Controversies in ACLS Drugs: What, When, Why

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Disclosures

- Research Grants: AHA, NIH, Kaneka, General Electric, Bristol-Myers Squibb
- ILCOR (Vice-Chair ALS)
- American Heart Association (paid and volunteer)
  - 2015 ACLS guidelines editor (paid – done Dec 2016)
  - Member, Research Task Force and Clinical – GWTG

Epinephrine in Cardiac Arrest

Epinephrine Versus Placebo

"Patients receiving adrenaline during cardiac arrest had no statistically significant improvement in the primary outcome of survival to hospital discharge although there was a significantly improved likelihood of ROSC."

Jacobs et al. *Resuscitation* 82 (2011) 1138-1143.

Epinephrine Versus Placebo

Table 2
Outcomes for patients receiving placebo versus adrenaline.

Outcome	Placebo (n = 262), n (%)	Adrenaline (n = 272), n (%)	OR (95% CI)	p-Value
ROSC achieved pre-hospital	22 (8.4%)	64 (23.5%)	3.4 (2.0–5.6)	<0.001
Admitted to hospital	34 (13.0%)	69 (25.4%)	2.3 (1.4–3.6)	<0.001
Survived to hospital discharge	5 (1.9%)	11 (4.0%)	2.2 (0.7–6.3)	0.15
CPC 1 or 2	5 (100%)	9 (81.8%)	n/a	0.31

- Pre-hospital ROSC: 8.4% (placebo) vs 23.5% (epinephrine)
- ED to hospital admission: 13% (placebo) vs 25.4% (epinephrine)
- Hospital discharge: 1.9% (placebo) vs 4% (epi) [NS] (50% relative reduction in mortality though not enough patients for statistical significance – thus, caution with interpretation of "negative" trial)

Jacobs et al. *Resuscitation* 82 (2011) 1138-1143.

VF/VT versus PEA/asystole

	Shockable ($n=245$)			Non-shockable ($n=289$)		
	Placebo	Adrenaline	OR (95% CI) p-Value	Placebo	Adrenaline	OR (95% CI) p-Value
ROSC achieved pre-hospital	17 (13.5%)	32 (26.9%)	2.4 (1.2–4.5) $p=0.009$	5 (3.7%)	32 (20.9%)	6.9 (2.6–18.4) $p<0.001$
Admitted to hospital	19 (15.1%)	33 (27.7%)	2.2 (1.2–4.1) $p=0.01$	15 (11%)	36 (23.5%)	2.5 (1.3–4.8) $p=0.005$
Survived to hospital discharge	5 (4.0%)	9 (7.6%)	2.0 (0.6–6.0) $p=0.23$	0 (0%)	2 (1.3%)	n/a

Jacobs et al. *Resuscitation* 82 (2011) 1138-1143.

VF/VT versus PEA/asystole

	Shockable ($n=245$)			Non-shockable ($n=289$)		
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Jacobs et al. *Resuscitation* 82 (2011) 1138-1143.

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

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Manabu Hasegawa, MD
Takeru Abe, MA
Takashi Nagata, MD
Yoshifumi Wakata, MD
Shogo Miyazaki, PhD

Context Epinephrine is widely used in cardiopulmonary resuscitation for out-of-hospital cardiac arrest (OHCA). However, the effectiveness of epinephrine use before hospital arrival has not been established.

Objective To evaluate the association between epinephrine use before hospital arrival and short- and long-term mortality in patients with cardiac arrest.

Design, Setting, and Participants Prospective, nonrandomized, observational propensity analysis of data from 417 188 OHCAs occurring in 2005-2008 in Japan in which patients aged 18 years or older had an OHCA before arrival of emergency medical service (EMS) personnel, were treated by EMS personnel, and were transported to the hospital.

Main Outcome Measures Return of spontaneous circulation before hospital arrival, survival at 1 month after cardiac arrest, survival with good or moderate cerebral performance (Cerebral Performance Category [CPC] 1 or 2), and survival with no, mild, or moderate neurological disability (Overall Performance Category [OPC] 1 or 2).

Results Return of spontaneous circulation before hospital arrival was observed in 2786 of 15 030 patients (18.5%) in the epinephrine group and 23 042 of 402 158 patients (5.7%) in the no-epinephrine group ($P<.001$); it was observed in 2446 (18.3%) and 1400 (10.5%) of 13 401 propensity-matched patients, respectively ($P<.001$). In the total sample, the numbers of patients with 1-month survival and survival with CPC 1 or 2 and OPC 1 or 2, respectively, were 805 (5.4%), 205 (1.4%), and 211 (1.4%) with epinephrine and 18 906 (4.7%), 8903 (2.2%), and 8831 (2.2%) without epinephrine (all $P<.001$). Corresponding numbers in propensity-matched patients were 687 (5.1%), 173 (1.3%), and 178 (1.3%) with epinephrine and 944 (7.0%), 413 (3.1%), and 410 (3.1%) without epinephrine (all $P<.001$). In all patients, a positive association was observed between prehospital epinephrine and return of spontaneous circulation before hospital arrival (adjusted odds ratio [OR], 2.36; 95% CI, 2.22-2.50; $P<.001$). In propensity-matched patients, a positive association was also observed (adjusted OR, 2.51; 95% CI, 2.24-2.80; $P<.001$). In contrast, among all patients, negative associations were observed between prehospital epinephrine and long-term outcome measures (adjusted ORs: 1-month survival, 0.46 [95% CI, 0.42-0.51]; CPC 1-2, 0.31 [95% CI, 0.26-0.36]; and OPC 1-2, 0.32 [95% CI, 0.27-0.38]; all $P<.001$). Similar negative associations were observed among propensity-matched patients (adjusted ORs: 1-month survival, 0.54 [95% CI, 0.43-0.68]; CPC 1-2, 0.21 [95% CI, 0.10-0.44]; and OPC 1-2, 0.23 [95% CI, 0.11-0.45]; all $P<.001$).

Conclusion Among patients with OHCA in Japan, use of prehospital epinephrine was significantly associated with increased chance of return of spontaneous circulation before hospital arrival but decreased chance of survival and good functional outcomes 1 month after the event.

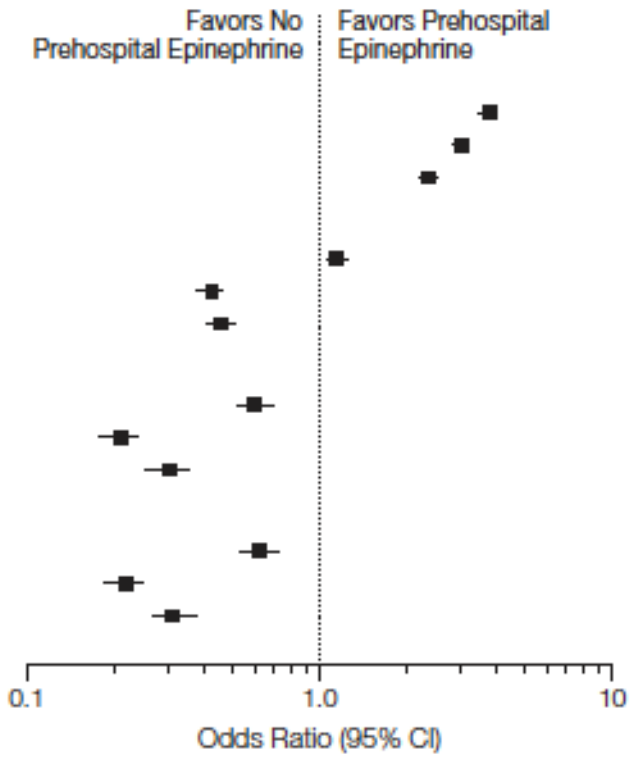
JAMA. 2012;307(11):1161-1168 www.jama.com

EPINEPHRINE IS WIDELY USED IN cardiopulmonary resuscitation (CPR) for patients with out-of-hospital cardiac arrest (OHCA).[1-3] However, its effectiveness in CPR has not been established. Epinephrine is associated with increased myocardial oxygen consumption and ventricular arrhythmias during the period after resuscitation.[4] Concern has been raised regarding increased myocardial dysfunction[5,6] and disturbed cerebral microcirculation after cardiac arrest.[7] Findings in support of epinephrine use include animal studies that show a beneficial short-term effect of epinephrine,[8,9] and evidence of increased cerebral and coronary perfusion by redirected peripheral blood flow has been reported.[10,11]

To verify the effectiveness of epinephrine in CPR, the influences of other factors, such as patients, bystanders, CPR by bystanders, life support by emergency medical service (EMS) personnel, and time from call to the scene or hospital arrival, need to be con-

Figure 2. Results of Unconditional Logistic Regression Analyses Comparing Prehospital Epinephrine Use vs No Prehospital Epinephrine Use in Patients With Out-of-Hospital Cardiac Arrest

Model	Total No. of Cases	No. (%) With Outcome		Odds Ratio (95% CI)
		Epinephrine	No Epinephrine	
ROSC				
Unadjusted	417 155	2786 (18.5)	23 042 (5.7)	3.75 (3.59-3.91)
Adjusted for selected variables[a]	412 078	2692 (18.6)	22 804 (5.7)	3.06 (2.93-3.21)
Adjusted for all covariates[b]	391 046	2556 (18.6)	21 629 (5.7)	2.36 (2.22-2.50)
1-Month survival				
Unadjusted	417 186	805 (5.4)	18 906 (4.7)	1.15 (1.07-1.23)
Adjusted for selected variables[a]	412 078	772 (5.3)	18 637 (4.7)	0.43 (0.39-0.46)
Adjusted for all covariates[b]	391 046	733 (5.3)	17 677 (4.7)	0.46 (0.42-0.51)
CPC 1 or 2				
Unadjusted	417 187	205 (1.4)	8903 (2.2)	0.61 (0.53-0.70)
Adjusted for selected variables[a]	412 078	197 (1.4)	8781 (2.2)	0.21 (0.18-0.24)
Adjusted for all covariates[b]	391 046	187 (1.4)	8329 (2.2)	0.31 (0.26-0.36)
OPC 1 or 2				
Unadjusted	417 187	211 (1.4)	8831 (2.2)	0.63 (0.55-0.73)
Adjusted for selected variables[a]	412 078	202 (1.4)	8710 (2.2)	0.22 (0.19-0.25)
Adjusted for all covariates[b]	391 046	192 (1.4)	37 732 (2.2)	0.32 (0.27-0.38)



CPC indicates Cerebral Performance Category; OPC, Overall Performance Category; ROSC, return of spontaneous circulation. Different sample sizes in the 3 models result from increasing numbers of cases with missing data as the number of independent variables increased.

[a] Selected variables included age, sex, bystander eyewitness, relationship of bystander to patient, bystander chest compression, bystander rescue breathing, use of public-access automated external defibrillator by bystander, first documented rhythm, and time from call to arrival at the scene for the model with ROSC as a dependent variable. For other models, ROSC and the above selected variables were adjusted.

[b] All covariates included all variables in Table 1 plus 46 dummy variables for the 47 prefectures in Japan for the model with ROSC as a dependent variable. For other models, ROSC, all variables in Table 1, and 46 dummy variables for the 47 prefectures in Japan were adjusted.

Conclusions

"Among patients with prehospital arrest in Japan, use of prehospital epinephrine was specifically associated with increased chance of ROSC but decreased chance of survival and good functional neurological outcome 1 month after the event ."

BMJ

BMJ 2013;347:f6829 doi: 10.1136/bmj.f6829 (Published 10 December 2013)

RESEARCH

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

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Abstract

Objectives To evaluate the effectiveness of pre-hospital adrenaline (epinephrine) administered by emergency medical services to patients with out of hospital cardiac arrest.

Design Controlled propensity matched retrospective cohort study, in which pairs of patients with or without (control) adrenaline were created with a sequential risk set matching based on time dependent propensity score.

Setting Japan's nationwide registry database of patients with out of hospital cardiac arrest registered between January 2007 and December 2010.

Participants Among patients aged 15-94 with out of hospital cardiac arrest witnessed by a bystander, we created 1990 pairs of patients with and without adrenaline with an initial rhythm of ventricular fibrillation or pulseless ventricular tachycardia (VF/VT) and 9058 pairs among those with non-VF/VT.

Main outcome measures Overall and neurologically intact survival at one month or at discharge, whichever was earlier.

Results After propensity matching, pre-hospital administration of adrenaline by emergency medical services was associated with a higher proportion of overall survival (17.0% *v* 13.4%; unadjusted odds ratio 1.34, 95% confidence interval 1.12 to 1.60) but not with neurologically intact survival (6.6% *v* 6.6%; 1.01, 0.78 to 1.30) among those with VF/VT; and higher proportions of overall survival (4.0% *v* 2.4%; odds ratio 1.72, 1.45 to 2.04) and neurologically intact survival (0.7% *v* 0.4%; 1.57, 1.04 to 2.37) among those with non-VF/VT.

Conclusions Pre-hospital administration of adrenaline by emergency medical services improves the long term outcome in patients with out of hospital cardiac arrest, although the absolute increase of neurologically intact survival was minimal.

Introduction

Pre-hospital cardiopulmonary resuscitation for patients with out of hospital cardiac arrest commonly includes administration of adrenaline (epinephrine) by emergency medical services. Despite extensive research on its effectiveness, there is no definite evidence to support its routine use. Whether pre-hospital use of adrenaline improves long term prognoses remains uncertain, although it unequivocally increases return of spontaneous circulation.[1 2] Recent randomised controlled trials showed slightly favourable (but non-significant) effects of pre-hospital adrenaline in improving long term survival,[3 4] whereas observational studies have not indicated any significant favourable effects and some large scale registry based studies have even shown detrimental long term effects.[5-10]

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Extra material supplied by the author [posted as supplied] (see http://www.bmj.com/content/347/bmj.f6829?tab=related#webextra)

Appendix 1: Evaluation of patient imbalance between groups after propensity score matching

Table 3| **Logistic regression analyses among matched patients. Odds ratios for comparison between patients with out of hospital cardiac arrest who received pre-hospital adrenaline (epinephrine) administered by emergency medical services and controls**

	Odds ratio (95% CI)	
	Unadjusted*	**Adjusted†**
Ventricular fibrillation/ventricular tachycardia		
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)
Non-ventricular fibrillation/ventricular tachycardia		
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)

*Bivariate analysis after propensity score matching.

†Adjusted for presumed cause (cardiac/non-cardiac origin), time from onset of CPR by emergency medical services to hospital arrival, and type of bystander (family/non-family), and time from onset of CPR to first defibrillation with multivariate logistic regression model.

‡Power=0.87.

§Power not calculated because OR was nearly 1.

¶Power >0.99.

**Power=0.50.

Conclusions

"Prehospital administration of adrenaline (epinephrine) improves long term outcome of patients with out of hospital cardiac arrest."

So, what was the difference?

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- Time dependent propensity score analysis → risk set matching

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- Time dependent propensity score analysis → risk set matching

- Issues without risk set matching:
  - A → ROSC with defibrillation at 3 minutes (no epi)
  - B → ROSC with first-dose epinephrine at 15 minutes
  - C → ROSC with first-dose epinephrine at 2 minutes

Conclusion

"Our findings contradict the harmful long term effects of adrenaline shown in previous observational studies, including a recent Japanese study that used the SAME database"

VF/VT versus PEA/asystole

	Shockable ($n=245$)			Non-shockable ($n=289$)		
	Placebo	Adrenaline	OR (95% CI) p-Value	Placebo	Adrenaline	OR (95% CI) p-Value
ROSC achieved pre-hospital	17 (13.5%)	32 (26.9%)	2.4 (1.2–4.5) $p=0.009$	3.7%	20.9%	.6–18.4) 001
Admitted to hospital	19 (15.1%)	33 (27.7%)	2.2 (1.2–4.1) $p=0.01$	15 (11%)	36 (23.5%)	2.5 (1.3–4.8) $p=0.005$
Survived to hospital discharge	5 (4.0%)	9 (7.6%)	2.0 (0.6–6.0) $p=0.23$	0 (0%)	2 (1.3%)	n/a

Jacobs et al. *Resuscitation* 82 (2011) 1138-1143.

Time To Epinephrine – PEA/Asystole

BMJ 2014;348:g3028 doi: 10.1136/bmj.g3028 (Published 20 May 2014)

RESEARCH

Time to administration of epinephrine and outcome after in-hospital cardiac arrest with non-shockable rhythms: retrospective analysis of large in-hospital data registry

OPEN ACCESS

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Abstract

Objective To determine if earlier administration of epinephrine (adrenaline) in patients with non-shockable cardiac arrest rhythms is associated with increased return of spontaneous circulation, survival, and neurologically intact survival.

Design Post hoc analysis of prospectively collected data in a large multicenter registry of in-hospital cardiac arrests (Get With The Guidelines-Resuscitation).

Setting We utilized the Get With The Guidelines-Resuscitation database (formerly National Registry of Cardiopulmonary Resuscitation, NRCPR). The database is sponsored by the American Heart Association (AHA) and contains prospective data from 570 American hospitals collected from 1 January 2000 to 19 November 2009.

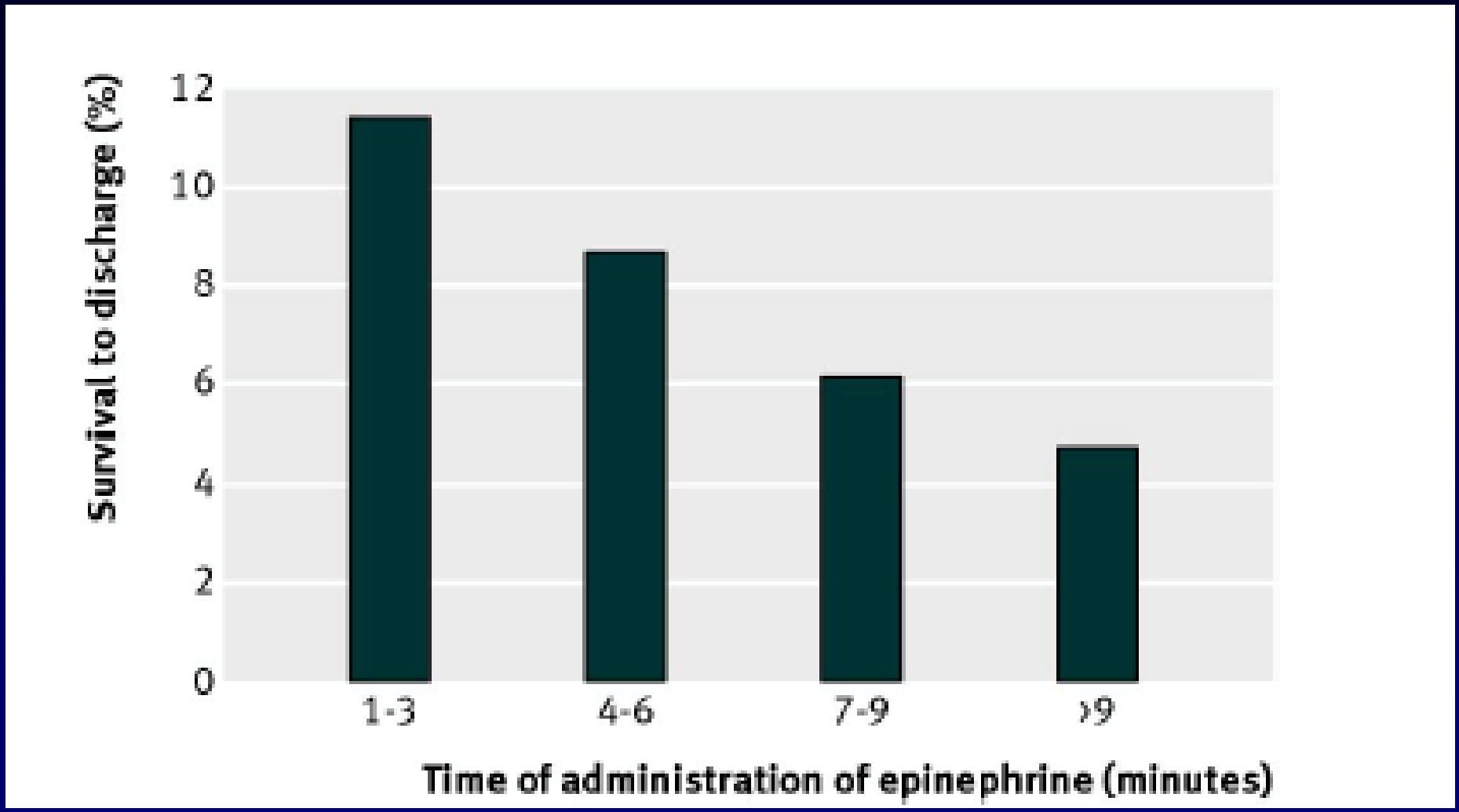
Participants 119 978 adults from 570 hospitals who had a cardiac arrest in hospital with asystole (55%) or pulseless electrical activity (45%) as the initial rhythm. Of these, 83 490 arrests were excluded because they took place in the emergency department, intensive care unit, or surgical or other specialty unit, 10 775 patients were excluded because of missing or incomplete data, 524 patients were excluded because they had a repeat cardiac arrest, and 85 patients were excluded as they received vasopressin before the first dose of epinephrine. The main study population therefore comprised 25 095 patients. The mean age was 72, and 57% were men.

Main outcome measures The primary outcome was survival to hospital discharge. Secondary outcomes included sustained return of spontaneous circulation, 24 hour survival, and survival with favorable neurologic status at hospital discharge.

Results 25 095 adults had in-hospital cardiac arrest with non-shockable rhythms. Median time to administration of the first dose of epinephrine was 3 minutes (interquartile range 1-5 minutes). There was a stepwise decrease in survival with increasing interval of time to epinephrine (analyzed by three minute intervals): adjusted odds ratio 1.0 for 1-3 minutes (reference group); 0.91 (95% confidence interval 0.82 to 1.00; P=0.055) for 4-6 minutes; 0.74 (0.63 to 0.88; P<0.001) for 7-9 minutes; and 0.63 (0.52 to 0.76; P<0.001) for >9 minutes. A similar stepwise effect was observed across all outcome variables.

Conclusions In patients with non-shockable cardiac arrest in hospital, earlier administration of epinephrine is associated with a higher

Time To Epinephrine – PEA/Asystole



(Donnino et al. *British Medical Journal 2014*)

Original Investigation | CARING FOR THE CRITICALLY ILL PATIENT

Time to Epinephrine and Survival After Pediatric In-Hospital Cardiac Arrest

Lars W. Andersen, MD; Katherine M. Berg, MD; Brian Z. Saindon, BS; Joseph M. Massaro, PhD; Tia T. Raymond, MD; Robert A. Berg, MD; Vinay M. Nadkarni, MD; Michael W. Donnino, MD; for the American Heart Association Get With the Guidelines–Resuscitation Investigators

IMPORTANCE Delay in administration of the first epinephrine dose is associated with decreased survival among adults after in-hospital, nonshockable cardiac arrest. Whether this association is true in the pediatric in-hospital cardiac arrest population remains unknown.

OBJECTIVE To determine whether time to first epinephrine dose is associated with outcomes in pediatric in-hospital cardiac arrest.

DESIGN, SETTING, AND PARTICIPANTS We performed an analysis of data from the Get With the Guidelines–Resuscitation registry. We included US pediatric patients (age <18 years) with an in-hospital cardiac arrest and an initial nonshockable rhythm who received at least 1 dose of epinephrine. A total of 1558 patients (median age, 9 months [interquartile range [IQR], 13 days–5 years]) were included in the final cohort.

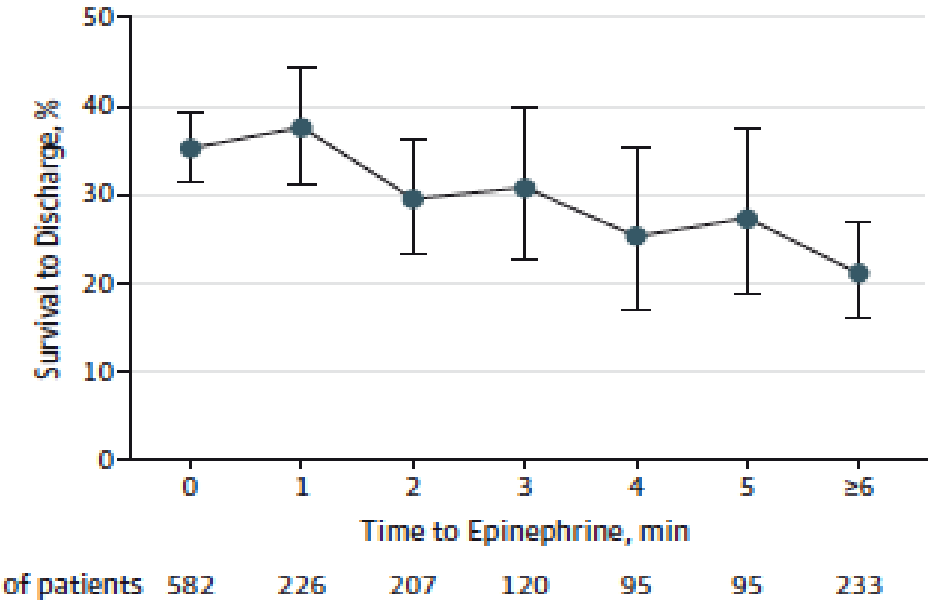
EXPOSURE Time to epinephrine, defined as time in minutes from recognition of loss of pulse to the first dose of epinephrine.

MAIN OUTCOMES AND MEASURES The primary outcome was survival to hospital discharge. Secondary outcomes included return of spontaneous circulation (ROSC), survival at 24 hours, and neurological outcome. A favorable neurological outcome was defined as a score of 1 to 2 on the Pediatric Cerebral Performance Category scale.

RESULTS Among the 1558 patients, 487 (31.3%) survived to hospital discharge. The median time to first epinephrine dose was 1 minute (IQR, 0-4; range, 0-20; mean [SD], 2.6 [3.4] minutes). Longer time to epinephrine administration was associated with lower risk of survival to discharge in multivariable analysis (multivariable-adjusted risk ratio [RR] per minute delay, 0.95 [95% CI, 0.93-0.98]). Longer time to epinephrine administration was also associated with decreased risk of ROSC (multivariable-adjusted RR per minute delay, 0.97 [95% CI, 0.96-0.99]), decreased risk of survival at 24 hours (multivariable-adjusted RR per minute delay, 0.97 [95% CI, 0.95-0.99]), and decreased risk of survival with favorable neurological outcome (multivariable-adjusted RR per minute delay, 0.95 [95% CI, 0.91-0.99]). Patients with time to epinephrine administration of longer than 5 minutes (233/1558) compared with those with time to epinephrine of 5 minutes or less (1325/1558) had lower risk of in-hospital survival to discharge (21.0% [49/233] vs 33.1% [438/1325]; multivariable-adjusted RR, 0.75 [95% CI, 0.60-0.93]; $P = .01$).

CONCLUSIONS AND RELEVANCE Among children with in-hospital cardiac arrest with an initial nonshockable rhythm who received epinephrine, delay in administration of epinephrine was associated with decreased chance of survival to hospital discharge, ROSC, 24-hour survival, and survival to hospital discharge with a favorable neurological outcome.

Figure 3. Time to Epinephrine and Survival to Hospital Discharge After Pediatric In-Hospital Nonshockable Cardiac Arrest (N = 1558)



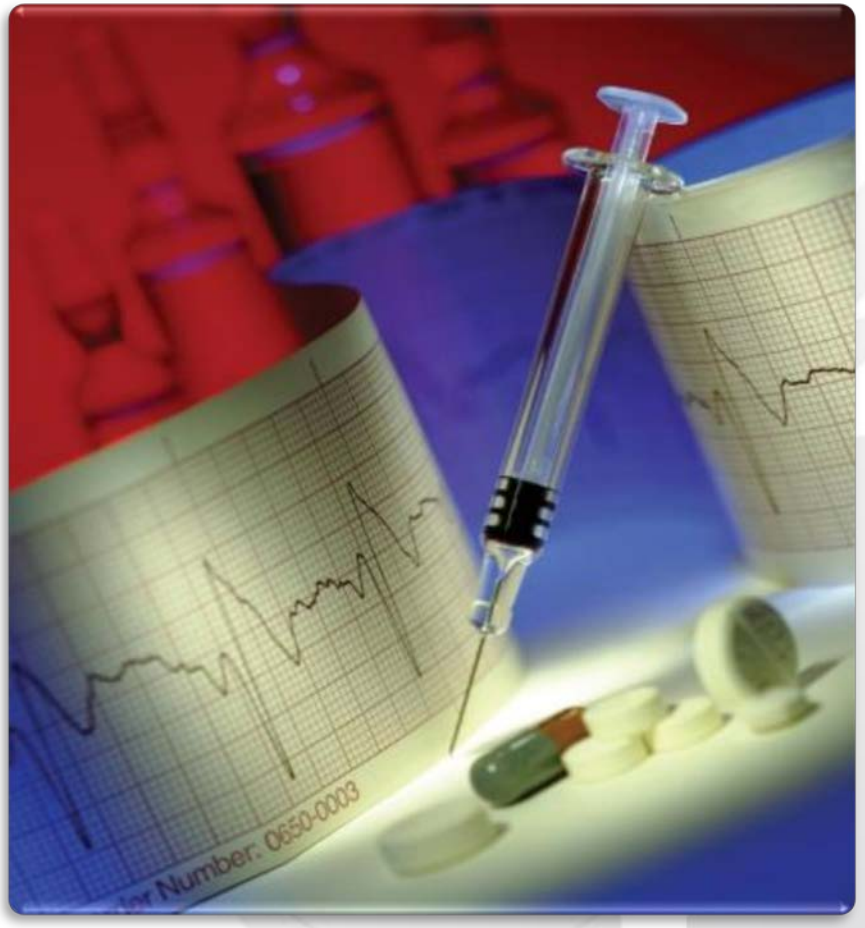
Longer time to epinephrine administration was associated with lower risk of survival to discharge in multivariable analysis (risk ratio per minute delay, 0.95 [95% CI, 0.93-0.98]; $P < .001$). Error bars indicate exact binomial 95% confidence intervals.

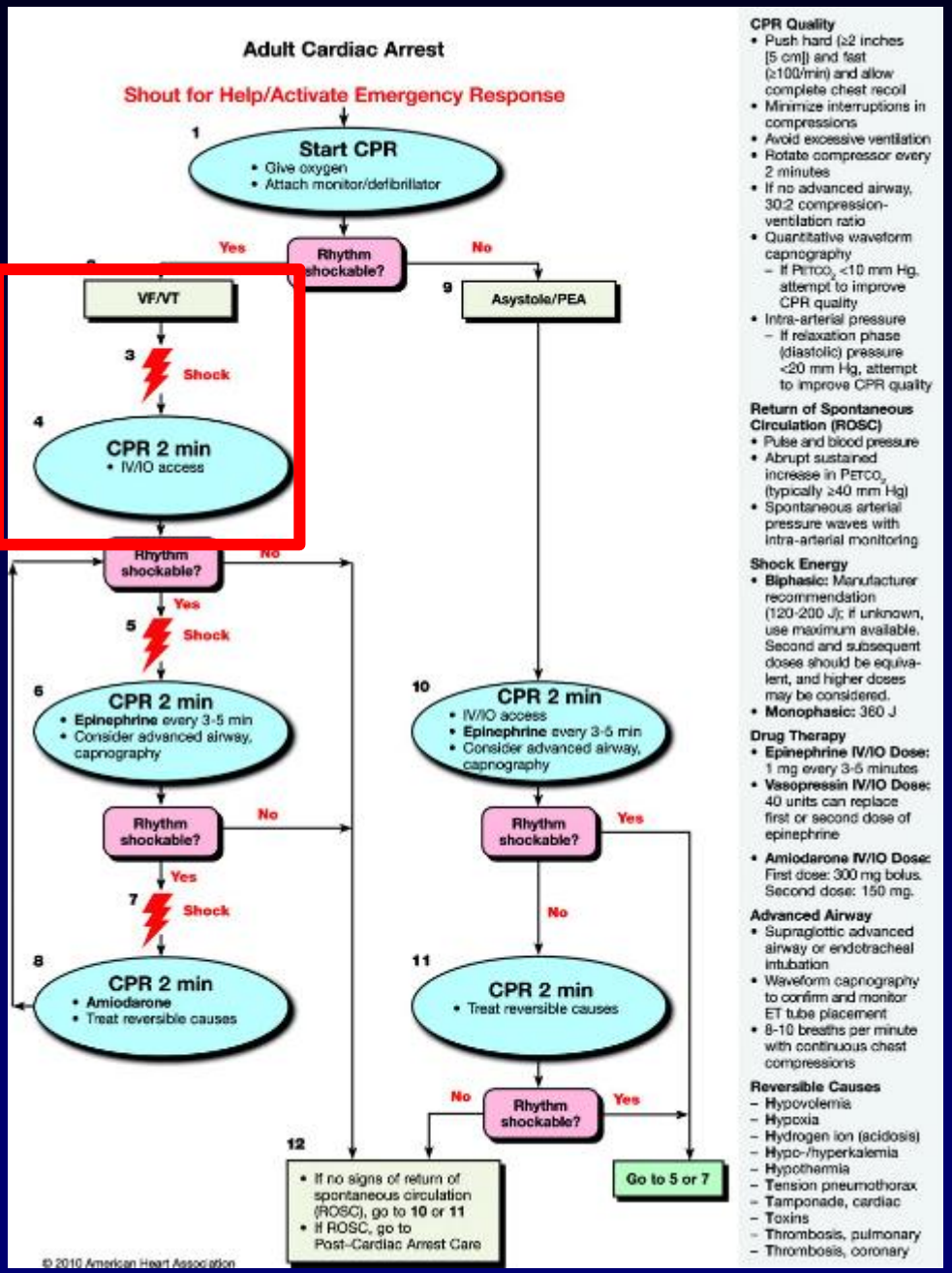
VASOPRESSORS FOR RESUSCITATION: EPINEPHRINE

American Heart Association.
GUIDELINES 2015 CPR & ECC

- Administer epinephrine as soon as feasible after the onset of cardiac arrest due to an initial nonshockable rhythm

- Association between early administration of epinephrine and increased ROSC, survival to hospital discharge, and neurologically intact survival




Adult Cardiac Arrest
Shout for Help/Activate Emergency Response
1
Start CPR
• Give oxygen
• Attach monitor/defibrillator
Rhythm shockable?
Yes
No
VF/VT
9
Asystole/PEA
3
Shock
4
CPR 2 min
• IV/IO access
Rhythm shockable?
No
Yes
5
Shock
6
CPR 2 min
• Epinephrine every 3-5 min
• Consider advanced airway, capnography
10
CPR 2 min
• IV/IO access
• Epinephrine every 3-5 min
• Consider advanced airway, capnography
Rhythm shockable?
No
Yes
7
Shock
Rhythm shockable?
Yes
No
8
CPR 2 min
• Amiodarone
• Treat reversible causes
11
CPR 2 min
• Treat reversible causes
No
Rhythm shockable?
Yes
12
• If no signs of return of spontaneous circulation (ROSC), go to 10 or 11
• If ROSC, go to Post-Cardiac Arrest Care
Go to 5 or 7
© 2010 American Heart Association
CPR Quality
• Push hard (≥2 inches [5 cm]) and fast (≥100/min) and allow complete chest recoil
• Minimize interruptions in compressions
• Avoid excessive ventilation
• Rotate compressor every 2 minutes
• If no advanced airway, 30:2 compression-ventilation ratio
• Quantitative waveform capnography
– If PETCO2 <10 mm Hg, attempt to improve CPR quality
• Intra-arterial pressure
– If relaxation phase (diastolic) pressure <20 mm Hg, attempt to improve CPR quality
Return of Spontaneous Circulation (ROSC)
• Pulse and blood pressure
• Abrupt sustained increase in PETCO2 (typically ≥40 mm Hg)
• Spontaneous arterial pressure waves with intra-arterial monitoring
Shock Energy
• Biphasic: Manufacturer recommendation (120-200 J); if unknown, use maximum available. Second and subsequent doses should be equivalent, and higher doses may be considered.
• Monophasic: 360 J
Drug Therapy
• Epinephrine IV/IO Dose: 1 mg every 3-5 minutes
• Vasopressin IV/IO Dose: 40 units can replace first or second dose of epinephrine
• Amiodarone IV/IO Dose: First dose: 300 mg bolus. Second dose: 150 mg.
Advanced Airway
• Supraglottic advanced airway or endotracheal intubation
• Waveform capnography to confirm and monitor ET tube placement
• 8-10 breaths per minute with continuous chest compressions
Reversible Causes
– Hypovolemia
– Hypoxia
– Hydrogen ion (acidosis)
– Hypo-/hyperkalemia
– Hypothermia
– Tension pneumothorax
– Tamponade, cardiac
– Toxins
– Thrombosis, pulmonary
– Thrombosis, coronary

Early administration of epinephrine (adrenaline) in patients with cardiac arrest with initial shockable rhythm in hospital: propensity score matched analysis

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Additional material is published online only. To view please visit the journal online.

Cite this as: *BMJ* 2016;353:i1577
http://dx.doi.org/10.1136/bmj.i1577

Accepted: 24 February 2016

ABSTRACT

OBJECTIVES

To evaluate whether patients who experience cardiac arrest in hospital receive epinephrine (adrenaline) within the two minutes after the first defibrillation (contrary to American Heart Association guidelines) and to evaluate the association between early administration of epinephrine and outcomes in this population.

DESIGN

Prospective observational cohort study.

SETTING

Analysis of data from the Get With The Guidelines-Resuscitation registry, which includes data from more than 300 hospitals in the United States.

PARTICIPANTS

Adults in hospital who experienced cardiac arrest with an initial shockable rhythm, including patients who had a first defibrillation within two minutes of the cardiac arrest and who remained in a shockable rhythm after defibrillation.

INTERVENTION

Epinephrine given within two minutes after the first defibrillation.

MAIN OUTCOME MEASURES

Survival to hospital discharge. Secondary outcomes included return of spontaneous circulation and survival to hospital discharge with a good functional outcome. A propensity score was calculated for the receipt of epinephrine within two minutes after the first defibrillation, based on multiple characteristics of patients, events, and hospitals. Patients who received epinephrine at either zero, one, or two minutes after the first defibrillation were then matched on the propensity score with patients who were "at risk" of receiving epinephrine within the same minute but who did not receive it.

RESULTS

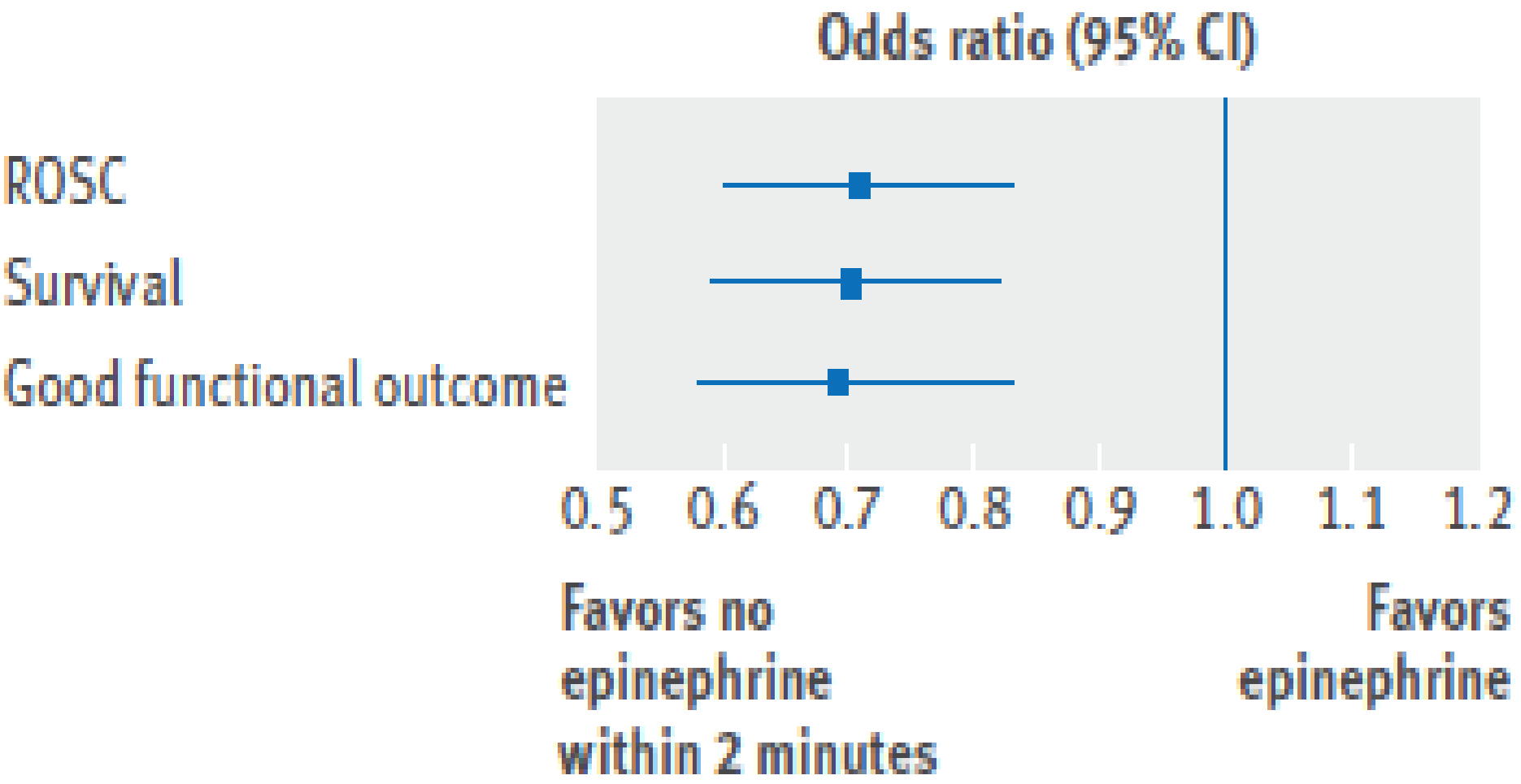
2978 patients were matched on the propensity score, and the groups were well balanced. 1510 (51%) patients received epinephrine within two minutes after the first defibrillation, which is contrary to current American Heart Association guidelines. Epinephrine given within the first two minutes after the first defibrillation was associated with decreased odds of survival in the propensity score matched analysis (odds ratio 0.70, 95% confidence interval 0.59 to 0.82; P<0.001). Early epinephrine administration was also associated with a decreased odds of return of spontaneous circulation (0.71, 0.60 to 0.83; P<0.001) and good functional outcome (0.69, 0.58 to 0.83; P<0.001).

CONCLUSION

Half of patients with a persistent shockable rhythm received epinephrine within two minutes after the first defibrillation, contrary to current American Heart Association guidelines. The receipt of epinephrine within two minutes after the first defibrillation was associated with decreased odds of survival to hospital discharge as well as decreased odds of return of spontaneous circulation and survival to hospital discharge with a good functional outcome.

Introduction

Epinephrine (adrenaline) has been used in resuscitation after cardiac arrest for decades and the provision of epinephrine is currently suggested by both the American Heart Association (AHA) and the European Resuscitation Council (ERC) in both shockable and non-shockable rhythms.[1,2] Despite this, the utility of



Early administration of epinephrine in patients with cardiac arrest and initial shockable rhythm. Andersen LW, Kurth T, Chase M, Berg KM, Cocchi MN, Callaway C, Donnino MW; BMJ. 2016 6;353

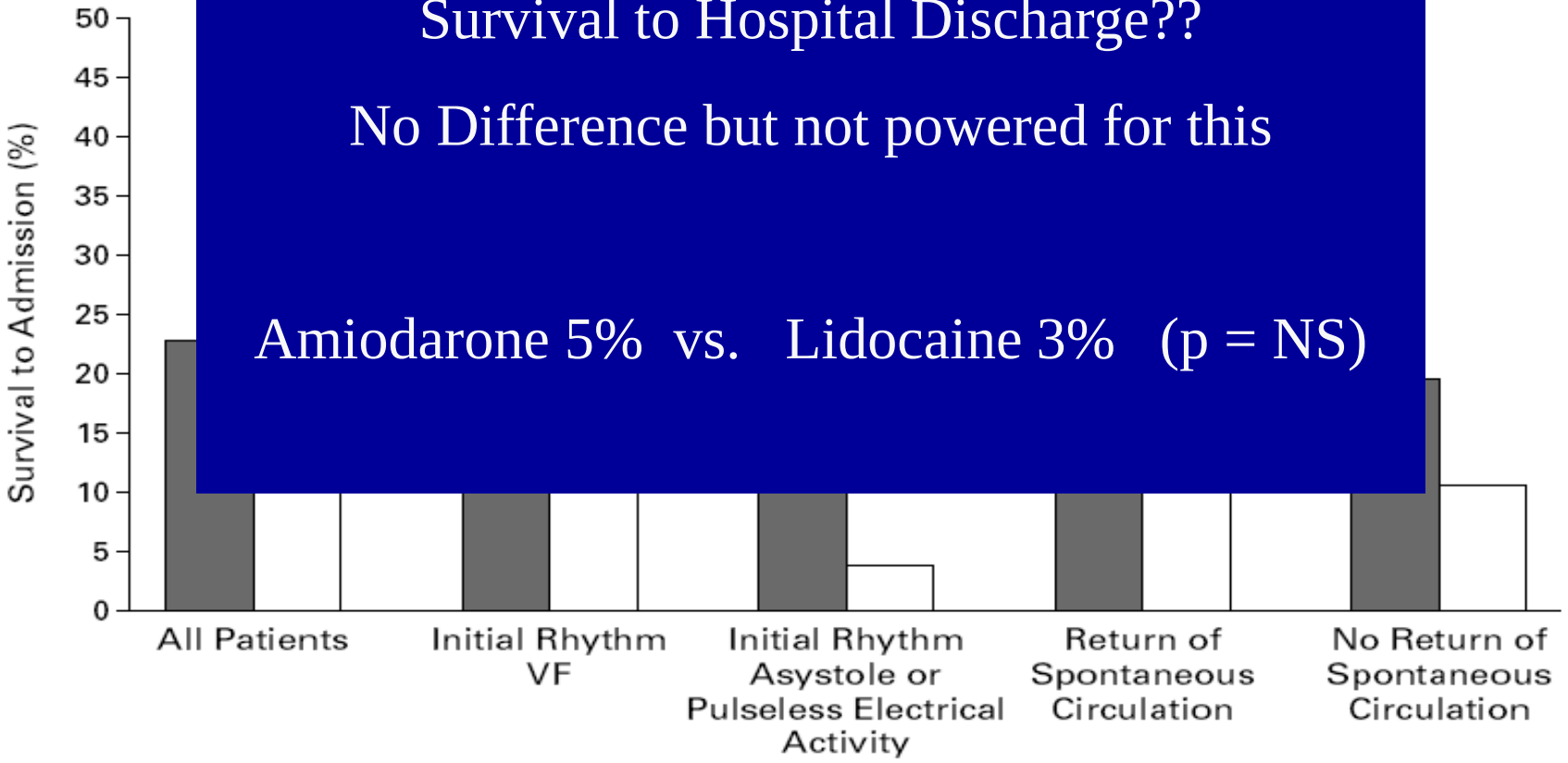
Epinephrine Conclusions

- Controversy: Epinephrine "not proven" and may be harmful or counterproductive

- Current Guidelines:
  - PEA/asystole → early and every 3-5 min
  - VFIB/VT → after the 2nd/3rd defibrillation

- MY opinion: Maybe it depends – timing, context, rhythm, alternative options/etiology of arrest may all factor in…Dosage also unknown…However, I don't think anyone should die without epinephrine

Amiodarone Vs. Lidocaine



No. Surviving/Total No.					
Amiodarone	41/80	35/141	4/34	10/24	31/156
Lidocaine	20/167	19/134	1/27	3/11	17/156

(Dorian et. al. NEJM)

Amiodarone vs. Lidocaine

- Bottom Line: Amiodarone currently has "the nod" but the study was small and had some flaws including provision of lipoprotein with deleterious effects to lidocaine group. Thus, giving lidocaine is acceptable alternative

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- Currently, being reproduced with Phase III trial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

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

P.J. Kudenchuk, S.P. Brown, M. Daya, T. Rea, G. Nichol, L.J. Morrison, B. Leroux, C. Vaillancourt, L. Wittwer, C.W. Callaway, J. Christenson, D. Egan, J.P. Ornato, M.L. Weisfeldt, I.G. Stiell, A.H. Idris, T.P. Aufderheide, J.V. Dunford, M.R. Colella, G.M. Vilke, A.M. Brienza, P. Desvigne-Nickens, P.C. Gray, R. Gray, N. Seals, R. Straight, and P. Dorian, for the Resuscitation Outcomes Consortium Investigators*

Amiodarone vs. Lidocaine

Table 3. Outcomes According to Trial Group in the Per-Protocol Population.*

Outcome	Amiodarone (N=974)	Lidocaine (N=993)	Placebo (N=1059)	Amiodarone vs. Placebo		Lidocaine vs. Placebo		Amiodarone vs. Lidocaine	
				Difference (95% CI)	P Value	Difference (95% CI)	P Value	Difference (95% CI)	P Value
				percentage points		*percentage points*		*percentage points*	
Primary outcome: survival to discharge — no./total no. (%)†	237/970 (24.4)	233/985 (23.7)	222/1056 (21.0)	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
Secondary outcome: modified Rankin score ≤3 — no./total no. (%)‡	182/967 (18.8)	172/984 (17.5)	175/1055 (16.6)	2.2 (−1.1 to 5.6)	0.19	0.9 (−2.4 to 4.2)	0.59	1.3 (−2.1 to 4.8)	0.44
Mechanistic (exploratory) outcomes									
Return of spontaneous circulation at ED arrival — no./total no. (%)	350/974 (35.9)	396/992 (39.9)	366/1059 (34.6)	1.4 (−2.8 to 5.5)	0.52	5.4 (1.2 to 9.5)	0.01	−4.0 (−8.3 to 0.3)	0.07
Admitted to hospital — no. (%)	445 (45.7)	467 (47.0)	420 (39.7)	6.0 (1.7 to 10.3)	0.01	7.4 (3.1 to 11.6)	<0.001	−1.3 (−5.7 to 3.1)	0.55
Modified Rankin score in all patients‡	5.0±1.9	5.1±1.8	5.2±1.8	−0.14 (−0.30 to 0.02)	0.09	−0.06 (−0.22 to 0.10)	0.45	−0.08 (−0.24 to 0.08)	0.34

Amiodarone vs. Lidocaine

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Anti-Arrythmic Conclusions

- My take: Antiarrhythmic drugs appear to have some benefit compared to placebo, however there does not appear to be a difference between amiodarone and lidocaine

- Could we have made some assumptions about the IO that are not true?