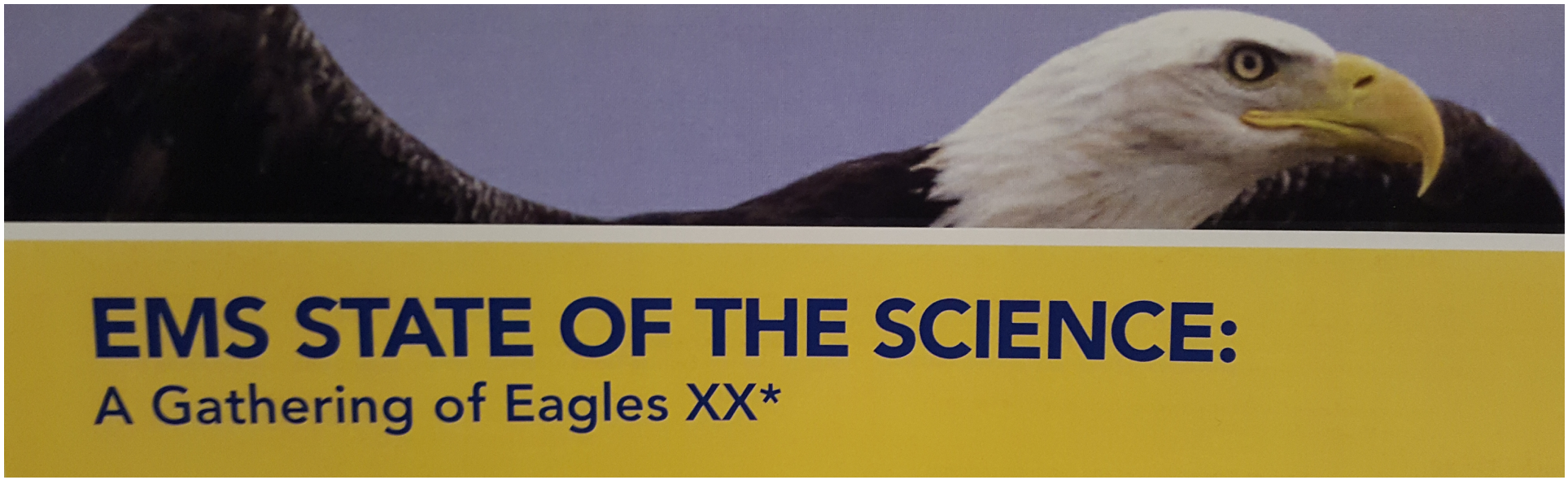
Doubling Down on Nitro is not a Bad Bet

Scott Gilmore, MD, EMT-P, FACEP, FAEMS

Medical Director

St. Louis Fire Department

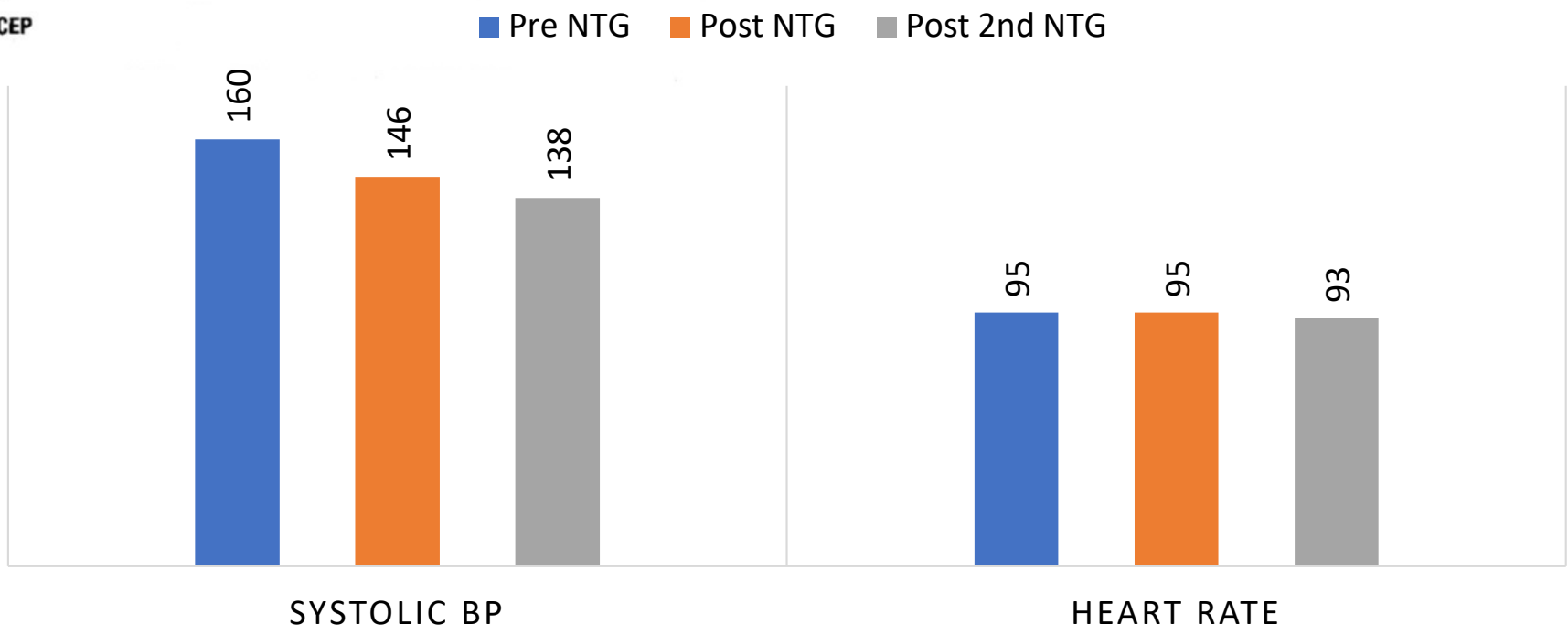


What does the asterisk truly mean?

STAY THIRSTY FOR KNOWLEDGE, *my friends*

Safety of Prehospital Nitroglycerin

[redacted]
Richard Wuerz, MD
Greg Swope, EMT-P
Steven Meador, MD, FACEP
C James Holliman, MD, FACEP
Gregory S Roth, MD

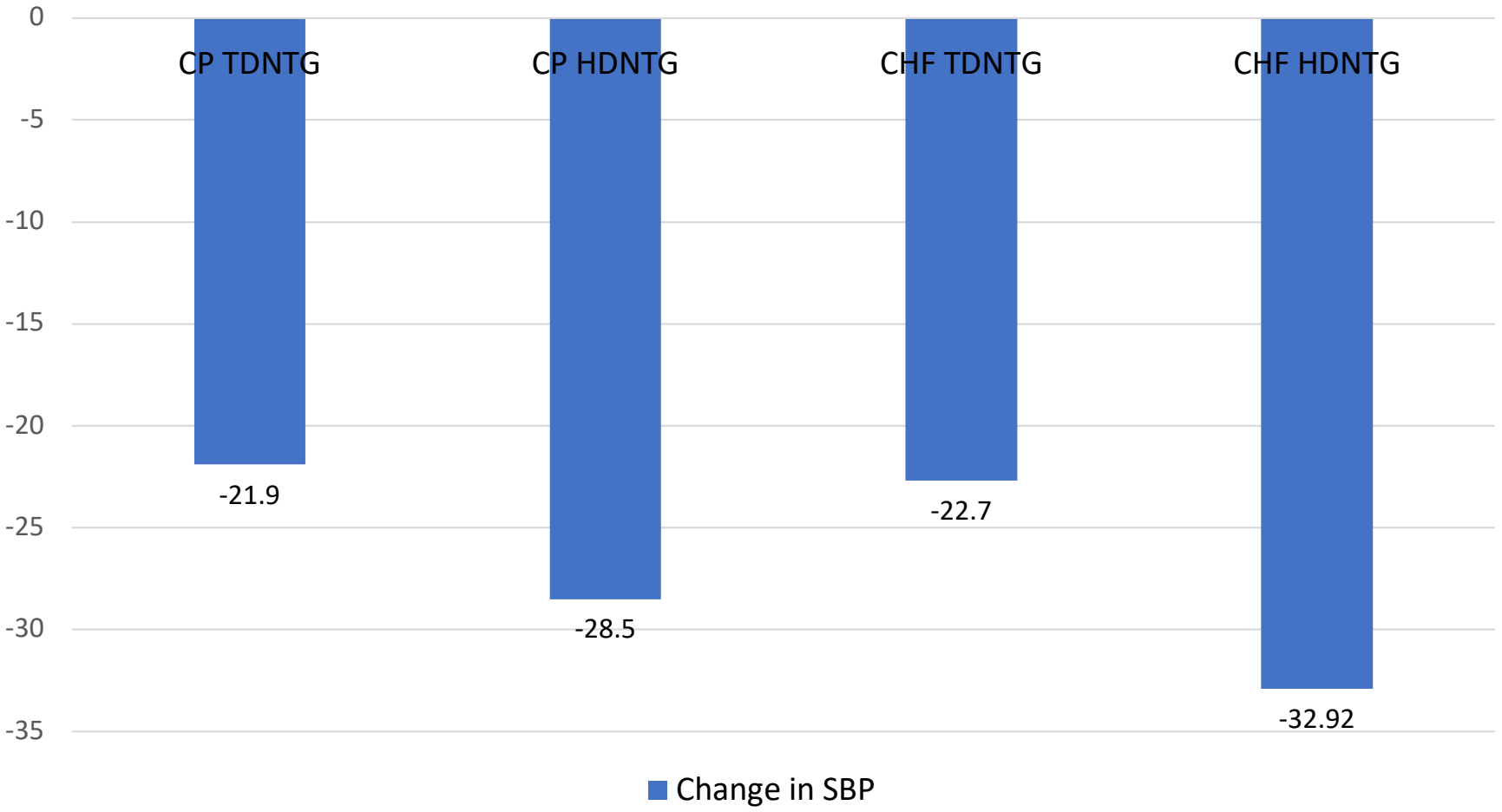


Adverse Event Rate 1.33%

Ann Emerg Med. 1994;23 (1):31-36.

Rates of Nitroglycerin Administration for EMS Treatment of Chest Pain and Congestive Heart Failure [Abstract]

Cole JS, Brice JH, Alonso-Serra HM and Delbridge TR



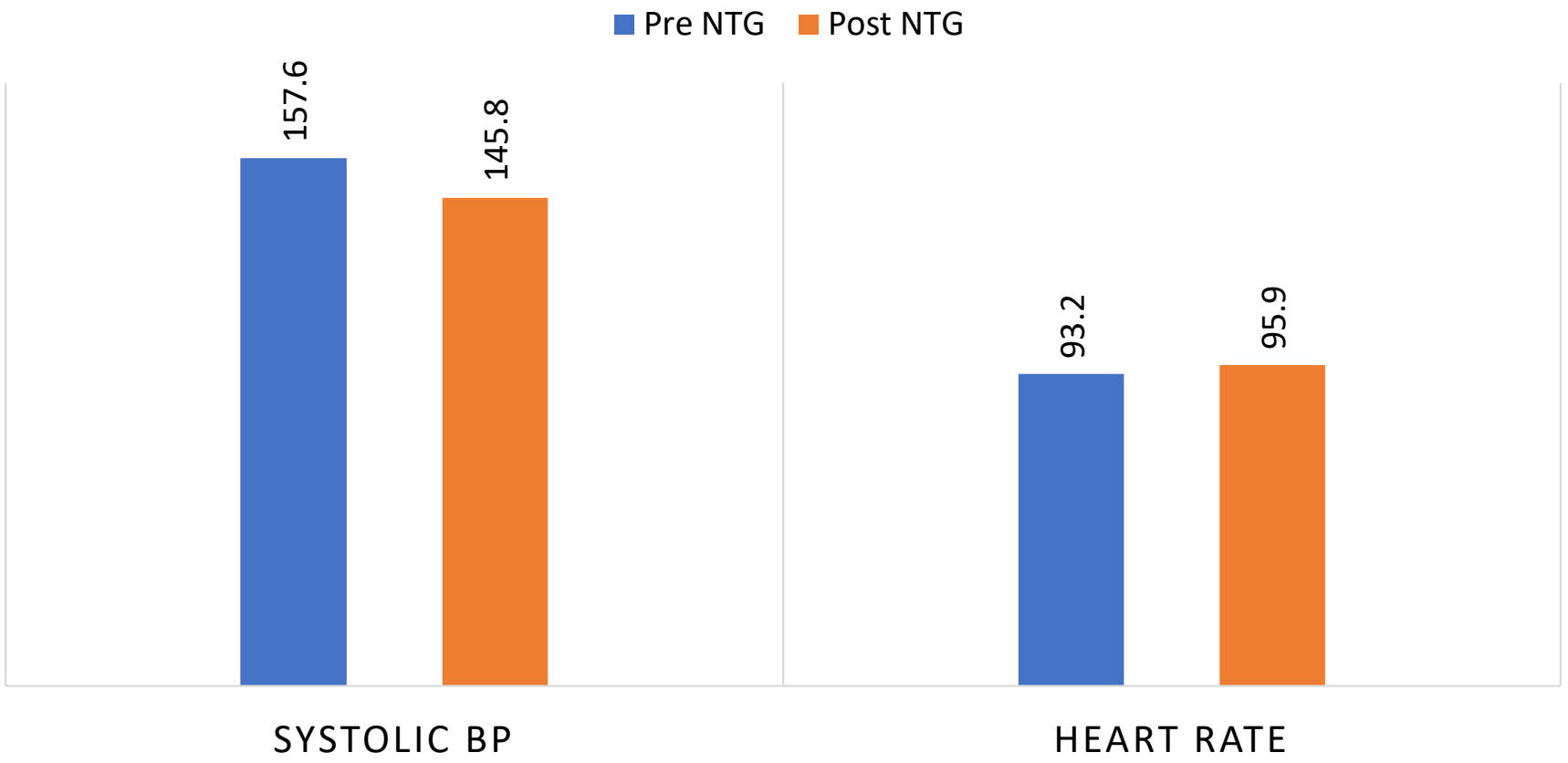
Adverse Event Rate 0.4% in HDNTG and 3.2% in TDNTG

Prehosp Emerg Care. 1998;2:255.

Original Articles

Effects of Prehospital Nitroglycerin on Hemodynamics and Chest Pain Intensity

Steven Engelberg, RPA-C, Adam J. Singer, MD, Janice Moldashel, MD,
Joseph Sciammarella, MD, Henry C. Thode, PhD, Mark Henry, MD



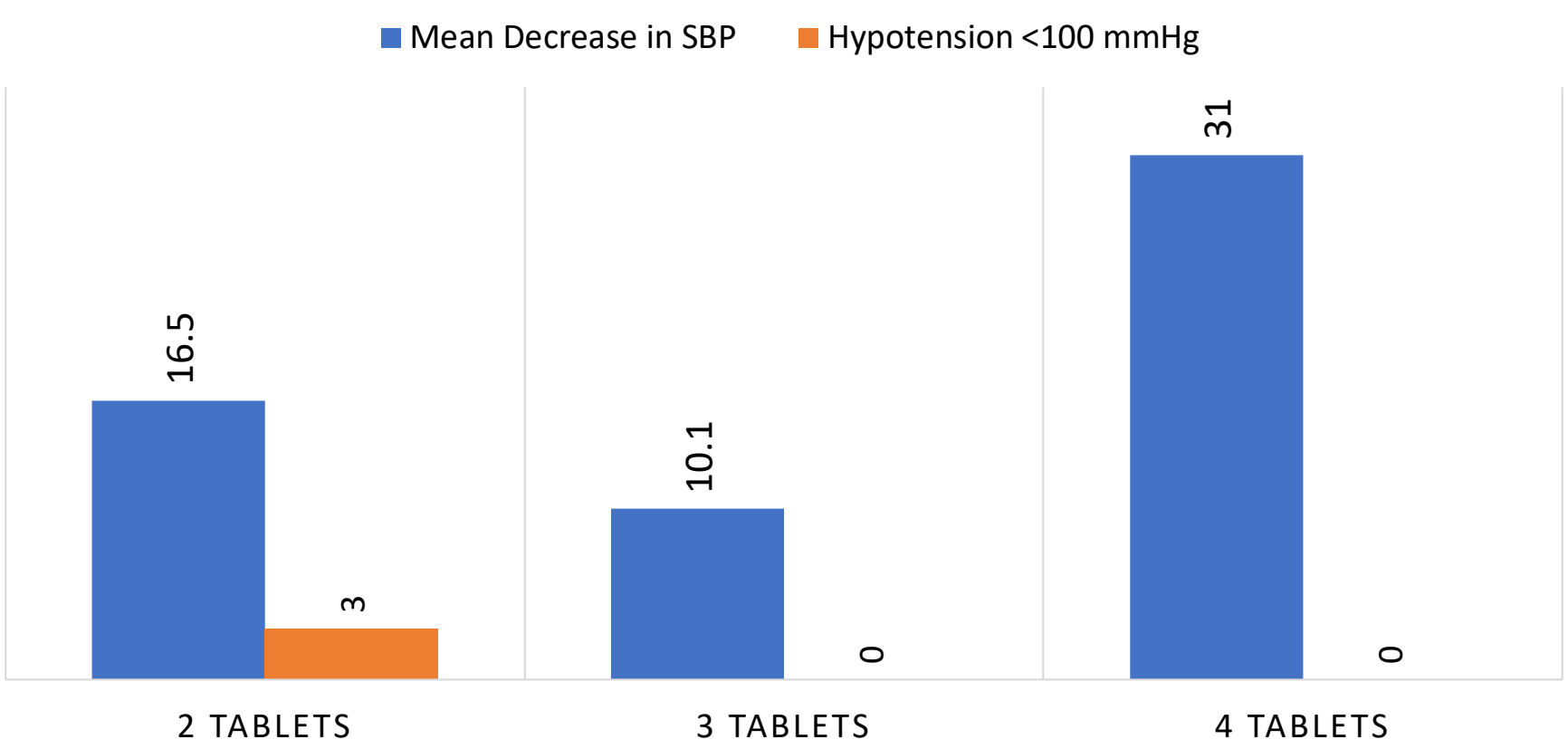
Adverse Event Rate 0.7%

Prehosp Emerg Care. 2000;4:290-293.

ORIGINAL RESEARCH

Prehospital High-dose Sublingual Nitroglycerin Rarely Causes Hypotension

Brian M. Clemency, DO; Jeffrey J. Thompson, MD; Gina N. Tundo; Heather A. Lindstrom, PhD



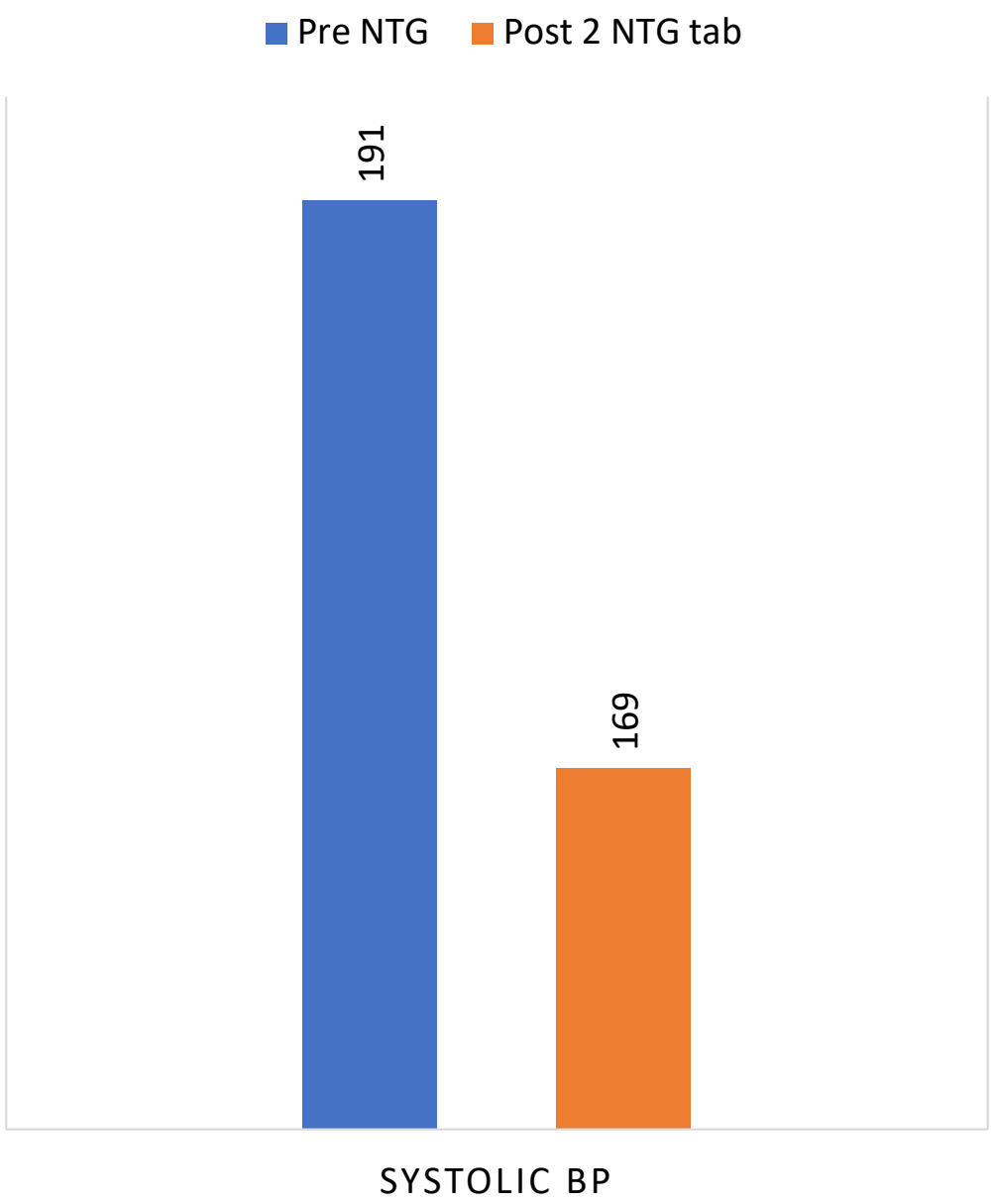
Prehosp Disaster Med. 2013;28 (5):477-481

DRUGS/PROCEDURES
First Responder:
EMT: **Nitroglycerin** Assist the patient with self-administration of his or her own ***nitroglycerin***. (As long as the systolic blood pressure is greater than 90 mmHg and the patient is still short of breath, ***nitroglycerin*** is self-administered every 5 minutes for a maximum of three doses.)
Paramedic: CPAP Cardiac monitor 12 lead EKG **Nitroglycerin** 0.8 mg sublingual every 5 minutes, as long as the systolic blood pressure remains greater than 90 mm Hg

There is no limit to the amount of nitroglycerin tablets that can be administered by a paramedic for pulmonary edema. The administration of nitroglycerin is contraindicated if erectile dysfunction medications have been taken within the last 24 hours (48 hours for tadalafil).


IMO 9000695
TITAN URANUS
HONG KONG

No IVF boluses given as rescue therapy



Why is this?

01

Bioavailability of sublingual NTG is 38.5% ± 25.6%

- Statistically, at max, only about 60% of NTG dose

02

Amount of NTG not absorbed after 8 minutes is 2.7 to 65.8% (mean 31.4 ± 18.9%)

03

NTG shown to peak in blood within 2 minutes

- Falls to 50% of peak levels in the blood at 7.5 minutes

What does this mean?

- Is an IV necessary for the first dose?
- Is there a limit to the amount of NTG that can be given?
- Is there a better way to give NTG?

Turbo-Charged Treatment:
Push Doses of IV Nitroglycerin

Marc Conterato, MD, FACEP
Office for the Medical Director, NMHAS
Joint Hennepin County EMS Services

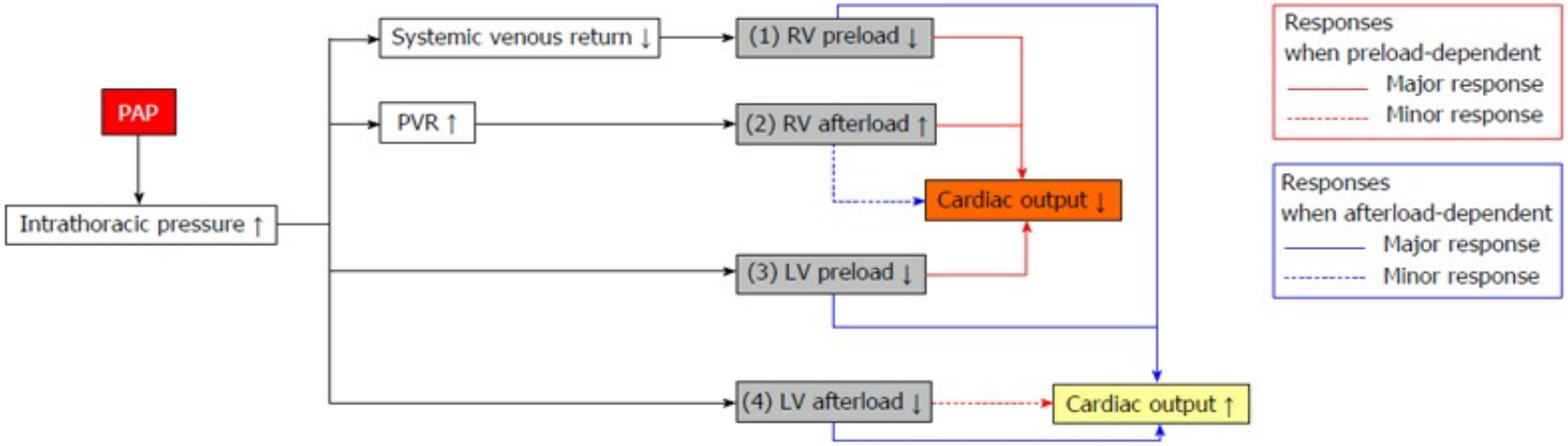
NORTH
MEMORIAL HEALTH

CHF and Pulmonary Edema

- Ideal treatments are:
  - High-flow oxygen
  - NIPPV (CPAP or Bilevel CPAP)
  - Nitroglycerin
  - SPEED!!

CPAP facts

- CPAP diminishes systemic venous return and RV preload by increasing intrathoracic pressure.
- CPAP alters pulmonary total vascular resistance (PVR), which is the major determinant of RV afterload, via an alternation in lung volume.
- It takes **~60-300 seconds** for CPAP to have positive effects in acute CHF/Pulmonary edema.



NORTH MEMORIAL HEALTH

CPAP facts

- When you take off the NIPPV mask to administer SL Nitroglycerin, the beneficial effects of NIPPV goes away and takes as long as 60-90 seconds to be re-established!!

Nitroglycerin facts:

NTG	Cost	Bioavailability	Onset	Peak effect	Duration
SL tab	$35/200 tab	38-50%	1-3 minutes	5 minutes	25 minutes
SL spray	$300/5oz	38-50%	1-3 minutes	4-15 minutes	25 minutes
IV	$5/5mg per 5ml	100%	Immediate	Immediate	3-5 minutes
IV	$35/50gm in 250ml	100%	Immediate	Immediate	3-5 minutes

Nitroglycerin facts:

- **Eagles survey on NTG for CHF/Pulmonary edema treatment.**
  - 800 mcg-2000 mcg SL as the initial dose
  - 400 mcg-800 mcg SL every 2-5 minutes
  - Some use of IV nitroglycerin drips (40-80 mcg/min)

What is SCAPE?

- **Sympathetic surge crashing pulmonary edema (SCAPE)**-a condition characterized by a vicious cycle of profound hypertension induced pulmonary edema, dyspnea and increased air hunger leading to catecholamine surge, worsening hypertension, respiratory failure, and death.
- In these situations, rapid afterload reduction in the first several minutes of care, coupled with non-invasive ventilation, can result in rapid resolution of symptoms.
- It appears that only *very high doses of nitrates* are effective in producing clinically meaningful improvements in this specific subset of patients with profound elevations of blood pressure resulting in life-threatening pulmonary edema

Nitroglycerin and CHF/Pulmonary edema:

- Treatment of severe decompensated heart failure with high dose nitroglycerin: a feasibility and safety analysis: Levy, Compton, Welch, et al. Annals of Emergency Medicine, 2007.
- Use of nitroglycerin by bolus prevents intensive care unit admission in patients with acute hypertensive heart failure: Suprat Saely Wilson, PharmD et al. AJEM, 2017.
- Weingart, S. “Sympathetic Crashing Acute Pulmonary Edema” EMCrit Podcast #1, 2009. http://emcrit.org/podcasts/scape

Treatment of SCAPE with IVB NTG

- 1. Continuous monitoring of pulse oximetry, ECG and BP (min. q 2 minutes)
- 2. Administration of 0.8mg of sublingual nitroglycerin
- 3. Initiation of peripheral intravenous access
- 4. Initiation of continuous positive airway pressure (CPAP) ventilatory support at 5-15 cm H20
- 5. Administration of intravenous nitroglycerin according to the following scheme
  - a. Systolic blood pressure ≥180mmHg, give 400mcg IVB
- 6. Re-dose every 2 minutes, until either:
  - a. Systolic blood pressure ≤140mmHg
  - b. Dyspnea resolves
- 7. Withhold further nitrates if systolic blood pressure <90mmHg at any point in the patient encounter, unless symptoms consistent with SCAPE recur.

Treatment of SCAPE with IVB NTG

- **Outcomes to be Measured:**
- **Primary Outcome:**
  - The primary outcome of this study is the incidence of systolic blood pressure <90mmHg at any point following the first dose of IVB NTG.

- **Secondary Outcome Measures:**
  - Change in pulse oximetry following IVB NTG. The initial oxygen saturation will be compared to the last oxygen saturation recorded prior to the handover of care to the receiving Emergency Department.

  - Change in systolic blood pressure following IVB NTG. The initial blood pressure will be compared to the final blood pressure recorded prior to the handover of care to the receiving Emergency Department, with success being defined as a reduction in systolic blood pressure of ≥20% from the initial baseline measurement.

  - Incidence of invasive airway management in the pre-hospital phase of care, and the incidence of invasive airway management occurring during the first 30 minutes of ED admission.

CHF/Pulmonary edema/SCAPE

- NIPPV is a highly effective for the treatment of these conditions.
- Removing the NIPPV mask to give SL NTG "resets the clock" for its beneficial effects.
- SL NTG can take a **long time** to onset and reach peak effects.
- IV NTG has immediate onset, safe to administer and **CHEAP!!**
- IV NTG is what will be started immediately in the ED when these patients arrive!

- **Special Thanks to:**
  Michael Perlmutter NRP, BSM, FTO; NMHAS
  University of MN School of Medicine, Class of 2021
  - **“My exit plan”**
- **@ConteratoMarc**

Push Doses of Epinephrine – When does this work

Jon Jui MD, MPH

Push Dose Epinephrine Uses in EMS

- Does it work?
- How easy is it to deploy?
- How effective is it?
- When can you expect a response?

Where did "Push dose epinephrine " come from?

EMCrit Podcast 6 – Push-Dose Pressors

July 10, 2009 by **Scott Weingart** — 57 Comments

Note: Please listen to the PDP update episode either before or immediately after listening to this one

Finally a non-intubation topic!

Bolus dose pressors and inotropes have been used by the anesthesiologists for decades, but they have not penetrated into standard emergency medicine practice. I don't know why. They are the perfect solution to short-lived hypotension, e.g. post-intubation or during sedation.

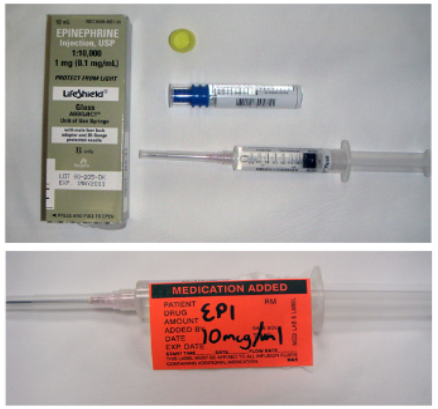
Push Dose Epinephrine : How To

EPINEPHRINE

Has alpha and beta1/2 effects so it is an inopressor
Do not give cardiac arrest doses (1 mg) to patients with a pulse

Mixing Instructions:

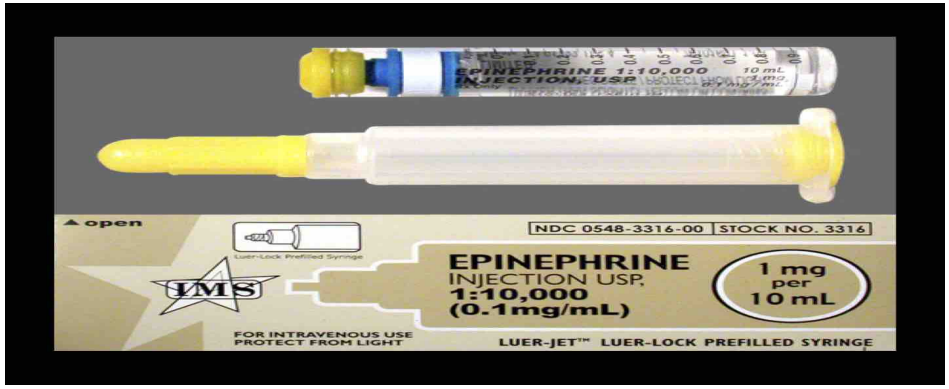
- Take a 10 ml syringe with 9 ml of normal saline
- Into this syringe, draw up 1 ml of epinephrine from the cardiac amp (Cardiac amp contains Epinephrine 100 mcg/ml)
- Now you have 10 mls of Epinephrine 10 mcg/ml



Onset-1 minute
Duration-5-10 minutes
Dose-0.5-2 ml every 2-5 minutes (5-20 mcg)

Which one should we chose ?

Push Dose Epinephrine OR Norepinephrine



Epinephrine vs Norepinephrine Potency

Agent	Alpha-1	Beta-1	Beta-2	Dopamine	Vasopressin-1
Dobutamine	+	+++++	+++	0	0
Dopamine	+++	++++	++	+++++	0
Epinephrine	+++++	++++	+++	0	0
Milrinone	0	0	0	0	0
Norepinephrine	+++++	+++	++	0	0
Phenylephrine	+++++	0	0	0	0
Vasopressin	0	0	0	0	+++++

Push Dose Epinephrine 2017

Age	Gender	Chief Complaint	Description	Initial BP/MAP	Final MAP	EMS Diagnosis	Hospital Dx	Survived
18	Male	Fever, increased work of breathing	Hx 21Q gene micro deletion, MR, J tube repair and fever, increased work of breathing	71/25 (40)	119/64 (82)	Septic Shock	Septic Shock, Colitis	Yes
69	Female	Weak	Hx of DM, renal failure, dialysis, CAD	74/42 (53)	95/54 (68)	Hypotension	Septic shock, RLL pneumonia, NSTEMI	No
49	Male	Overdose, unconcious	Schizophrenia, HTN, Found unconscious in assisted Living, possible OD on Zyprexa	69/41 (50)	104/72	Hypotension, overdose	Overdose, Hypotension	Yes
61	Male	Acutely weak, increased confusion	Schizophrenia, dementia	62/38 (46)	90/63 (72)	Septic Shock	Septic shock, respiratory failure	Uk
68	Male	Increased agitation, decreased mentation	resident of SNF, Hx of UTI	56/29 (38)	68/44 (52)	Septic Shock	Septic shock, gram negative bacteremia (Proteus)	Yes

61 yo Male

TIME	BLOOD PRESSURE	PULSE	RESP	GLASGOW COMA SCALE				EKG	SPO2	BLOOD GLUCOSE	PAIN SCALE
				E	V	M	TOTAL				
21:16	87 / 55 (66)	69	40	4	3	6	13				
21:20								SINUS TACHYCARDIA			
21:21	62 / 38 (46)	132	46	4	3	6	13		93%		
21:27										135	
21:28	81 / 51 (61)	117	44	4	3	6	13		92%		
21:33	60 / 39 (46)	130	48	4	3	6	13		95%		
21:36	90 / 63 (72)	115	30	4	3	6	13				

49 YO Male

TIME	BLOOD PRESSURE	PULSE	RESP	GLASGOW COMA SCALE				EKG	SPO2	BLOOD GLUCOSE	PAIN SCALE
				E	V	M	TOTAL				
22:42	69 / 41 (50)	86	8	2	1	1	4				
22:44								NORMAL SINUS RHYTHM			
22:46								NORMAL SINUS RHYTHM			
22:47										177	
22:55	84 / 53 (63)	84	8	2	1	1	4		97%		
23:00	98 / 64 (75)	83	8	2	1	1	4		99%		
23:06	122 / 79 (93)	87	10	1	1	1	3		99%		
23:12	100 / 68 (79)	79	8	1	1	1	3		97%		
23:14	95 / 62 (73)	85	10	1	1	1	3		98%		
23:16	91 / 69 (76)	84	10	1	1	1	3		98%		
23:19									100%		
23:20	76 / 52 (60)	80	12	1	1	1	3				
23:23									99%		
23:24									99%		
23:26	108 / 72 (84)	76	12	1	1	1	3				
23:31	104 / 72 (83)	80	12	1	1	1	3				

18 YO MALE

TIME	BLOOD PRESSURE	PULSE	RESP	GLASGOW COMA SCALE				EKG	SPO2	BLOOD GLUCOSE	PAIN SCALE
				E	V	M	TOTAL				
10:02	82 / P	140	86	2	1	4	7				
10:02								SINUS TACHYCARDIA			
10:12	71 / 25 (40)	72	84	2	1	4	7		100%		
10:12										195	
10:18	33 / 21 (25)	130	81	2	1	4	7		99%		
10:24	49 / 24 (32)	111	77	2	1	4	7				
10:27									95%		
10:30	98 / 74 (82)	92	92	2	1	4	7				
10:33	119 / 64 (82)	106	83	2	1	4	7		97%		

69 YO Female

TIME	BLOOD PRESSURE	PULSE	RESP	GLASGOW COMA SCALE				EKG	SPO2	BLOOD GLUCOSE	PAIN SCALE
				E	V	M	TOTAL				
16:51	88 / 50 (63)	89	16	4	5	6	15		95%		
16:54										167	
17:03	74 / 42 (53)	92	16	3	5	6	14				
17:08	89 / 43 (58)	95	22	3	4	5	12				
17:10								PACED RHYTHM			
17:14	73 / 31 (45)	87	16	2	2	4	8				
17:20	125 / 60 (82)	102	20	4	5	6	15		100%		
17:24	95 / 54 (68)	101	20	4	5	6	15				

Conclusions

- Push Dose Epinephrine is
  - Medically effective
  - Operationally feasible
  - Low Cost
  - High Benefit

The END

Confounding the Confounders:

Does Epinepherine Ever Work?

John M Gallagher, MD, FACEP
EMS System Medical Director
Wichita/Sedgwick County Kansas

Eagles 2018

- Conflicts:
  - None but looking


10 mL
NDC 0409-4921-34
EPINEPHRINE
Injection, USP
1:10,000
1 mg (0.1 mg/mL)
PROTECT FROM LIGHT
LifeShield®
Glass
ABBOJECT®
Unit of Use Syringe
with male luer lock adapter and 20-Gauge protected needle
℞ only
LOT 78-127-DK
EXP 1MAR2011
PRESS AND PULL TO OPE
Epinephrine
Injection, USP
1:1000
BACKORDER


GRIN &
BEAR IT


5
4
3
5
3
(0.5mg
each)
5
4
(6 min
apart)
3
5
5
2
3
10
5
3
How many epi doses
should we give?
5
3
3
(0.5mg
each)
3
3
4
(10 min
apart)
3
5
10
3
5
3
5
3

What about Zero?…

Future Cardiology

Epinephrine in Resuscitation: Curse or Cure?

Robert R Attaran; Gordon A Ewy

DISCLOSURES | Future Cardiol. 2010;6(4):473-482.

EMSWORLD | PATIENT CARE | EDUC/ TRNG | PT HANDLING/ TRANSPORT | COMMUNITY | OPS | LEADERSHIP | TECH | MIH-CP | PRODUCTS | CAREERS/ PERSONNEL | REVISTA | INTL NEWS | MENU

PATIENT CARE

PATIENT CARE

InterSystems, ZOLL Medical Corporation Collaborate to Integrate EMS into Care Continuum

PATIENT CARE

Literature Review: Prehospital Epi for Cardiac Arrest

By Angelo Salvucci, Jr., MD, FACEP Mar 28, 2012

Print Version

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HOME >> PATIENT CARE >> RESEARCH STUDY EXAMINES EPINEPHRINE'S EFFECTS ON CARDIAC ARREST

Research Study Examines Epinephrine's Effects on Cardiac Arrest

Epinephrine has been the mainstay of cardiac arrest, but is it effective?

Wed, Jun 13, 2012 | By David Page, MS, NREMT-P

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Did you know Adrenaline doesn't work for Cardiac Arrest?

13 June, 2017 EMS

Adrenaline may improve return of spontaneous circulation, but it **does not improve survival to discharge or neurologic outcome**. The timing of epinephrine may affect patient outcome, but **Basic Life Support measures are the most important aspect of resuscitation and patient survival.**

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Is Epinephrine During Cardiac Arrest Associated With Worse Outcomes in Resuscitated Patients?

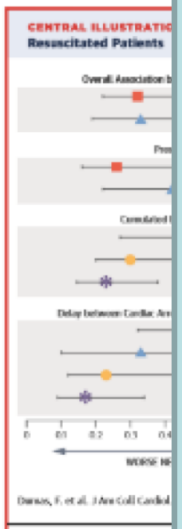
Florence Dumas, MD, PhD,*† Wulfran Bougouin, MD, MPH,*‡ Guillaume Geri, MD, MSc,*‡ Lionel Lamhaut, MD,*§ Adrien Bougle, MD,‡ Fabrice Daviaud, MD,‡ Tristan Morichau-Beauchant, MD,‡ Julien Rosencher, MD,‖ Eloi Marijon, MD, PhD,* Pierre Carli, MD, PhD,§ Xavier Jouven, MD, PhD,* Thomas D. Rea, MD, MPH,¶ Alain Cariou, MD, PhD*‡

an independent predictive factor, complicating the current debate on the benefit of this agent (26). However, this relationship has been already described when looking at observational data and the few randomized studies that were recently performed (5,27). We made multiple methodological efforts (using propensity score, cross-matching, and different sensitivity analysis) to discriminate the specific role of the intervention. The results were robust regardless of the methodological approach. To our knowledge, this is the first study depicting such a linear relationship between the dose and outcome, which is consistent with an increasing effect of the ascendant dose of the drug. Some studies have previously shown that repeated and increased doses of epinephrine could worsen the chances of survival (28,29).

Before incriminating the drug itself, our findings probably should provoke further discussion on the most appropriate scheme of treatment and its interaction regarding the resuscitation phases. Our sensitivity analyses showed that the role of epinephrine did not change according to ACLS delay or length of resuscitation but was clearly dependent on the timing of first administration. These last findings are consistent with other studies, emphasizing the potential benefit of an early dose of epinephrine (30–32).

Moreover, these observations concur with what Weisfeldt and Becker (33) previously described as the 3 phases of resuscitation in VF arrest: "the electrical phase" within the first few minutes after arrest, in which epinephrine should not be required; "the circulatory phase," during which time chest compressions and epinephrine could help reperfusion; and finally "the metabolic phase," when the drug may be detrimental in regard to the peripheral ischemia release of massively cytotoxic proteins. As supported by our results, it is highly probable that patients receiving late or repeated doses of epinephrine have little or low chance of survival. Currently, no existing alternative can bring these patients back from near-death except mechanical circulatory assistance in very select cases. Altogether, the scheme and timing of administration may be crucial to provide the appropriate effect of epinephrine.

This study highlights the need to assess the quality of resuscitation, such as the quality of CPR and ACLS response (34–36), to improve clinical practice (37,38). We may be able to better understand the role of epinephrine with careful investigation of its timing and dose in the context of intermediate outcomes such as the electrocardiographic waveform and rhythm transition, end-tidal carbon dioxide, and brain perfusion (31,39). Finally, our results highlight the need for additional studies with different



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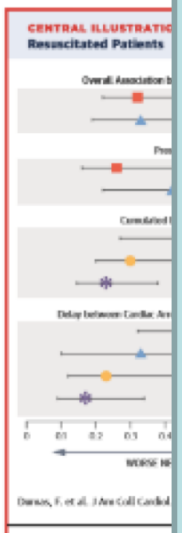

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an independent predictive factor, complicating the current debate on the benefit of this agent (26). However, this relationship has been already described when looking at observational data and the few randomized studies that were recently performed (5,27). We made multiple methodological efforts (using propensity score, cross-matching, and different sensitivity analysis) to discriminate the specific role of the intervention. The results were robust regardless of the methodological approach. To our knowledge, this is the first study depicting such a linear relationship between the dose and outcome, which is consistent with an increasing effect of the ascendant dose of the drug. Some studies have previously shown that repeated and increased doses of epinephrine could worsen the chances of survival (28,29).

Before incriminating the drug itself, our findings probably should provoke further discussion on the most appropriate scheme of treatment and its interaction regarding the resuscitation phases. Our sensitivity analyses showed that the role of epinephrine did not change according to ACLS delay or length of resuscitation but was clearly dependent on the timing of first administration. These last findings are consistent with other studies, emphasizing the potential benefit of an early dose of epinephrine (30–32).

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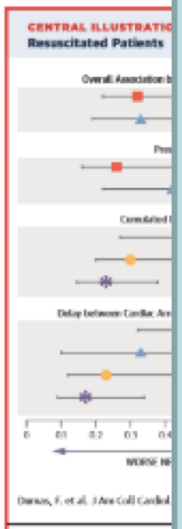

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So timing seems to matter.

But there’s more…

A thought exercise…

How well does albuterol work for patients with respiratory distress?

-Asthma Exacerbation

-Anxiety

-Pulmonary Embolism

-Pneumothorax

…just like respiratory distress,

not all cardiac arrest is the same

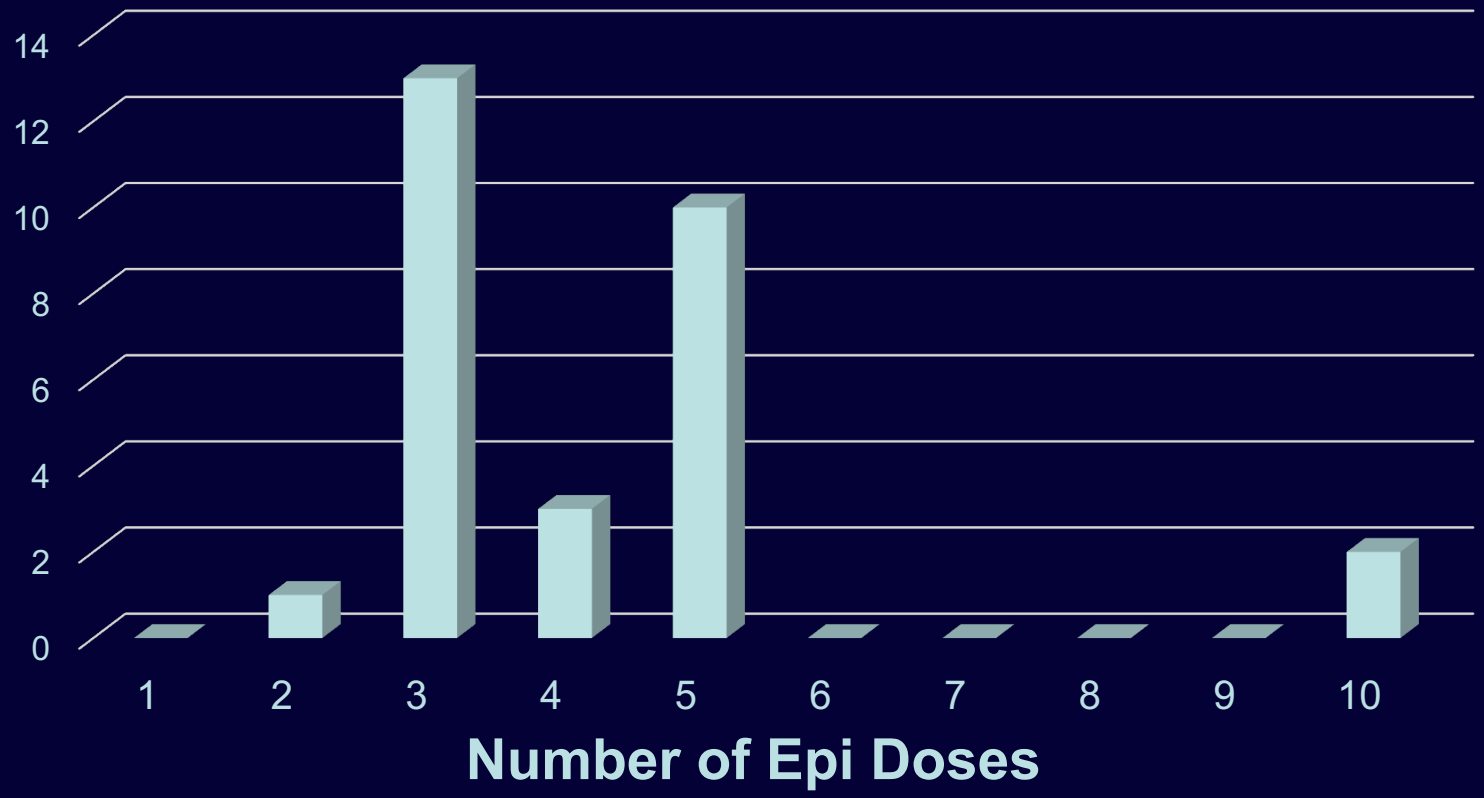
A thought exercise…

We have to be sure we are using (and studying) this medication in an appropriate pool of patients.

Hypothesis: Epi is no better than placebo in patients who receive terrible CPR.

-also doesn't work for patients who are long dead, or those who were actually seizures, etc…

So what did we do?



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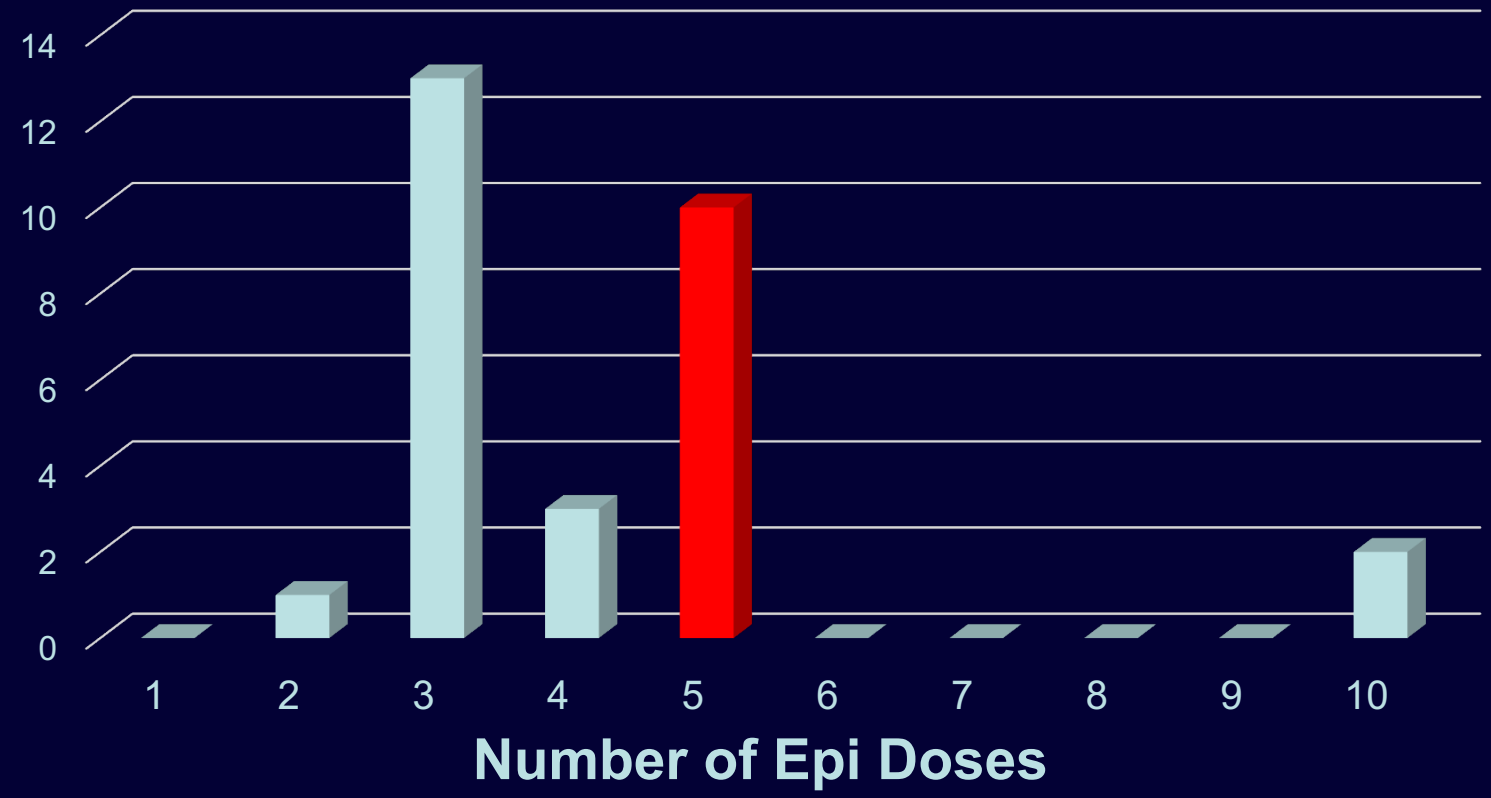

…and no change in CARES outcomes to date.

THANK YOU

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Emergency and EMS Physician

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