

Vasopressori ed Antiaritmici

cosa e quando?

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- Co-author, ERC guidelines, Advanced Life Support 2015

Epinephrine

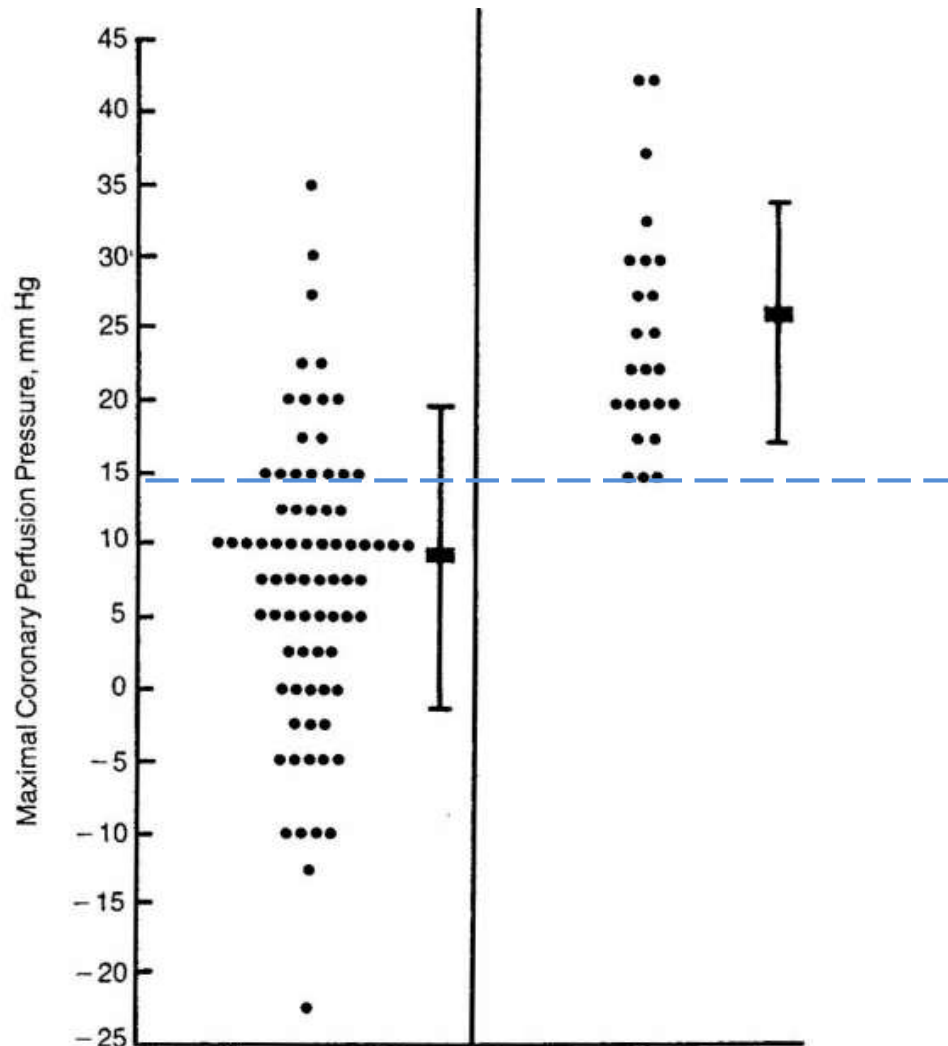
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Coronary perfusion pressure (CPP)



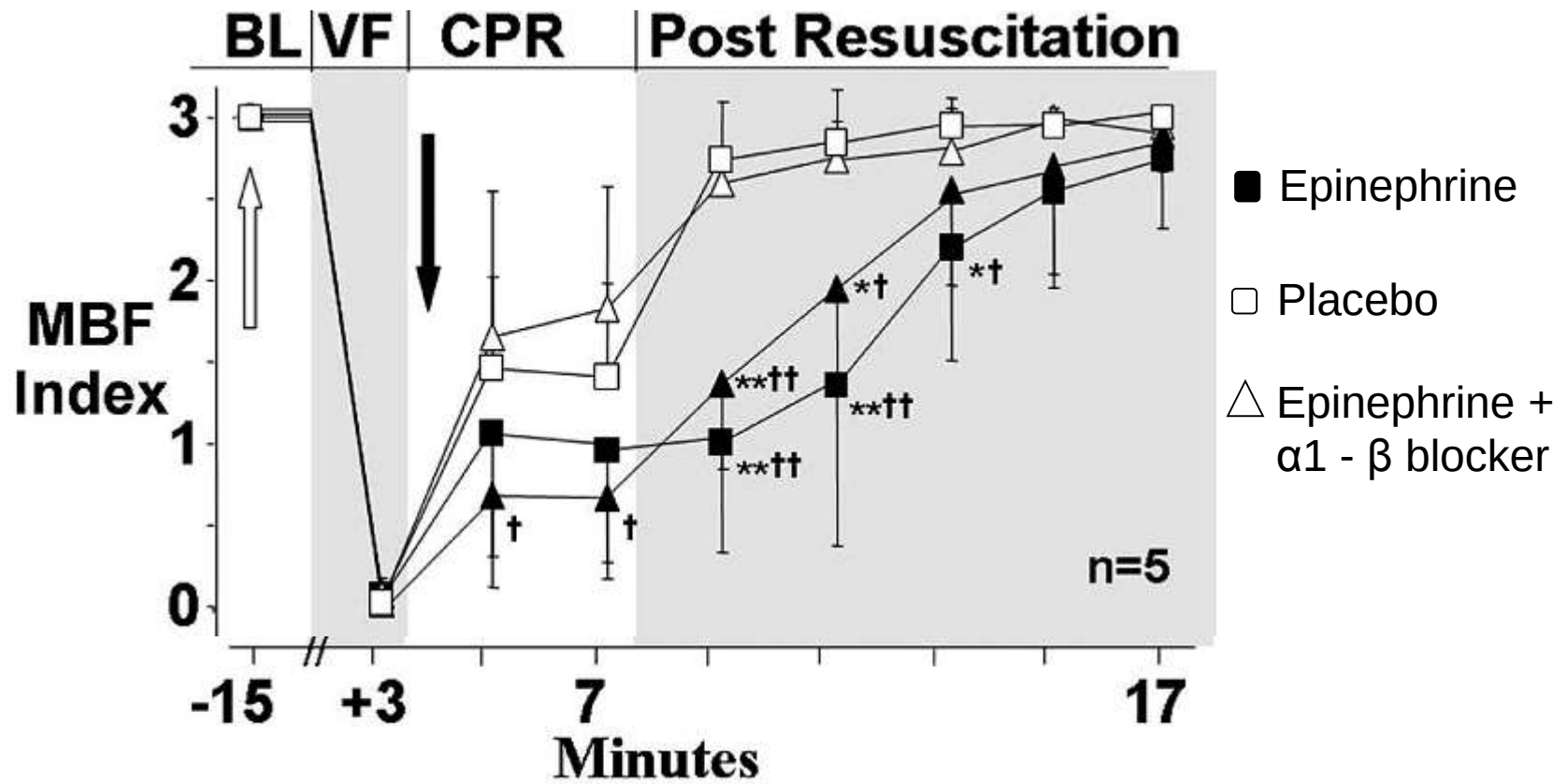
- # 100 pts
- ROSC only when $CPP \geq 15$ mmHg

Epinephrine

- It increases coronary blood flow
 - Michael JR et al. Circulation 1984;69:822-35
 - Brown CG et al. Circulation 1987;75:491-7
- It increases cerebral blood flow
 - Michael JR et al. Circulation 1984;69:822-35
 - Burnett AM et al. Resuscitation 2012; 83:1021–24
- Microcirculation?

Epinephrine reduces cerebral perfusion during cardiopulmonary resuscitation*

Giuseppe Ristagno, MD; Wanchun Tang, MD, FCCM; Lei Huang, MD; Alain Fymat, MD; Yun-Te Chang, MD; Shijie Sun, MD, FCCM; Carlos Castillo, MSEE; Max Harry Weil, MD, PhD, FCCM

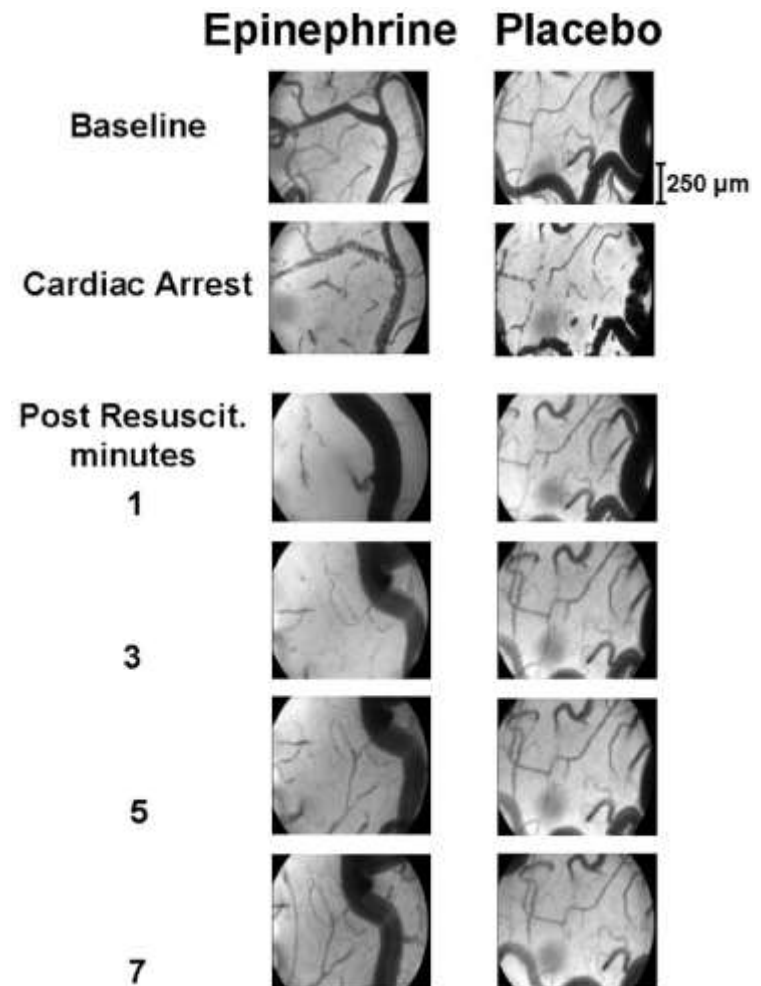


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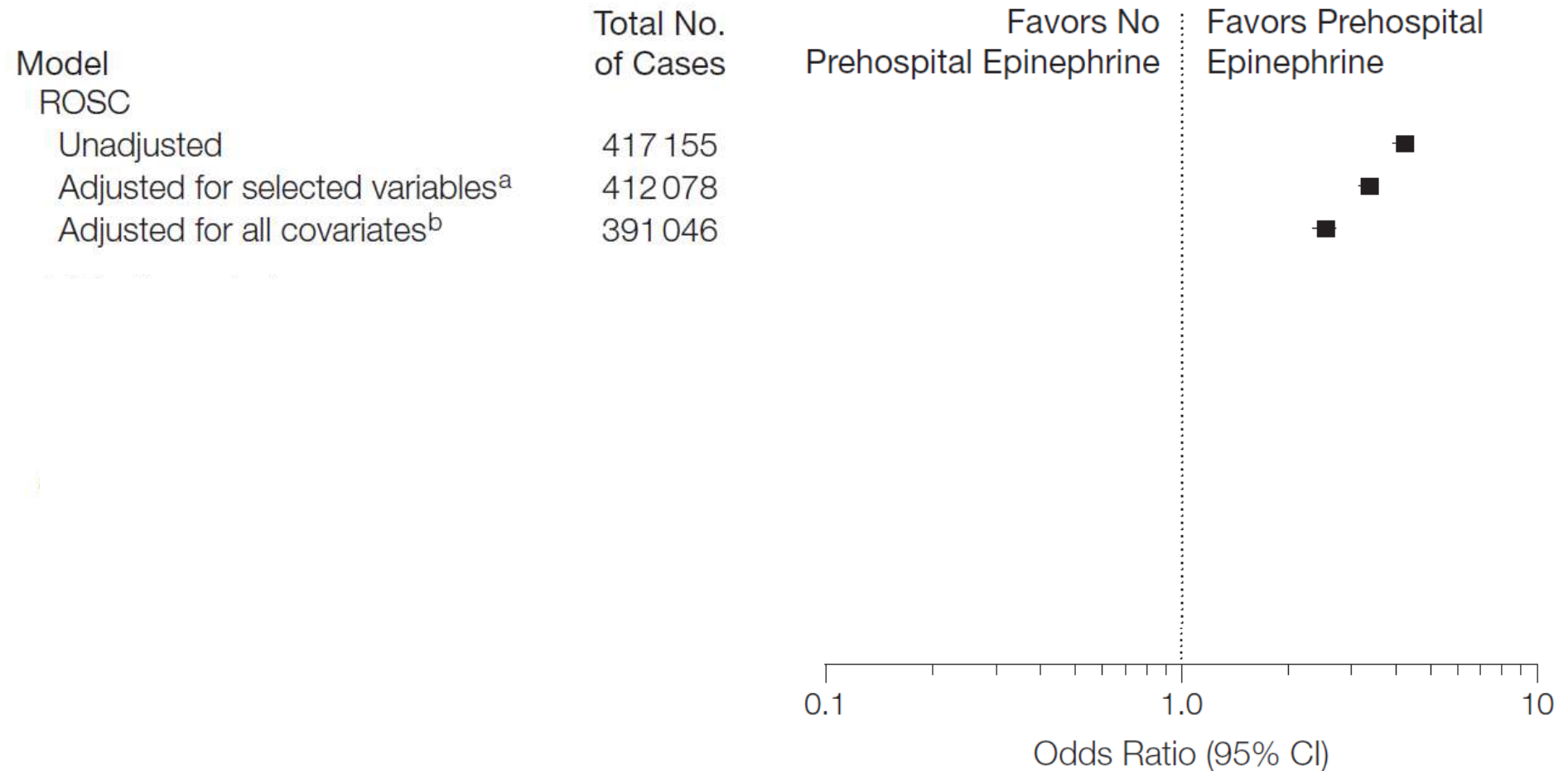
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Epinephrine:

- Increases arterial pressure
- Decreases cerebral microcirculation
- Decreases oxygen pressure (PbO_2) inside cerebral tissue



JAMA® Prehospital Epinephrine Use and Survival Among Patients With Out-of-Hospital Cardiac Arrest



Evaluation of pre-hospital administration of adrenaline (epinephrine) by emergency medical services for patients with out of hospital cardiac arrest in Japan: controlled propensity matched retrospective cohort study

	Unadjusted*	Adjusted†
Ventricular fibrillation/ventricular tachycardia (1990 pairs)		
Overall survival	1.34 (1.12 to 1.60)‡	1.36 (1.13 to 1.63)
Neurologically intact survival	1.01 (0.78 to 1.30)§	1.02 (0.78 to 1.33)
<u>Non-ventricular fibrillation/ventricular tachycardia (9058 pairs)</u>		
Overall survival	1.72 (1.45 to 2.04)¶	1.78 (1.49 to 2.13)
Neurologically intact survival	1.57 (1.04 to 2.37)**	1.55 (0.99 to 2.41)

Indications for adrenaline

- ASAP in non-VF/pVT rhythms
- After the 3rd shock in persistent VF/pVT
- However:

“Despite the widespread use of adrenaline during resuscitation, there is no placebo-controlled study that shows that the routine use of any vasopressor at any stage during human cardiac arrest increases neurologically intact survival to hospital discharge.”

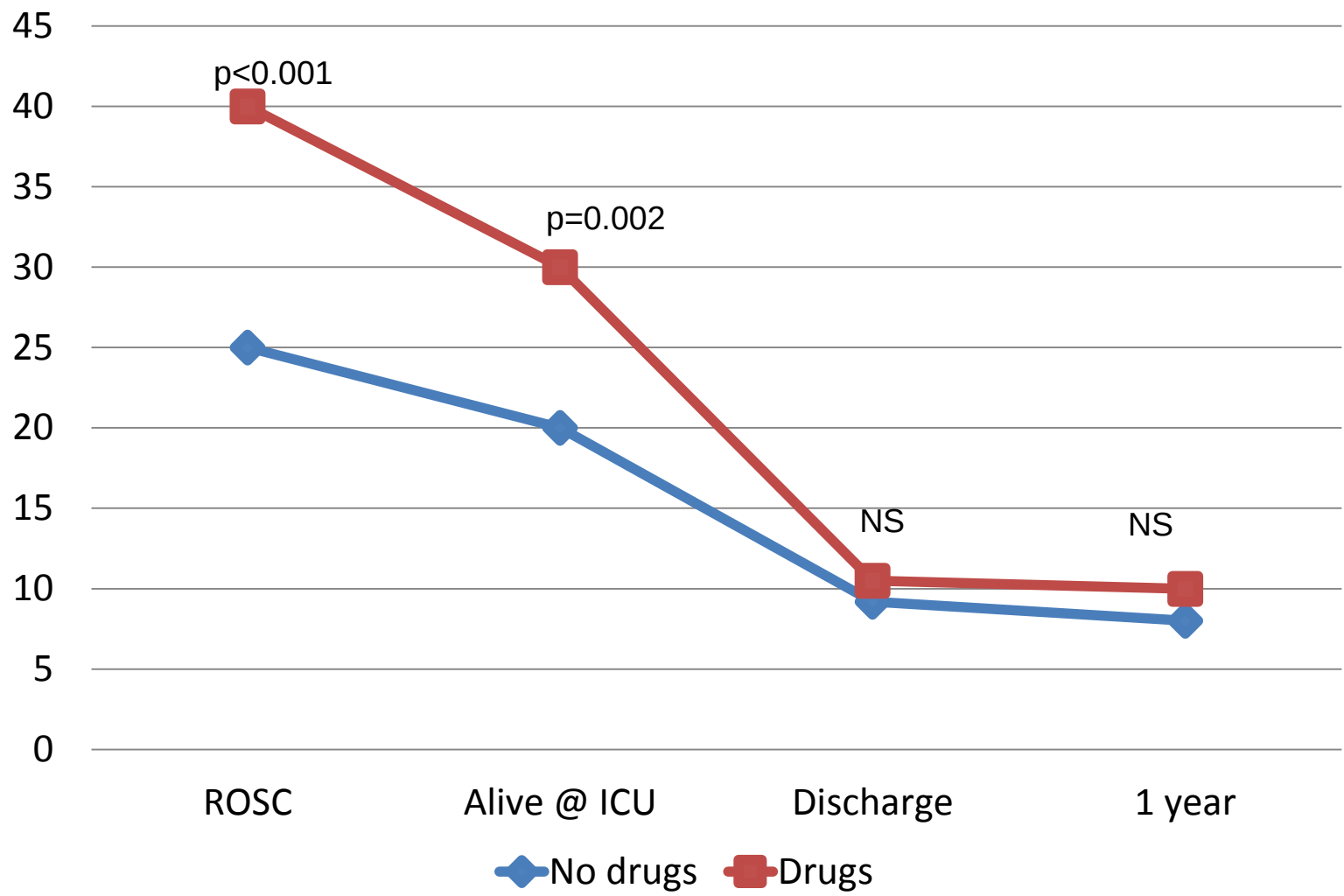
Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest: A Randomized Trial

Theresa M. Olasveengen; Kjetil Sunde; Cathrine Brunborg; et al.

- Randomised trial, non-traumatic OHCA
- 851 adult patients
- Intervention:
 - ALS with drugs
 - ALS with no drugs (1st venous access 5' after ROSC)
- Strict control of CPR quality

Intravenous Drug Administration During Out-of-Hospital Cardiac Arrest: A Randomized Trial

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Secondary analysis, epinephrine

	First rhythm VF/pulseless VT	
	No adrenaline (<i>n</i> = 156)	Adrenaline (<i>n</i> = 128)
Admitted to hospital	92 (59)	80 (63)
Admitted to ICU	82 (53)	51 (40)
Discharged alive	53 (34)	18 (14)
Discharged with CPC 1–2	51 (33)	15 (12)
Discharged if admitted ICU	65%	35%

	First rhythm asystole or pulseless electrical activity	
	No adrenaline (<i>n</i> = 325)	Adrenaline (<i>n</i> = 239)
Admitted to hospital	36 (11)	95 (40)
Admitted to ICU	26 (8)	53 (22)
Discharged alive	7 (2.2)	6 (2.5)
Discharged with CPC 1–2	6 (1.8)	4 (1.7)
Discharged if admitted ICU	27%	11%

Secondary analysis, epinephrine

	Odds Ratio Survival	95% CI
Initial VF/VT	15.60	7.75, 31.41
Witnessed arrest	2.33	1.08, 5.01
Male gender	1.59	0.79, 3.20
Age (per increased year)	0.96	0.95, 0.98
Response interval (per increased minute)	0.81	0.75, 0.88
Adrenaline	0.52	0.29, 0.92
Intubation	0.38	0.20, 0.72

Prehospital Assessment of the Role of Adrenaline: Measuring the Effectiveness of Drug administration In Cardiac arrest (PARAMEDIC)

- Randomised, placebo-controlled trial
- Primary endpoint: 30-day survival
- To be completed in 2018





Antiarrhythmics

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Antiarrhythmics

- In patients with VF/pVT:
- Amiodarone 300 mg should be given after 3 defibrillation attempts
 - A further 150-mg dose may be given after 5 defibrillation attempts
- Lidocaine 1 mg kg⁻¹ may be used as an alternative if amiodarone is not available

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Amiodarone, Lidocaine, or Placebo in Out-of-Hospital Cardiac Arrest

- Double-blind RCT (*ALPS* trial) in VF/pVT OHCA
- After ≥ 1 ineffective DC shock patients were randomised (1:1:1) to:
 - Amiodarone, Lidocaine or Placebo
- Primary end point: survival to discharge

ALPS trial: characteristics

- Captisol-enabled amiodarone (Nexterone[®] Baxter)
 - To avoid the haemodynamic effects of Polysorbate-80
- Either i.v. or i.o. administration route
- Powered to detect a 6% absolute difference between amiodarone and placebo
 - 3000 patients needed

ALPS trial: key process variables

Characteristic	Amiodarone (N=974)	Lidocaine (N=993)	Placebo (N=1059)
Time from initial call to first dose of trial drug in patients with non-EMS-witnessed cardiac arrest — min	19.3±7.1	19.3±7.6	19.3±7.3
Time from cardiac arrest to first dose of trial drug in patients with EMS-witnessed arrest — min	11.7±5.8	12.1±6.6	12.1±6.6
Trial drug given through intraosseous access — no./total no. (%)†	212/974 (21.8)	220/991 (22.2)	229/1054 (21.7)
No. of shocks before first dose of trial drug — median (IQR)	3 (2–4)	3 (2–4)	3 (2–4)

Rates of hospital admission

n = 3026

Amiodarone vs. Placebo

Difference
(95% CI)

P Value

*percentage
points*

6.0
(1.7 to 10.3)

0.01

Lidocaine vs. Placebo

Difference
(95% CI)

P Value

*percentage
points*

7.4
(3.1 to 11.6)

<0.001

Amiodarone vs. Lidocaine

Difference
(95% CI)

P Value

*percentage
points*

−1.3
(−5.7 to 3.1)

0.55

Rates of survival to discharge

n = 3026

Amiodarone vs. Placebo		Lidocaine vs. Placebo		Amiodarone vs. Lidocaine	
Difference (95% CI)	P Value	Difference (95% CI)	P Value	Difference (95% CI)	P Value
<i>percentage points</i>		<i>percentage points</i>		<i>percentage points</i>	
3.2 (-0.4 to 7.0)	0.08	2.6 (-1.0 to 6.3)	0.16	0.7 (-3.2 to 4.7)	0.70

Limitations

- Underpowered (predicted absolute difference in survival to discharge 6.3%; actual 3.4%)
 - $\approx 9,000$ patients needed
- Nexterone used instead of Polysorbate-80
 - Generalisability?
- Survival according to administration route?

Survival to discharge according to route of administration

	Amiodarone	Lidocaine	Placebo	Amiodarone vs Placebo Difference (95% CI) P	Lidocaine vs Placebo Difference (95% CI) P	Amiodarone vs Lidocaine Difference (95% CI) P
Route of access²						
IO, n (%) [N=212;218;227]	41 (19.3%)	45 (20.6%)	51 (22.5%)	-3.1% (-10.7%, 4.5%) P=0.42	-1.8% (-9.5%, 5.8%) P=0.64	-1.3% (-8.9%, 6.3%) P=0.74
IV, n (%) [N=758;765;824]	196 (25.9%)	188 (24.6%)	170 (20.6%)	5.2% (1.1%, 9.4%) P=0.01	3.9% (-0.2%, 8.1%) P=0.06	1.3% (-3.1%, 5.6%) P=0.56

ALPS trial: conclusions

- In patients with VF/pVT resistant to ≥ 1 shock, both amiodarone and lidocaine are associated with increased survival to hospital admission as compared to placebo
- There is a non-significant trend towards increased survival to discharge as well
- Amiodarone $\equiv$ Lidocaine

Conclusions

- Both vasopressors and antiarrhythmics are still recommended in cardiac arrest
 - Same dosage and indications as per previous recommendations
- Their impact on survival to discharge needs to be confirmed
 - Adrenaline trial underway
 - Amiodarone to be retested in adequately-powered trials



Thank you for your attention!

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