Therapeutic Hypothermia

ICU management of the Post-Cardiac Arrest Patient

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Speaker disclosures

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Case: History

- 37 yo 4th year dental student collapses while taking an exam
- She remains untouched for 5 minutes
- Proctor checks for a pulse
- Starts CPR, calls for AED
- AED → shock advised
- Shocked once into perfusing rhythm

Case: 37 yo VF arrest

- Time to ROSC = 8 minutes
- 911 called, patient remains comatose
- Patient arrives to the ED
  - 25 min after arrest, 15 min after ROSC
  - Sinus tachycardia @ 110 beats per minute
  - BP = 132/80

Case: 37 yo VF arrest

- Quick neurologic assessment
  - Eyes were closed
  - Not making any verbal sounds
  - Decorticate posturing
  - GCS = 5 (E-1; V-1; M-3)

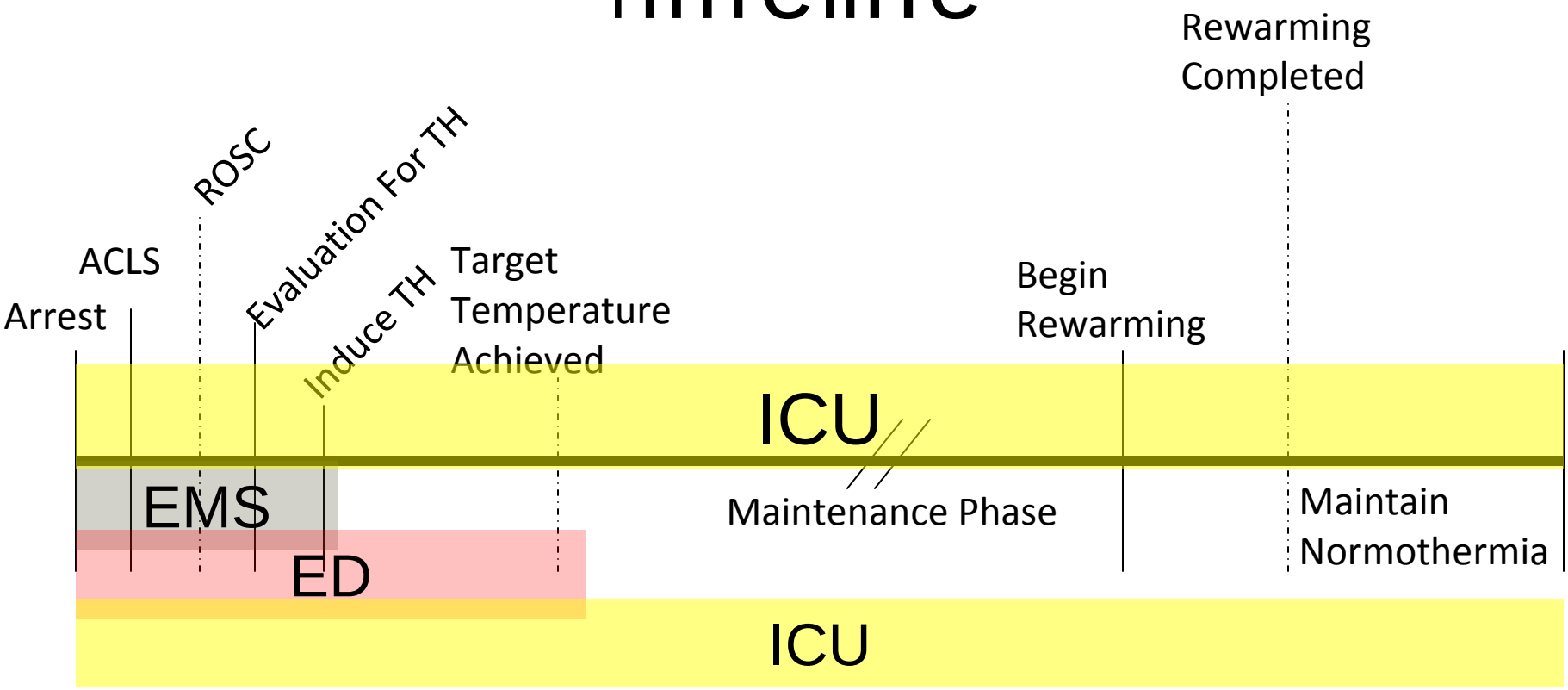
Should this woman be cooled?

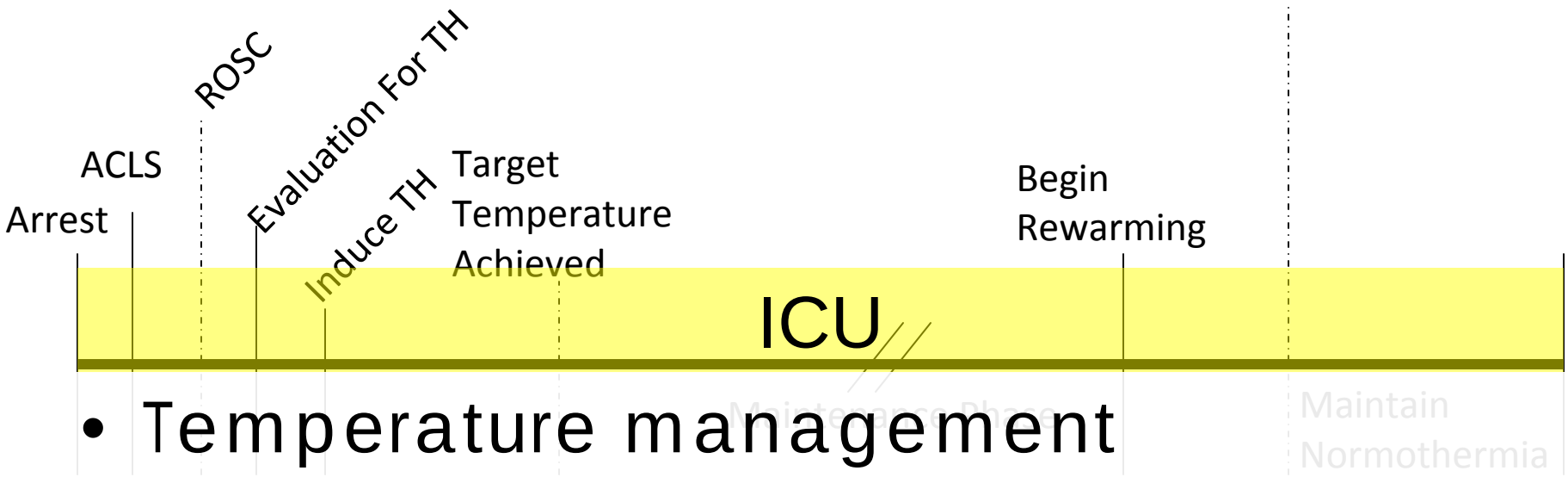
Case: 37 yo VF arrest

- Orally intubated
- EKG – NSR with nonspecific ST changes
- 2L of chilled saline infused through peripheral IVs ~ 1 ¼ hours post-ROSC
- Ice packs placed in groin and axillae
- Arterial line and CVC placed
- Patient is transported to the ICU

What's next?

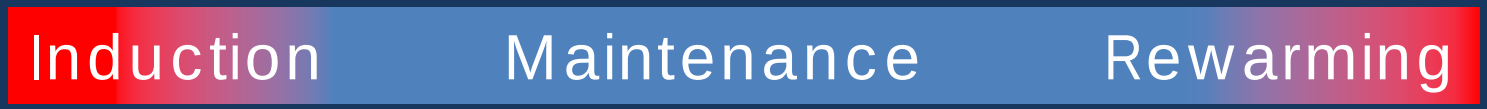
Timeline


Rewarming
Completed
ROSC
Evaluation For TH
ACLS
Arrest
Induce TH
Target
Temperature
Achieved
Begin
Rewarming
ICU
EMS
ED
Maintenance Phase
Maintain
Normothermia
ICU



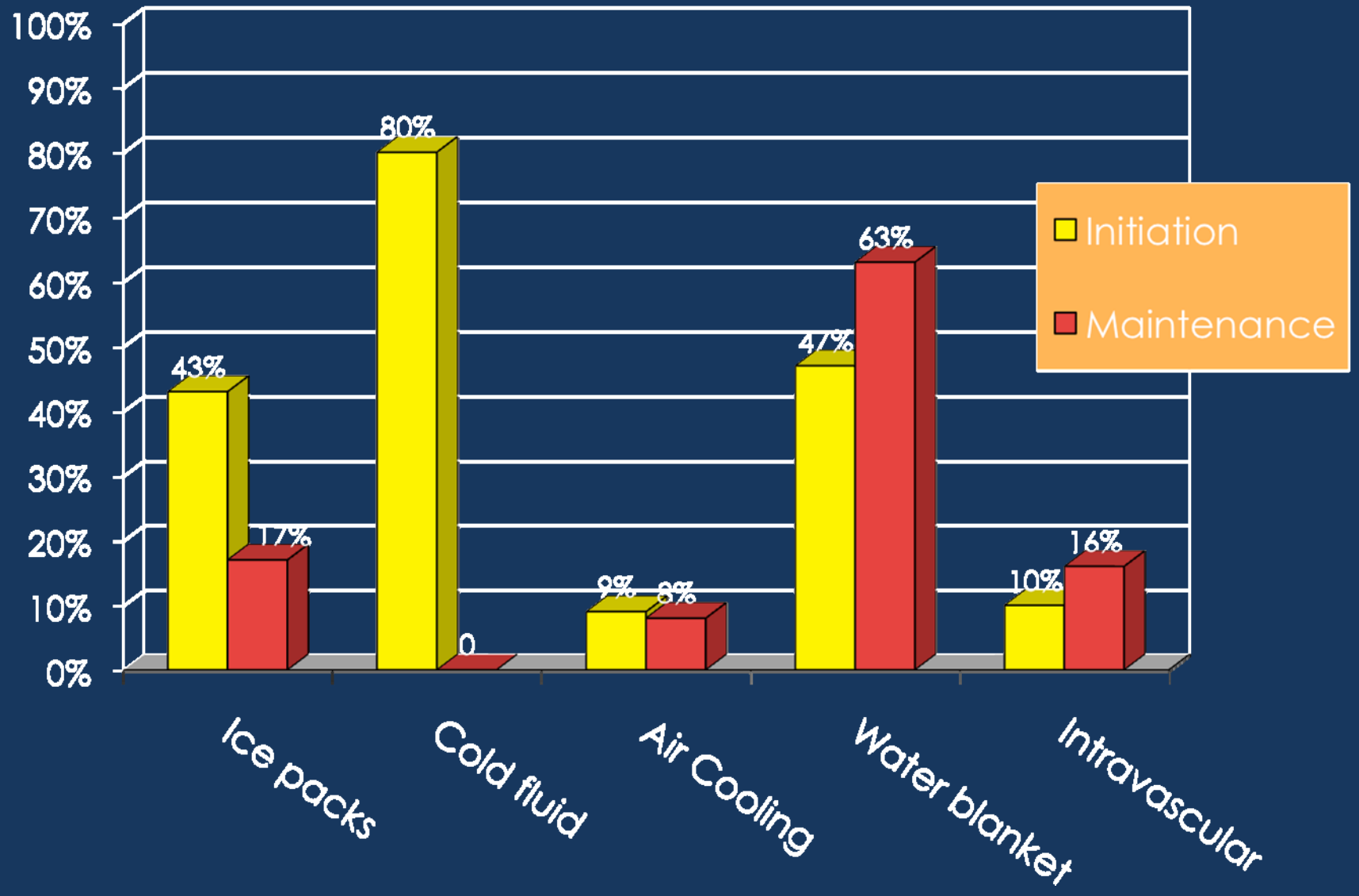
- Temperature management
- Paralysis and sedation
- Seizures
- Ventilator management
- Fluid and electrolyte shifts
- Infection surveillance/control
- Glucose control
- Resuscitation strategies

Temperature Management



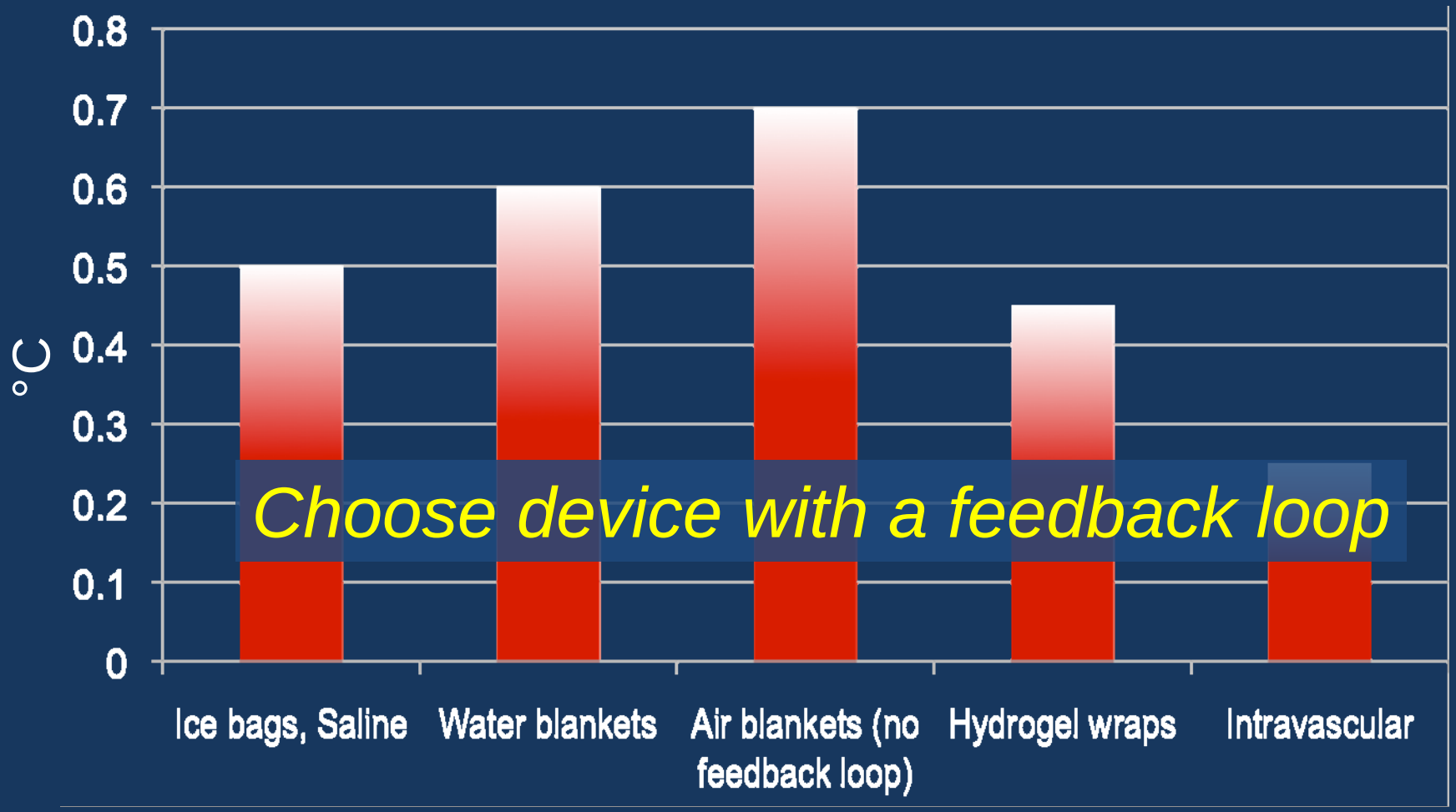
- Induction
  - Getting to desired goal (33°C)
- Maintenance
  - Keeping the patient at the desired temp for a predefined period of time
- Rewarming
  - Returning to normothermia

How are people cooled?



Nielsen N, et al. Acta Anaesthesiol Scand. 2009; 53: 926-34.

Temperature Deviation



Hoedemaekers CW, et al. Crit Care. 2007; 11(4): R91.

Temperature Monitoring

- PA catheter
- Esophageal
- Bladder
  - If patient has adequate UO
    - 0 – 30 cc/hr – varies per manufacturer
- Rectal/skin/tympanic less accurate

How long to cool?

Maintenance

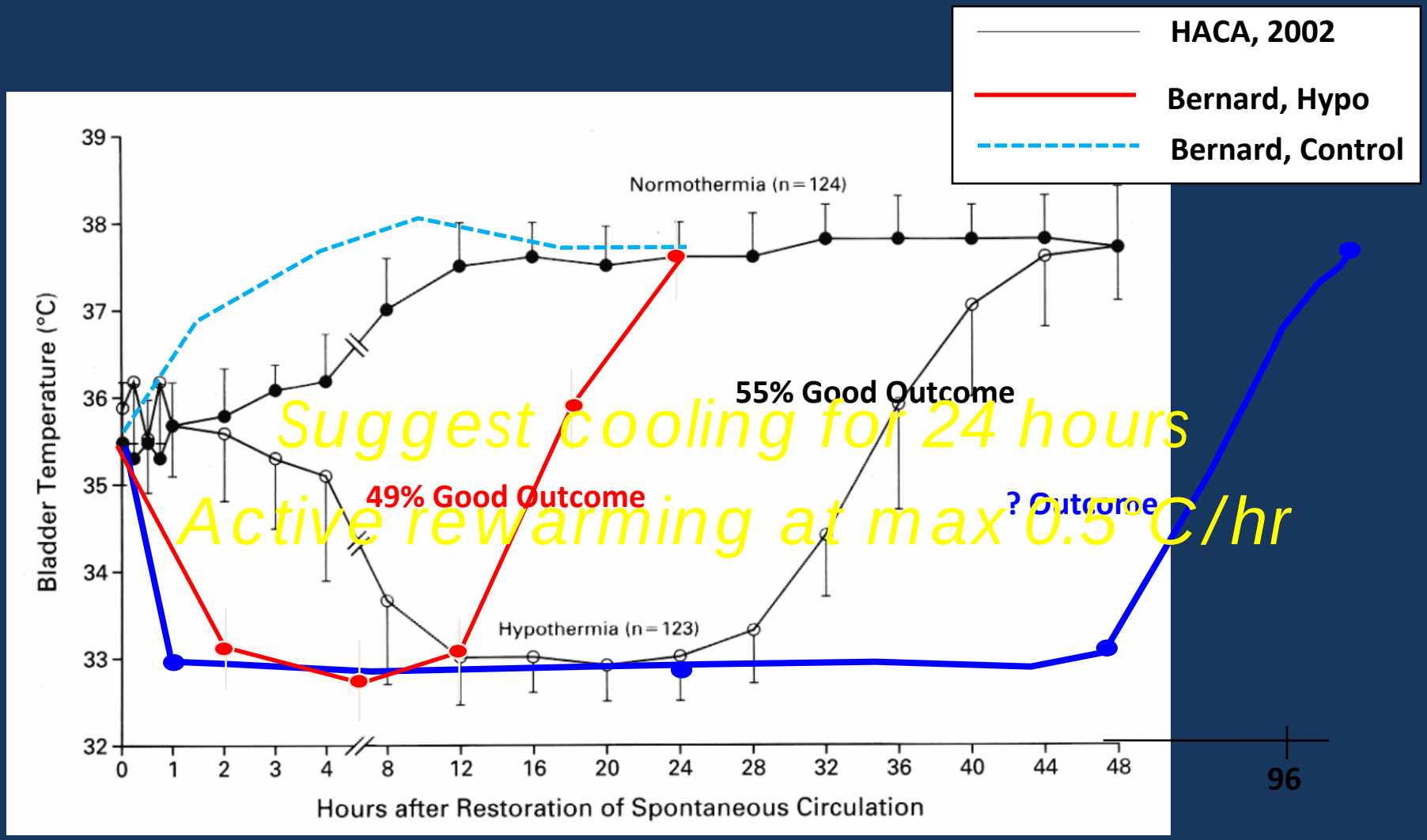
- Bernard: 12 hours
- HACA: 24 hours from onset of cooling
- Nielsen: 12 – 48 hours (93% for 24 hours)
- Nagao: Tailored to the patient
  - < 15 minutes to ROSC → 24 hours
  - 15-30 minutes to ROSC → 48 hours
  - > 30 minutes to ROSC → 72 hours
- Experimental data suggests apoptotic period = 7 days

How fast to rewarm?

- Rapid rewarming associated with increased ICP in stroke/TBI patients
- Bernard: 6 hrs with heated-air blankets
- HACA: Passive rewarming over 8 hrs
- Nielsen: 4 – 12+ hrs (no difference in outcomes)
- Nagao: Rewarmed to 35°C, maintained 24 hrs, then further rewarming

Nielsen N, et al. Acta Anaesthesiol Scand. 2009; 53: 926-34.

How long to cool?



Sedation

- Reduces oxygen consumption
- Can prevent shivering
- More rapid cooling
- Used in 2 NEJM trials
- May delay prognostication
- May contribute to hypotension

Sedation

- Short acting
  - Propofol
  - Dexmedetomidine
- Use published sedation scale

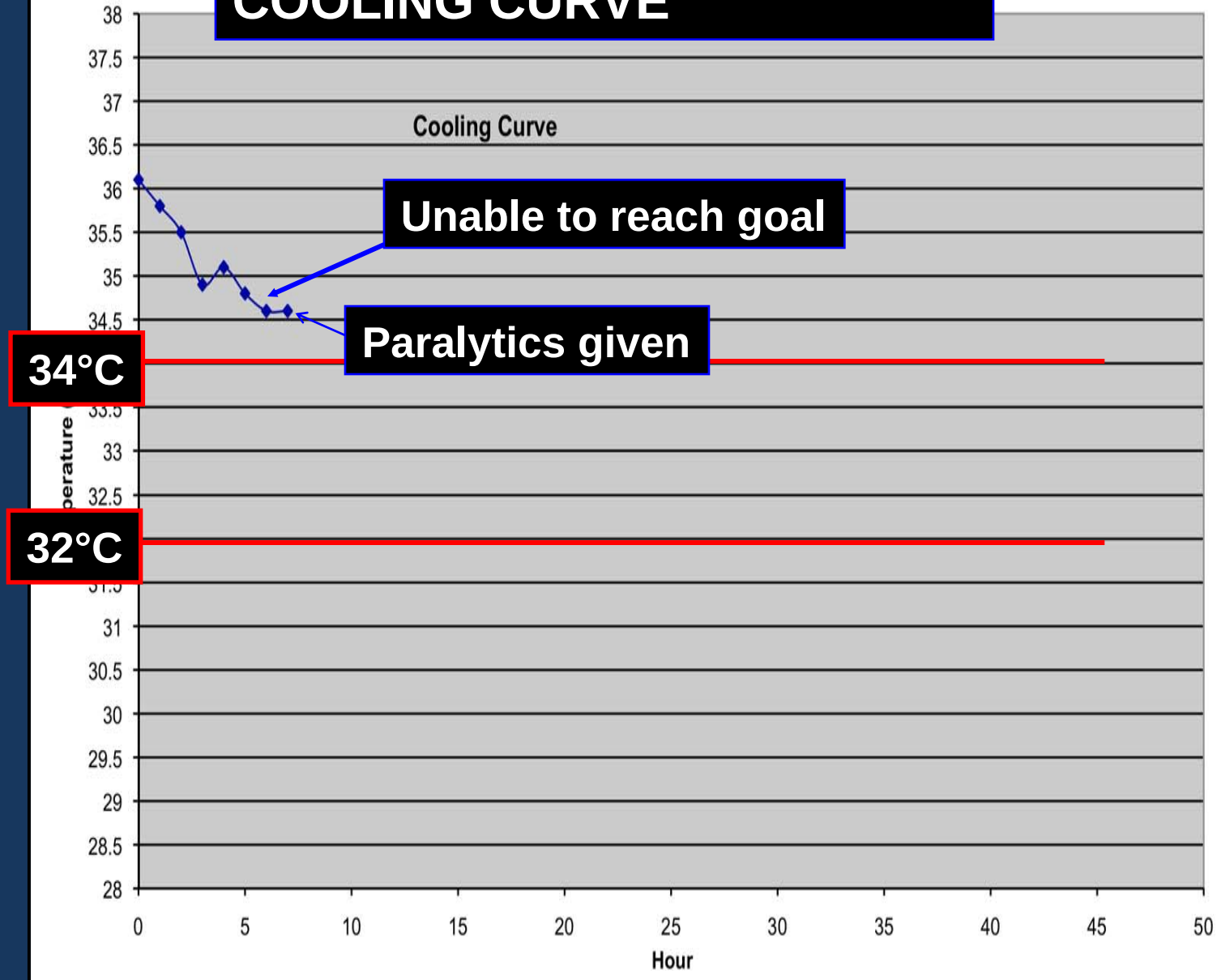
Richmond Agitation Sedation Scale (RASS) *

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to *voice* **(≥10 seconds)**	Verbal Stimulation
-2	Light sedation	Briefly awakens with eye contact to *voice* **(<10 seconds)**	
-3	Moderate sedation	Movement or eye opening to *voice* **(but no eye contact)**	
-4	Deep sedation	No response to voice, but movement or eye opening to *physical* stimulation	Physical Stimulation
-5	Unarousable	No response to *voice or physical* stimulation	

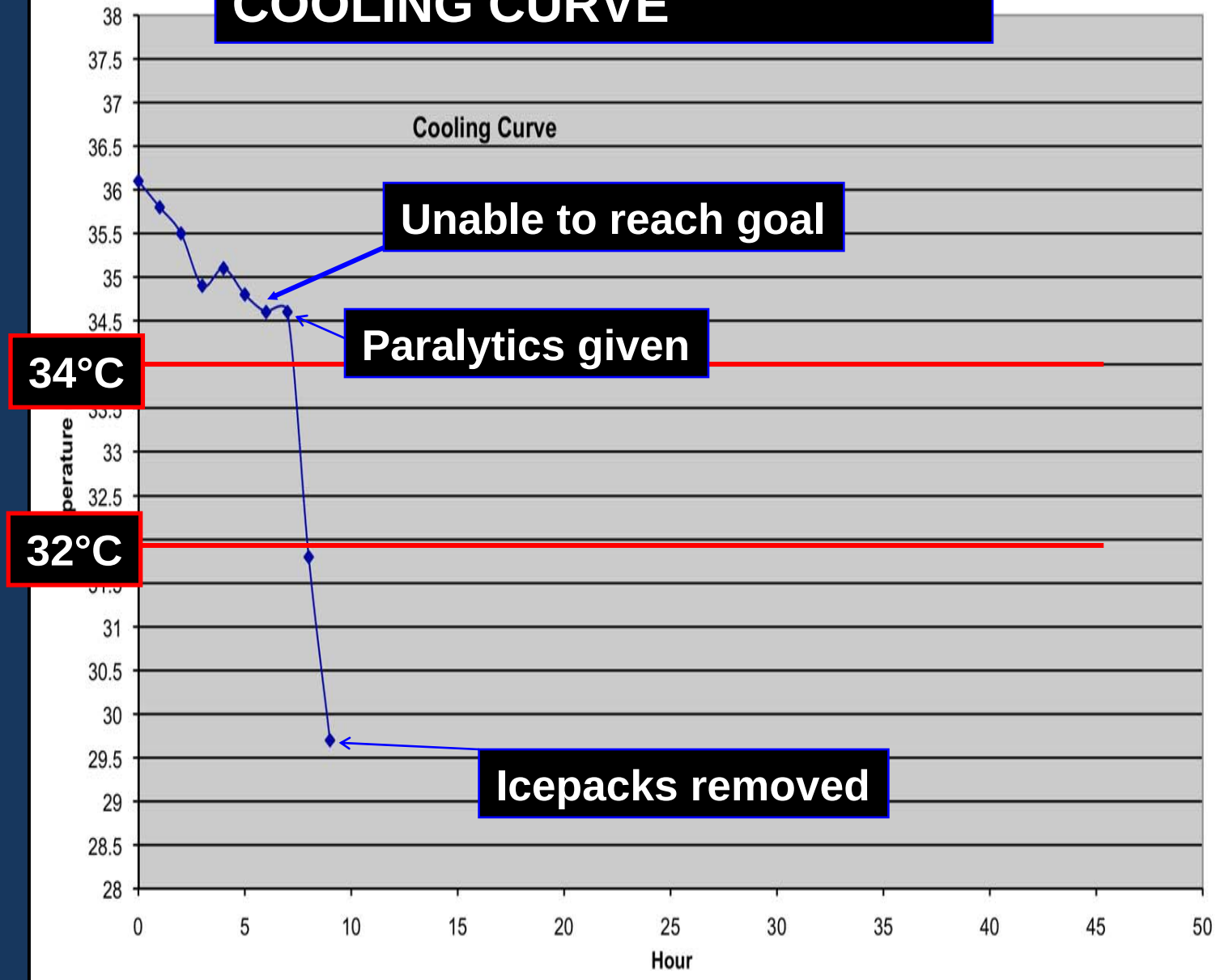
Case: 37 yo VF arrest

- Arrives in the ICU
- T° probe bladder catheter placed
- Surface cooling initiated and target set @ 33°C
- Propofol gtt started

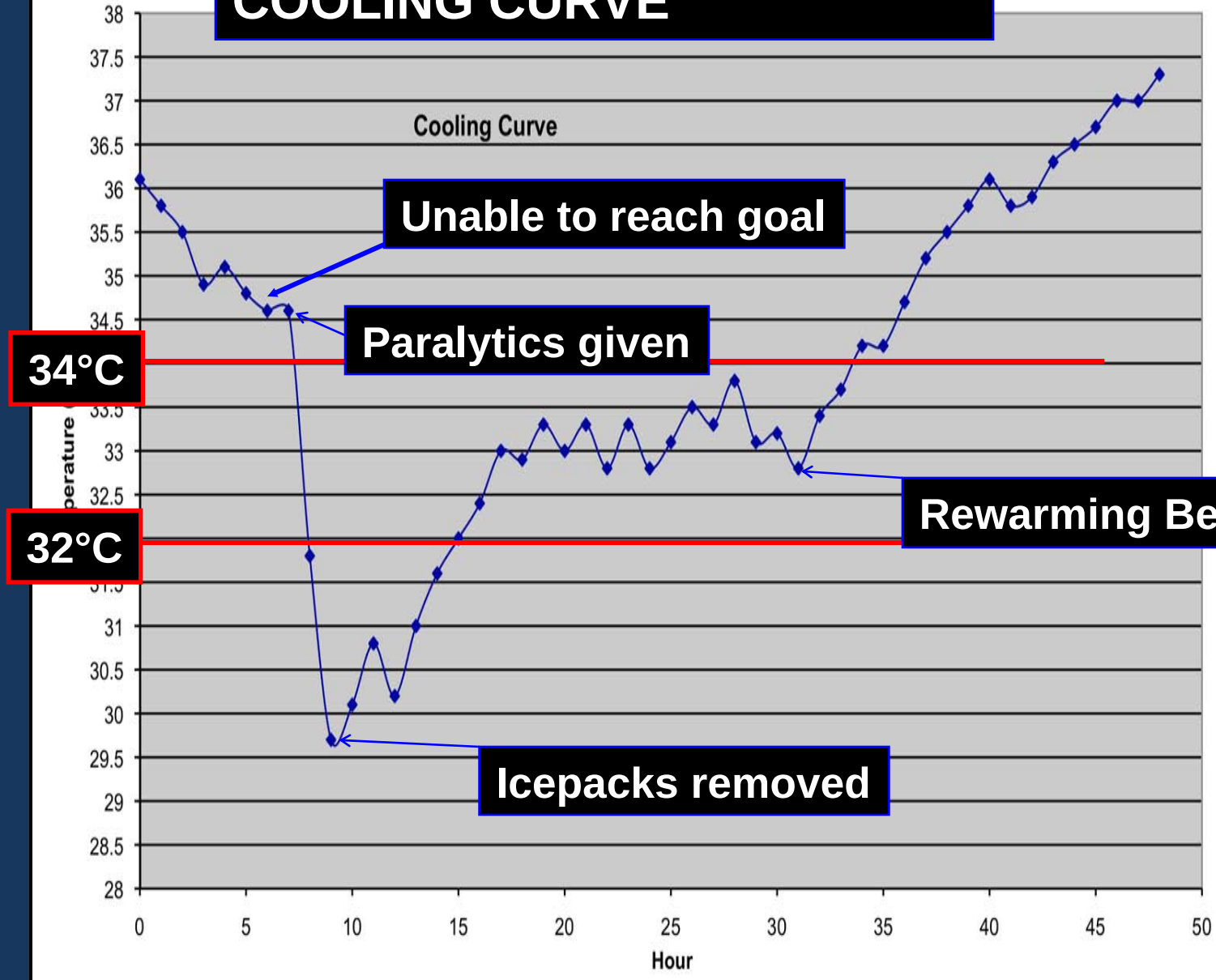
COOLING CURVE



COOLING CURVE



COOLING CURVE



Paralysis

- Eliminates shivering
  - Decrease MVO_2
- No associated hypotension
- Continuous paralysis in 2 NEJM studies
- Must sedate prior to paralyzing
- Seizures may be concealed
- Continuous EEG monitoring recommended

Seizures

- Occur in 5 – 15% who achieve ROSC
  - 10 – 40% of those who remain comatose
- Increase cerebral metabolism 3-fold
- Thiopental and phenytoin are neuroprotective in animal model
- No data on seizure prevention
- Good neuro outcomes reported in patients initially with status epilepticus

Zandbergen EG, et al. Neurology. 2006; 66: 62-68.
Ingvar M. Ann N Y Acad Sci. 1986; 462: 194–206.
Sunde K, et al. Resuscitation. 2006; 69: 29-32

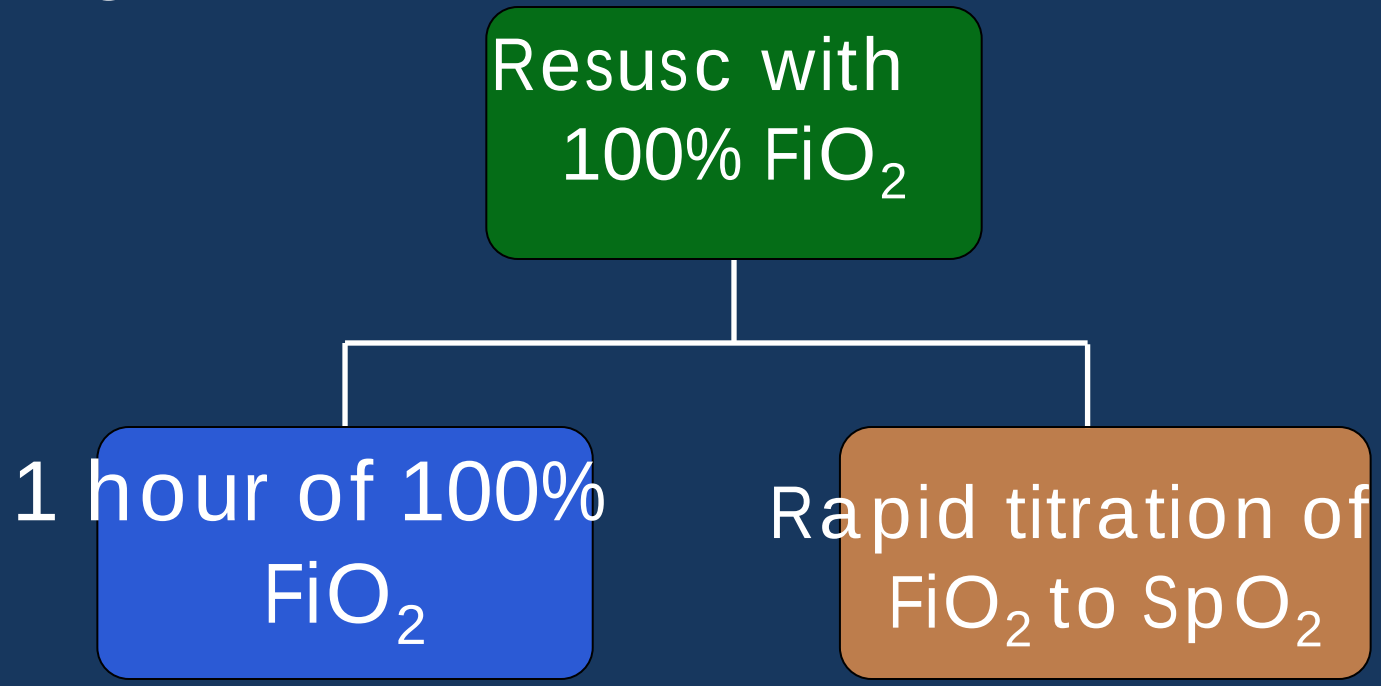
Ventilator Management

- Most patients with ROSC don't have ALI
- Standard ventilator mode/strategy
- Guidelines emphasize 100% FiO_2 during CPR
- Clinicians frequently maintain 100% O_2
- Early hyperoxia harms postischemic neurons

Oximetry-Guided Reoxygenation Improves Neurological Outcome After Experimental Cardiac Arrest

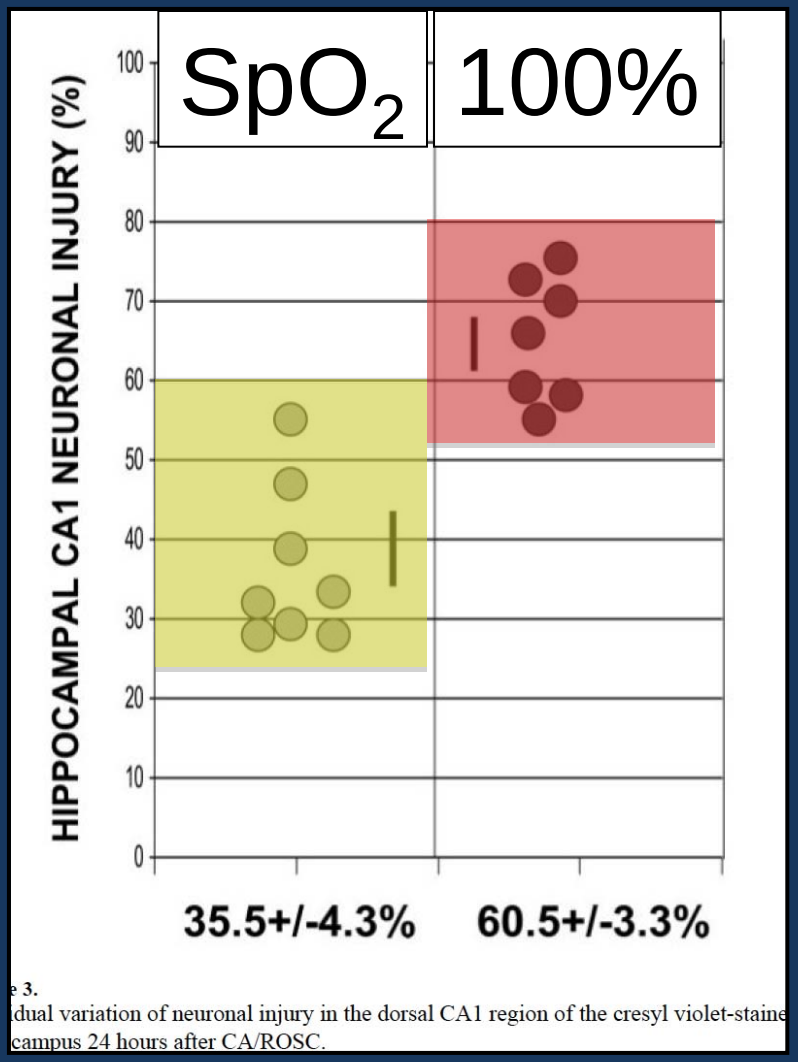
Irina S. Balan, PhD, **Gary Fiskum, PhD**, **Julie Hazelton, MS**, **Cynthia Cotto-Cumba, MD**, and **Robert E. Rosenthal, MD**
From the Departments of Anesthesiology (I.S.B., G.F., J.H., R.E.R.) and Surgery (C.C.-C., R.E.R.), Program in Trauma, University of Maryland School of Medicine, Baltimore, Md

- 100% FiO_2 v SpO_2 guided oxygenation
- Dog model cardiac arrest with ROSC

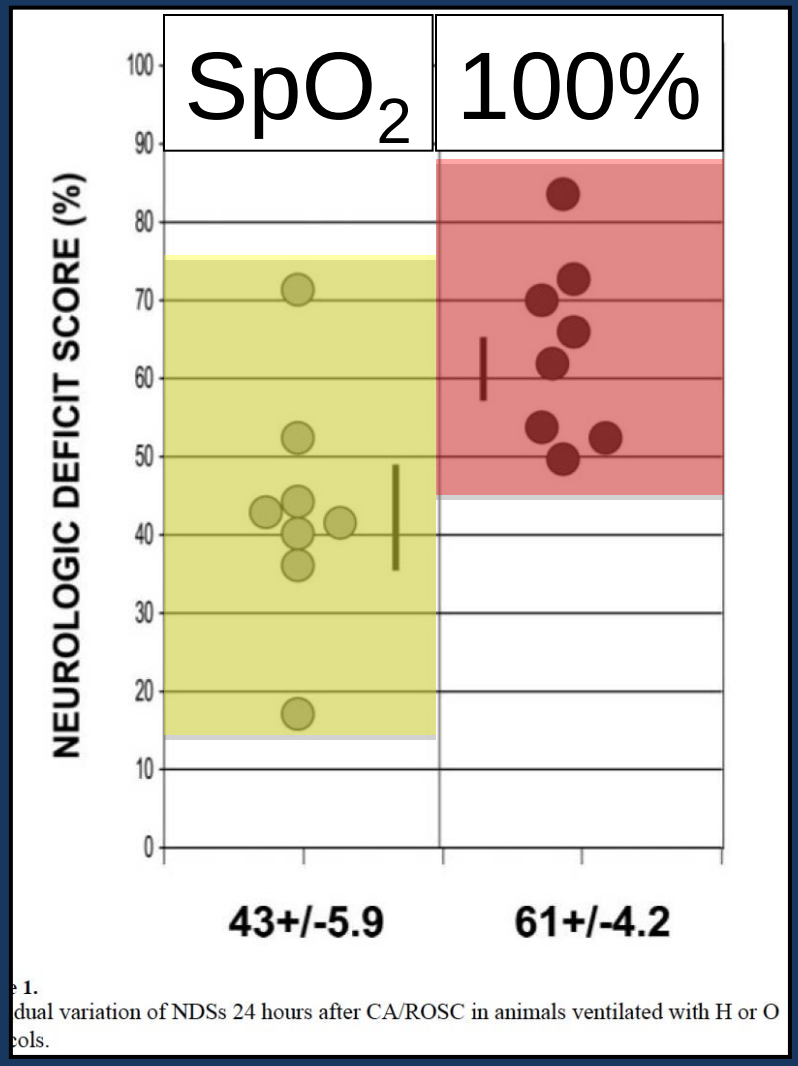


Balan IS, et al.STROKE. 2006; 37: 3008-13.

Ventilator Management



e 3.
idual variation of neuronal injury in the dorsal CA1 region of the cresyl violet-staine
campus 24 hours after CA/ROSC.



e 1.
dual variation of NDSs 24 hours after CA/ROSC in animals ventilated with H or O
cols.

Balan IS, et al. STROKE. 2006; 37: 3008-13.

Ventilator Management

- Cerebrovascular reactivity to $PaCO_2$ preserved
- No data to support specific $PaCO_2$
- Hyperventilation may produce cerebral ischemia
- Hypoventilation may increase ICP

Target normocarbia

Balan IS, et al.STROKE. 2006; 37: 3008-13.

Fluid and Electrolytes

- Cold diuresis
  - Venoconstriction, ↑ANP, ↓ADH, & tubular dysfunction
- If uncorrected
  - Hypovolemia → hypoperfusion
  - Hemoconcentration → hyperviscosity
- Rewarming, may unmask hypovolemia
- IVF load (w/o K^+) pre- and during rewarming

Fluid and Electrolytes

- Decreased electrolytes
  - K^+, Mg, Phos
- Diuresis induced renal excretion
- Intracellular electrolyte shifts
  - Shift extracellular with rewarming
  - Prevented with slow controlled rewarming
- Replace to low normal during cooling
  - If increased, treat before rewarming

Infection

- Infe
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- Sup e
- Pne or
  ven on
  – U
- No cs

TABLE 4. COMPLICATIONS DURING THE FIRST SEVEN DAYS AFTER CARDIAC ARREST.*

COMPLICATION	NORMOTHERMIA	HYPOTHERMIA
	no./total no. (%)	
Bleeding of any severity†	26/138 (19)	35/135 (26)
Need for platelet transfusion	0/138	2/135 (1)
Pneumonia	40/137 (29)	50/135 (37)
Sepsis	9/138 (7)	17/135 (13)
Pancreatitis	2/138 (1)	1/135 (1)
Renal failure	14/138 (10)	13/135 (10)
Hemodialysis	6/138 (4)	6/135 (4)
Pulmonary edema	5/133 (4)	9/136 (7)
Seizures	11/133 (8)	10/136 (7)
Lethal or long-lasting arrhythmia	44/138 (32)	49/135 (36)
Pressure sores	0/133	0/136

*None of the comparisons between the two groups, performed with the use of Pearson's chi-square test, indicated significant differences.

Infection

- Must be vigilant
  - Signs/symptoms not available
- Inspect lines/tubes, skin, routine CXRs
- Suspect if sudden increase in work of cooling device (↓water temp)
  - Indicates increase heat production
- Have low threshold to start antibiotics

Glucose Control

- Hyperglycemia
  - Decrease insulin sensitivity
  - Decrease insulin secretion
- Tight glucose control (80-110 mg/dL)
  - Reduced mortality in surgical ICU patients
  - No difference in medical ICU patients
    - If ICU stay $\geq$ 3 days, mortality reduced
    - No difference in subset with neuro disease

Van den Berghe, et al. NEJM. 2001; 345: 1359-67.
Van den Berghe, et al. NEJM. 2006; 354: 449-61.

Intensive Care Med (2007) 33:2093–2100
DOI 10.1007/s00134-007-0876-8

ORIGINAL

Tuomas Oksanen
Markus B. Skrifvars
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Anne Kuitunen
Ville Pettilä
Jouni Nurmi
Maaret Castrén

Strict versus moderate glucose control after resuscitation from ventricular fibrillation

- RCT of 90 comatose OH-VF patients
  - Strict (72 – 108 mg/dL)
  - Moderate (108 – 144 mg/dL)
- No difference in 30 day mortality
  - More hypoglycemic episodes in strict

Recommend target value ≤ 144 mg/dL

Oksanen et al. ICM, 2007; 33: 2093-2100.

Resuscitation Strategies

- Post-cardiac arrest syndrome similar to sepsis
- 2005 AHA/ILCOR guidelines recommend hemodynamic optimization of patients post-arrest

"Providers should try to normalize oxygen content and transport"

AHA Post-Resuscitation Support Circulation, 2005

Goal-directed hemodynamic optimization in the post-cardiac arrest syndrome: A systematic review☆,☆☆

Alan E. Jones[a], Nathan I. Shapiro[b], J. Hope Kilgannon[c], Stephen Trzeciak[c,d,*],

- Literature review looking for studies using goal-directed resuscitation post-arrest
- Inclusion criteria
  - Clearly defined intervention consisting of a structured cardiovascular resuscitation protocol
  - Control group in which subjects received standard of care therapy
- NO studies found

Jones A, et al. Resuscitation. 2008; 77: 26-29.

Post-Cardiac Arrest Early Goal-Directed Therapy

Who needs this?
Resuscitated patients with:
- Pulseless < 60 min
- GCS Motor score < 6
- No other reason for coma
- Not DNR or DNI status
- If pregnant consult Ob/Gyn

Getting Started
- Stat ECG, echocardiogram, and cardiology consult
- Stat head CT
- Insert arterial pressure monitoring line in radial or femoral artery
- Initiate therapeutic hypothermia if indicated (after arterial line)
- Insert Presep® CVC in subclavian or internal jugular vein
- Notify Bed Coordinator for ICU bed and EEG fellow for EEG

- 500 ml IVF over 5 min q 20 min until CVP >8
- Use 2 liters of 4°C saline (peripheral IV preferred) if initiating therapeutic hypothermia
- If no CHF, continue IVF to get MAP ≥ 80, but CVP no >20
- Consider PA cath if CVP>15 or > 5 liters IVF or CHF or significant vasopressor need

MAP

< 80

CVP > 8

< 80

> 80

> 100

- If EF is normal, use NOREPI
- If ↓EF, start DOBUT (2.5-20mcg/min). If MAP↓, add DOPA or EPI
- If severe hypotension→ IABP

- Start IV NTG at 10 mcg/min. Titrate to MAP ≤ 100. Assure adequate CVP
- Consider lasix if CHF
- If tachycardic or ACS* w/ normal EF & $ScvO_2$ then consider esmolol

80-100
(Consider lower goal if ACS*,CHF,Shock)

$ScvO_2$ ≥ 65%

Yes

No

If evidence of shock is present:
- Optimize CVP if not already done (up to 20)
- Transfuse PRBC's if hemoglobin ≤ 10 mg/dl
- Dobutamine if not already initiated
- Consider PA Cath if CVP>15 or escalating vasopressors

$ScvO_2$<65% w/ shock?

No

Yes

- Re-evaluate to achieve goal
- Consider IABP

MAP, CVP, $ScvO_2$ goals achieved

Monitor serial lactate to rule out inadequate organ perfusion

* ACS=Acute coronary syndrome

Updated 5/16/06

Is it working?

"We can implement early goal-directed hemodynamic optimization while inducing TH w/o negatively impacting time to target T°"

- Analyzed first 18 patients since start of TH
- 18 historic controls from 2001-2005
- Examined differences in

– Vasoactive drug use
– Volume resuscitation
– Mortality
– Good neurologic outcomes

Gaieski et al. Resuscitation. 2009; 80: 418-424.

Percentage of Patients Reaching End-Point at Specific Time

Resuscitation End-Point (hr)	0	1	2	3	4	5	6
CVP ≥ 8 ≤ 20 mmHg	77.8	Intravenous Fluid Boluses					81.3
MAP 80-100 mmHg	50.0	Vasoactive Medications					83.3
ScvO2 > 65	83.3	Inotropic Agents and Blood					93.8
Target Temp 32-34°C	5.6	11.1	44.4	55.6	61.1	66.7	77.8

4°C Chilled Saline; Cooling Wraps

Gaieski et al. Resuscitation. 2009; 80: 418-424.

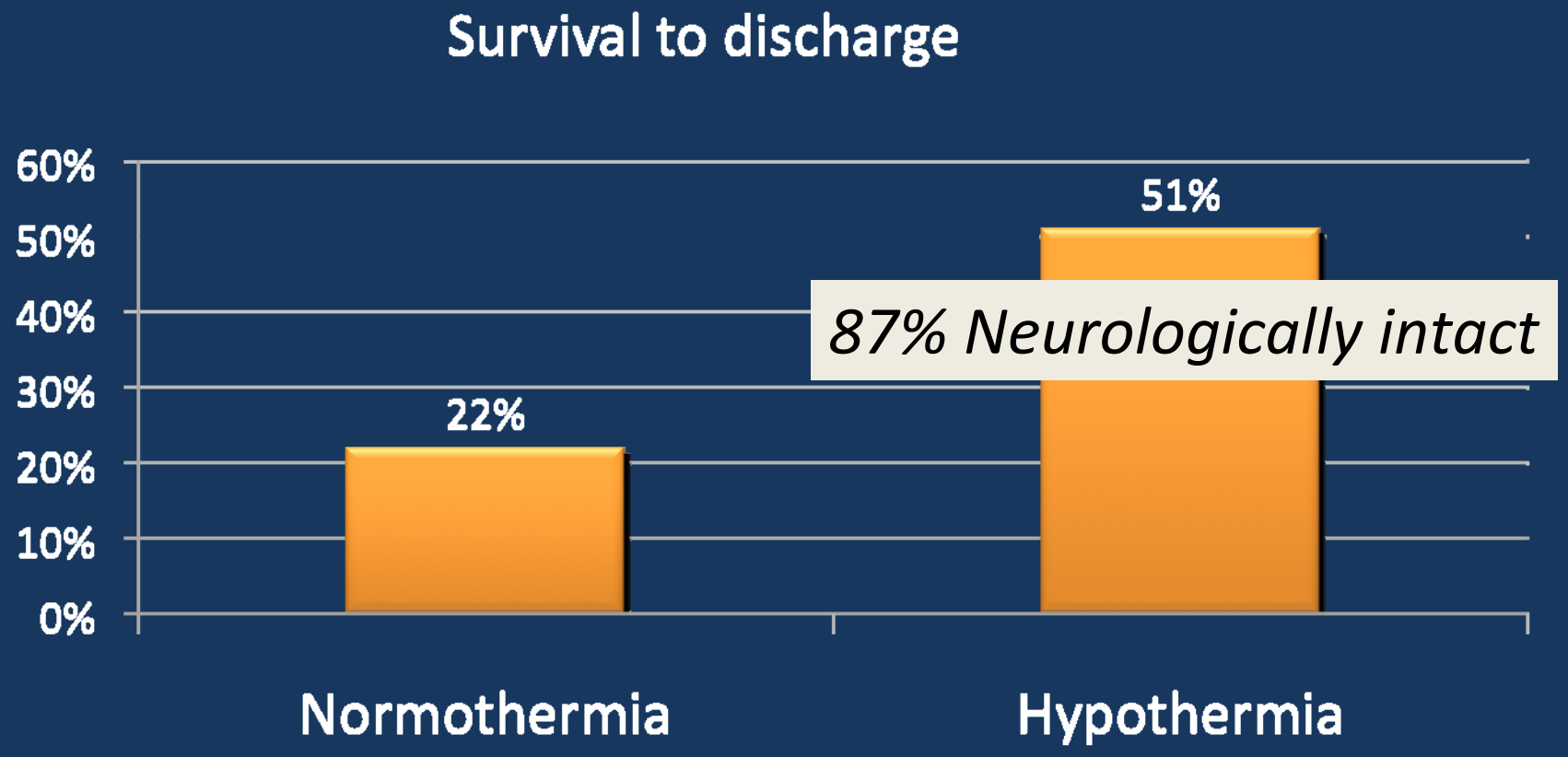
Vasoactive Agents

	Hour	EGDHO	Historic
Vasopressor	1	38.8	22.2
	6	38.8	50.0
	24	29.4	28.5
Inotrope	1	29.4	0.0
	6	38.8	0.0
	24	33.3	0.0
Vasodilator	1	27.7	11.1
	6	33.3	25.0
	24	17.6	14.2

Fluid Balance

		EGDHO	Historic
ED	Input	2543.3	812.5
	Output	117.6	125.0
	Balance	2425.7	687.5
12 Hours	Input	5761.0	1450.5
	Output	2006.6	1726.5
	Balance	3754.4	-276.0
24 Hours	Input	8624.1	4203.0
	Output	3057.7	2851.1
	Balance	5566.4	1351.9

Outcomes Data—76 patients



Resuscitation Strategies

- Reasonable goals for PCAR include
  - MAP of 65 to 100 mm Hg
    - Consider patient's normal BP
    - Cause of arrest
    - Severity of any myocardial dysfunction
  - CVP of 8 to 12 mm Hg
  - $ScvO_2$ 70%
  - Urine Output 1 mL/kg/hr
  - Normal or decreasing serum lactate level

Case: Conclusion

- HD#2 – extubated
- HD #3 – sitting up asking for diet soda
- Normal cath and EP studies
- Cause of arrest
  - Tako tsubo
- AICD placed
- Discharged HD # 11
- Practicing dentist in the Mid-Atlantic

Conclusions

- Hypothermia is a 3 phase process
- Consider routine paralysis for induction
- Treat cold diuresis with IVF
- Check electrolytes frequently and correct aggressively in induction and maintenance
- Monitor for infection, particularly pneumonia
- Consider empiric antibiotics
- Target glucose $\leq$ 144 mg/dL

Thank you!

Dave Gaieski
Ben Abella
Bob Neumar
Lance Becker
Roger Band
Sanjay Desai
Howard Cooper
Greg Marchand
Allen Wolfe
Kori Hudson
Brendan Furlong

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