7	86	58	7	1.99 [0.63, 3.36]	2017
1.2.2 Tibial IO v IV- hypovolaemia								
Hampton et al 2016- amiodarone	120	50.3	7	94	79.4	7	0.37 [-0.69, 1.43]	2016
Adams et al 2016- vasopressin	159	79	8	94	72	8	0.81 [-0.22, 1.85]	2016
Fulkerson et al 2016- vasopressin	158	78.8	7	86	70	8	0.91 [-0.17, 2.00]	2016
Burgert et al 2019- adrenaline	223	45	7	154	47.1	7	1.40 [0.19, 2.62]	2019
Yauger et al 2020- adrenaline	180	71	7	112	37	7	1.12 [-0.03, 2.28]	2020
1.2.3 Humeral IO v IV- normovolaemia								
Beaumont et al 2016- adrenaline	56	21	7	86	32	7	-1.04 [-2.18, 0.10]	2016
Burgert et al 2017- vasopressin	111.4	51.1	7	114.55	55	11	-0.06 [-1.00, 0.89]	2017
Long et al 2018- adrenaline	56	21.2	7	86	31.7	7	-1.04 [-2.18, 0.10]	2018
1.2.4 Humeral IO v IV- hypovolaemia								
Adams et al 2016- vasopressin	77	42	7	94	72	8	-0.27 [-1.29, 0.75]	2016
Holloway et al 2016- amiodarone	115.7	87.3	7	94.3	78.3	7	0.24 [-0.81, 1.29]	2016
Long et al 2018- adrenaline	150	50.3	7	154	47.6	7	-0.08 [-1.12, 0.97]	2018
Burgert et al 2019- adrenaline	150	48.9	7	154	47.1	7	-0.08 [-1.13, 0.97]	2019
Neill et al 2020- adrenaline	107	23.8	7	103	34.4	7	0.13 [-0.92, 1.18]	2020

Fig. 2 – Time to maximum concentration (TMAX)- peripheral IV v IO: animal studies Figure footer: Data presented as seconds, except[66] which reports as minutes. Where needed, data were extracted from figures using computer software. For some studies, the standard error was converted to standard deviation to facilitate plotting of the data.

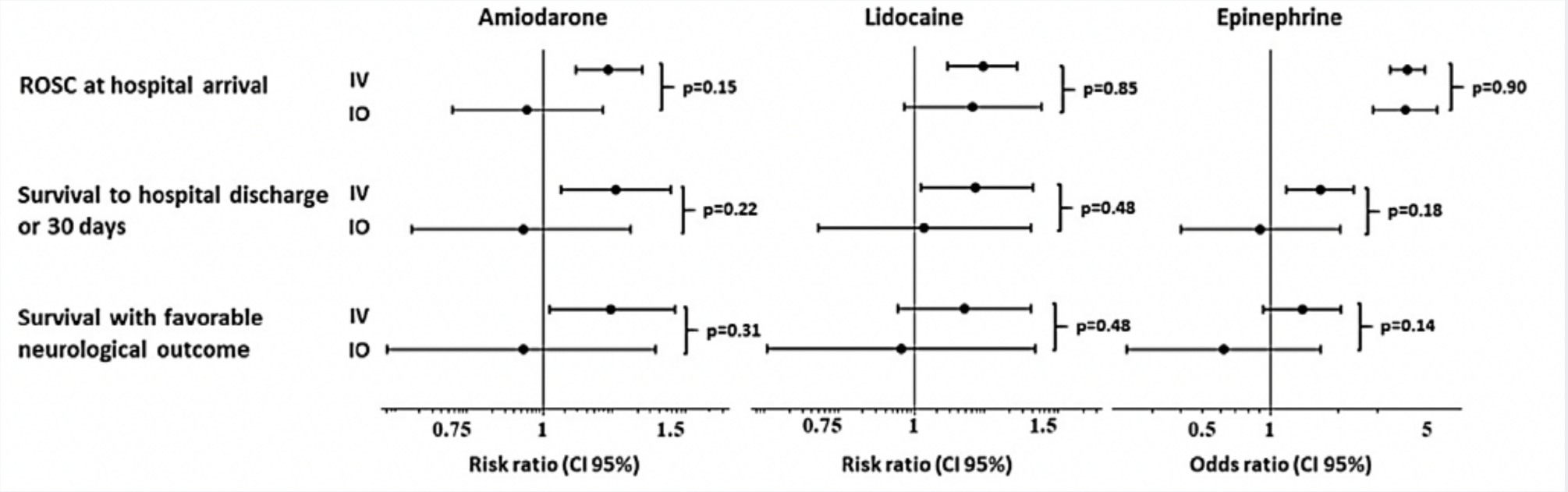
Review

Drug routes in out-of-hospital cardiac arrest: A summary of current evidence

Amy Hooper[a], Jerry P Nolan[b,c], Nigel Rees[d,e], Alison Walker[f,g], Gavin D Perkins[a,b], Keith Couper[a,b,]*

IO administration

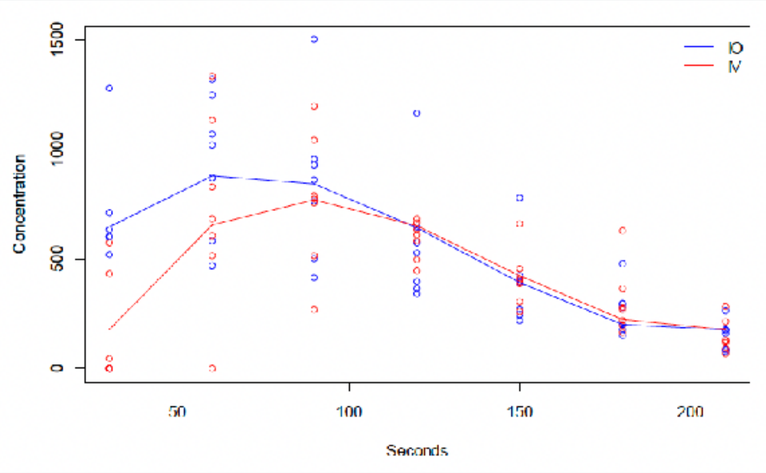
- May also depend on types of drugs
  - Certain drugs (e.g., amiodarone) may have reduced efficacy when given IO compared to IV



IO access in different location?

- Both tibial and sternal IO routes are an effective means of delivering drugs
  - Sternal IO routes - faster and greater dose delivered than tibial IO routes

- Humerus is better than ear vein in pig CPR models
  - Humerus is better than tibial IO routes in dogs and cats?

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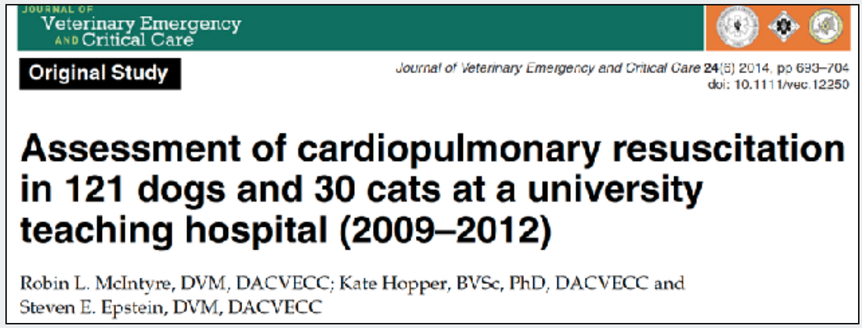
Experimental paper

Pharmacokinetics of intraosseous and central venous drug delivery during cardiopulmonary resuscitation☆,☆☆

Stephen L. Hoskins[a], Paulo do Nascimento Jr.[a,b], Rodrigo M. Lima[a,b], Jonathan M. Espana-Tenorio[a], George C. Kramer[a,*]

Prognosis of CPR in Veterinary Medicine



Return of spontaneous circulation (ROSC)

58%

Dog: 58%

Cat: 57%

ROSC>20 min

32%

Dog: 35%

Cat: 23%

ROSC > 24h

10%

Dog: 10%

Cat: 10%

Discharge

5%

Dog: 6%

Cat: 3%

Route for drug administration - Summary

- IV access is considered the gold standard
- IO administration is recommended alternative
  - If IV access is not successful within 2 minutes
- Endotracheal (ET) administration is an option
  - Less effective compared to IV and IO administration

High vs low dose epinephrine

- High dose epinephrine
  - Potentially improving initial ROSC
  - No survival benefit
  - Worse neurological outcomes