Randomized Clinical Trial of Pre-hospital Sodium Nitrite in Out-of Hospital Cardiac Arrest Patients

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Background

- **Survival from OHCA is less than 20%**
- **Administration of sodium nitrite during resuscitation increased survival by nearly 50% in animal model of cardiac arrest**
- ***Determine whether sodium nitrite given during resuscitation improves outcomes from out-of-hospital cardiac arrest***

Trial Setting/Design

- **Emergency medical services (EMS) agencies in Seattle and surrounding King County**
- **Individual OHCA patients double blind-randomized (1:1:1)**
  - **Intervention- 60 mg Sodium Nitrite**
  - **Intervention- 45 mg Sodium Nitrite**
  - **Control-Placebo (normal saline)**

Eligibility

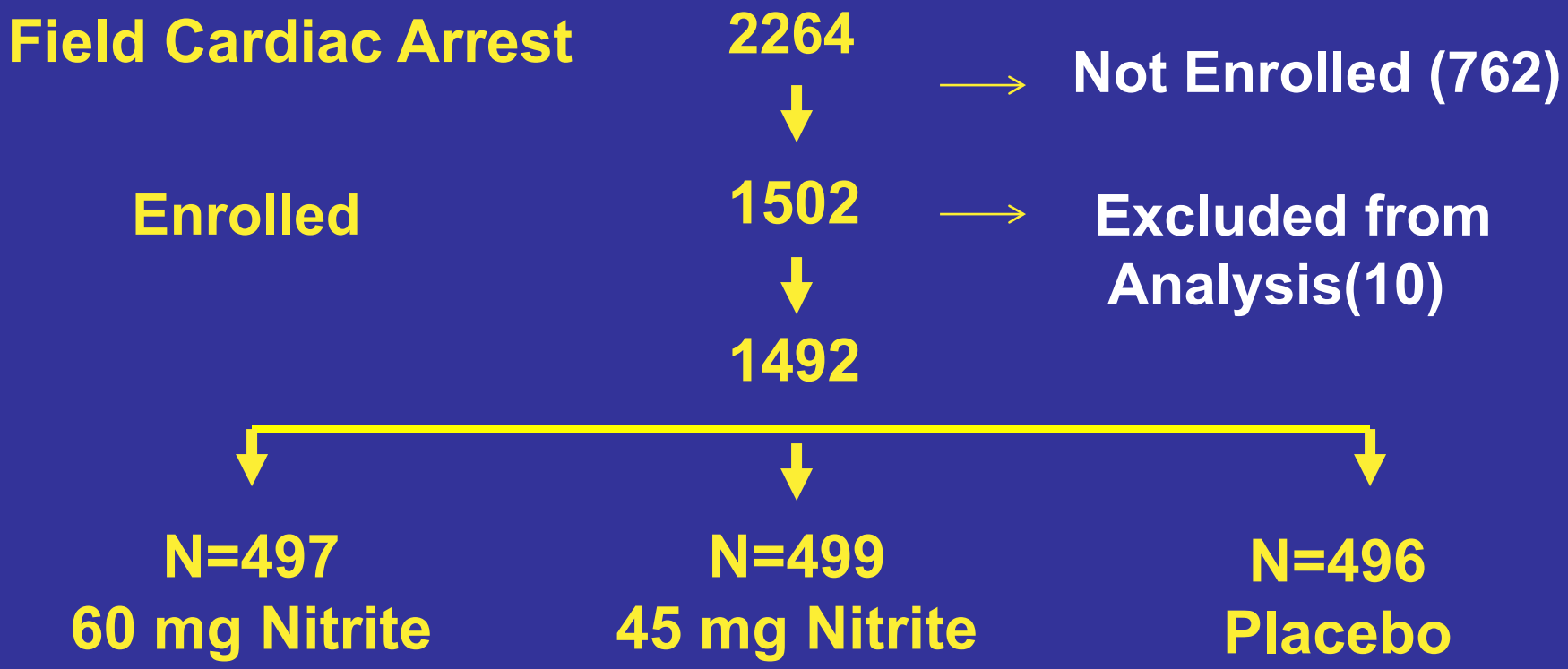
Inclusion Criteria

- Cardiac arrest with life support by paramedics
- Age 18+
- Intravenous/intraosseous access
- Unconscious

Exclusion Criteria

- Traumatic cardiac arrest
- Age < 18
- Known DNR
- Pregnant
- Prisoner
- Drowning

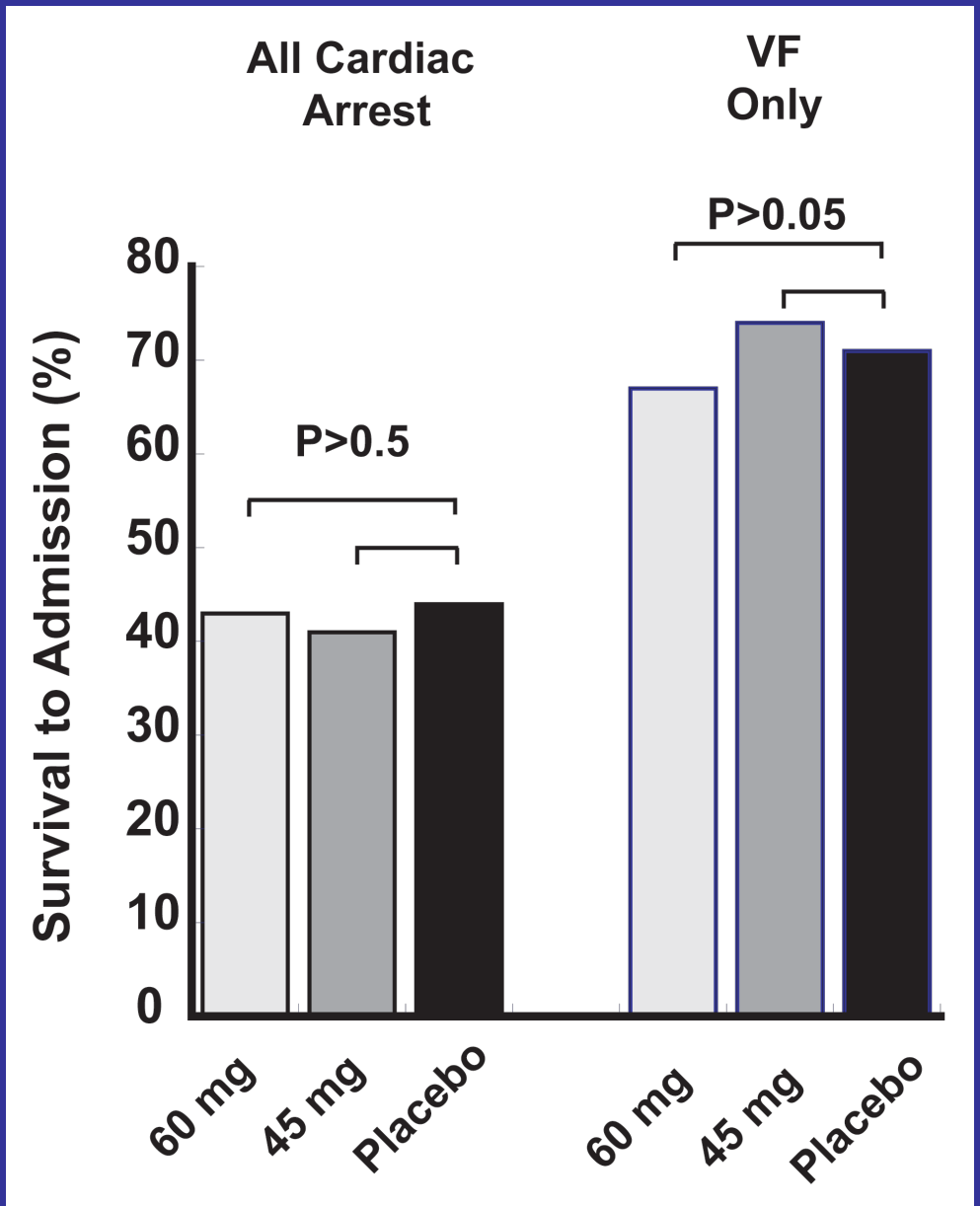
Trial Flow



Primary Outcome: Survival to Hospital Admission,
Important Secondary: Survival to Discharge

Characteristic	Randomization group		
	60 mg (n=497)	45 mg (n=499)	Placebo (n=496)
Age (years)	62±17	65±16	64±17
Men	66%	66%	67%
Initial rhythm			
Asystole	44.1%	45.9%	41.3%
Pulseless electrical activity	27.4%	30.9%	29.6%
Ventricular fibrillation	24.9%	19.0%	23.6%
Ventricular tachycardia	0.4%	0.2%	0.4%
Arrest before EMS arrival	87%	87%	90%
Witnessed arrest	43%	43%	44%
Time from call to first arrival (min)	5.7±2.0	6.1±3.3	6.0±4.5
Time from call to randomization (min)	22±8 (n=493)	22±10 (n=498)	22±10 (n=491)

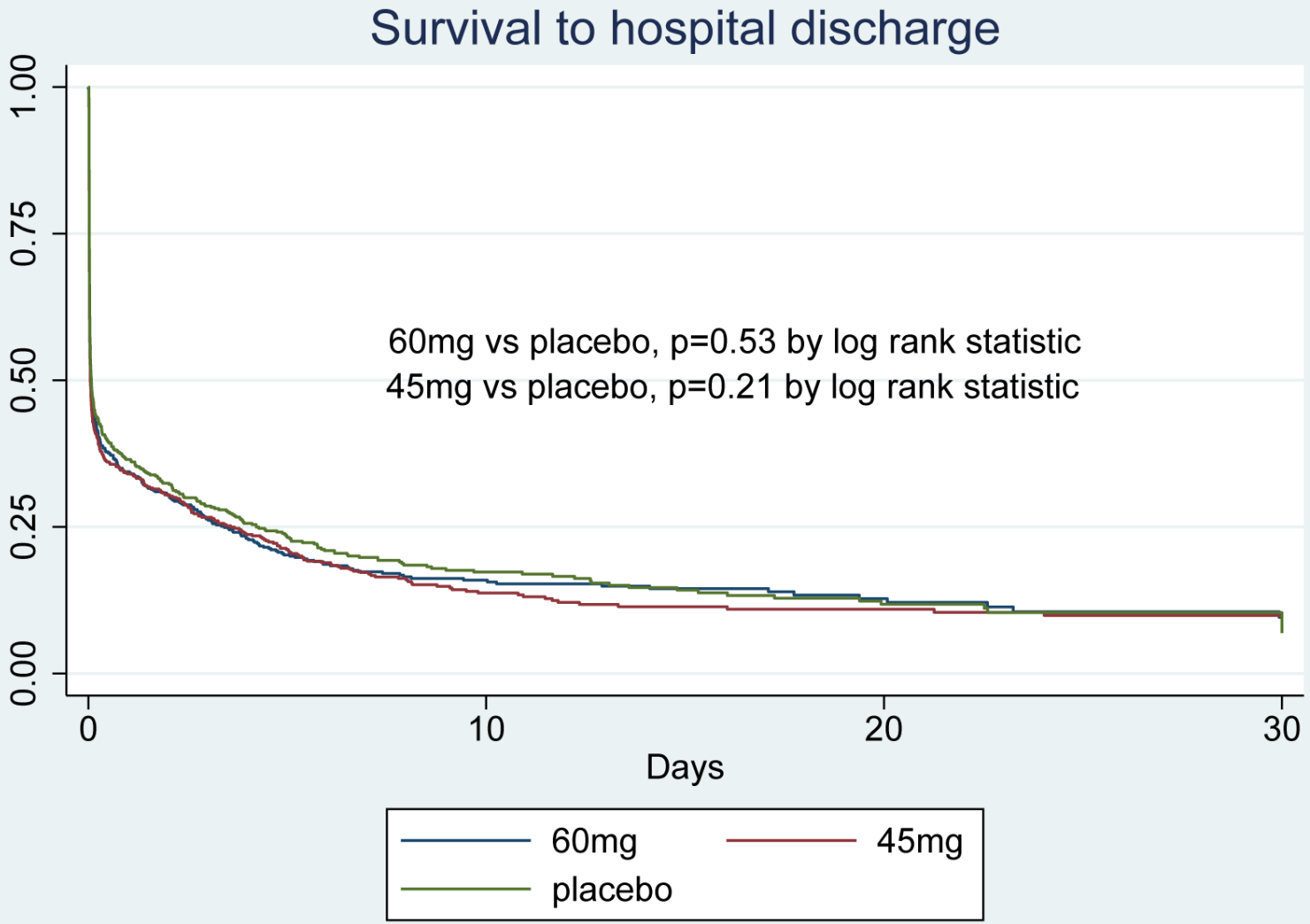
Outcomes - Survival to Hospital Admission



All Cardiac arrest
60 mg n= 212
45 mg n= 205
Placebo n= 218

VF
60 mg n=84
45 mg n=70
Placebo n=84

Post hoc Outcome - Survival to Discharge



Safety - prehospital

Event	Randomization group		
	60 mg (n=497)	45 mg (n=499)	Placebo (n=496)
ROSC	58%	53%	58%
Norepinephrine after randomization	16%	16%	15%
Epinephrine after randomization	95%	95%	95%
Epinephrine dose (mg)	3.1±1.7 (n=473)	3.1±1.6 (n=471)	3.2±2.0 (n=468)
Rearrest in field (ROSC)	156/294 (53%)	130/270 (48%)	139/291 (48%)
Systolic BP after randomization (mm/Hg)	128±43 (n=257)	127±41 (n=241)	130±44 (n=260)
Transported to hospital	55%	51%	56%

Safety - ED and hospital

Characteristic	Randomization group		
	60 mg (n=497)	45 mg (n=499)	Placebo (n=496)
First systolic blood pressure in hospital (mm/Hg)	117±35 (n=241)	114±34 (n=222)	122±36 (n=249)
Sustained hypotension	9/228 (3.9%)	11/216 (5.1%)	14/238 (5.9%)
pH first arterial blood gas	7.1±0.2 (n=235)	7.1±0.2 (n=222)	7.1±0.2 (n=235)
Pressors in first 24 hours	185/272 (68%)	173/255 (68%)	190/278 (68%)
Hospital targeted temperature management	139/272 (51%)	130/255 (51%)	136/278 (49%)
First hospital temperature	35.3±1.7 (n=226)	35.3±1.8 (n=205)	35.1±2.0 (n=220)
Withdrawal of life sustaining therapies	112/272 (41%)	109/255 (43%)	124/277 (45%)
Rearrest first 24 hours of hospitalization	74/271(27%)	65/249 (28%)	76/271 (28%)
ICU days (median)	5.3 (n=68)	5.1 (n=56)	4.6 (n=77)

Conclusions

- Sodium nitrite for out-of-hospital cardiac arrest did not significantly improve survival to hospital admission or to discharge
- Sodium nitrite is not associated with substantive or significant adverse effects on hemodynamics

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