

Get With The Guidelines® -Resuscitation: Physiologic-Directed CPR



March 20, 2019

Presenter:

Robert Michael Sutton MD MSCE FAAP FCCM
Associate Professor of Anesthesia, Critical Care, and
Pediatrics

Meet Our Presenter



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Associate Professor of Anesthesia, Critical Care, and Pediatrics

Chair: Resuscitation Committee at The Children's Hospital of Philadelphia

Medical Lead: Preventing Codes Outside the ICU

Co-Director: Resuscitation Science Research Program
Department of Anesthesiology and Critical Care Medicine
University of Pennsylvania School of Medicine

Personalizing Resuscitation with Physiologic-Directed CPR

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March 16th, 2019



Presenter Disclosure Information

Current Research Support:

NIH NHLBI (PI R01 – clinical)
NIH NHLBI (PI R01 – clinical)
NIH NHLBI (Co-I R01 – large animal)
NIH NICHD (Co-I R21 – large animal)
Mallinckrodt Pharma (Co-I – large animal)

Past Research Support:

NIH NICHD (PI K23)
Laerdal Foundation / Laerdal Corporation
Zoll medical

Intellectual Conflicts:

Chair Elect: AHA GWTG-R Pediatric Research Task Force
2015 and 2018 PALS writing group member
Member: ECC Systems of Care Committee
Member: ECC Pediatric Emphasis Group
Member: ECC Science Review Task Force

Speaking Honoraria:

Zoll Medical for Pediatric CPR Quality Talk



Objectives

At the conclusion of this talk, participants will be able to:

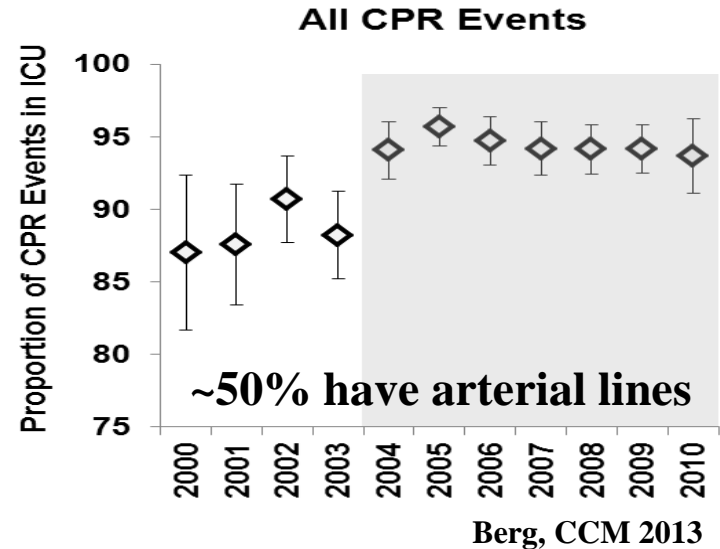
Understand the concept, the targets, and the potential practical application of physiologic-directed CPR.

Recommendation:

- For patients with invasive hemodynamic monitoring in place at the time of arrest, it may be reasonable for rescuers to use blood pressure to guide CPR quality. No specific values can be recommended.

Why?

- Arrests most often occur in ICUs
- Many have arterial lines in place
- Two randomized controlled animal studies demonstrated improved survival with such an approach (Sutton, Resuscitation 2013 and AJRCCM 2014)
- Not studied in humans... yet

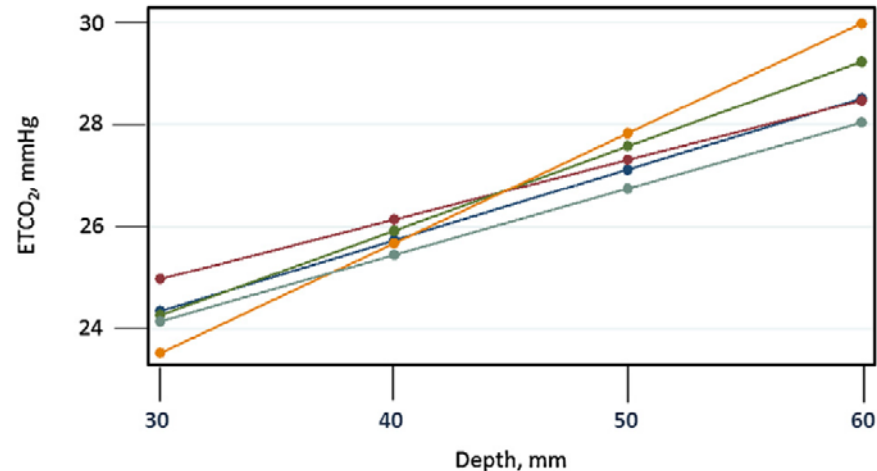


Recommendation:

- ETCO₂ monitoring may be considered to evaluate the quality of chest compressions, but specific values to guide therapy have not been established in children.

Why?

- No pediatric evidence to support that ETCO₂ monitoring during arrest improves outcomes...
- But ETCO₂ values during adult CPR correlate with CC depth and ventilation rate.
- Low end tidal associated with death



A 4 year old presents with fever, bacteremia, and hypotension. The child receives 60cc/kg of isotonic fluid. Blood pressure is now 100/50. Heart rate is normal for age. Extremities are warm. I would start the following vasopressor infusion:

- A. Epinephrine
- B. Norepinephrine
- C. Vasopressin
- D. Dobutamine
- E. None

A 4 year old intubated ICU patient has a cardiac arrest. An arterial line is in place at the time of the arrest. Etiology is presumed to be respiratory decompensation. With chest compressions alone, the arterial blood pressure is 100/50. The first vasopressor I would give to treat this cardiac arrest is:

- A. Epinephrine
- B. Norepinephrine
- C. Vasopressin
- D. Isoproterenol
- E. None

Rescuer-Centric Vs. Patient-Centric

Rescuer

Performance

“Mechanics”

Rate

Depth

Release Velocity

Interruptions



Time to
Shift the Focus

Patient

Physiology

CoPP

DBP

ETCO₂

NIRS (rSO₂)

Landmark Studies Change Talks

[Eur J Anaesthesiol.](#) 2018 Jul 16. doi: 10.1097/EJA.0000000000000855. [Epub ahead of print]

Near-infrared spectroscopy in vegetables and humans: An observational study.

Kahn RA¹, Anyanwu A.

Author information

Abstract

BACKGROUND: Cerebral near-infrared spectroscopy (NIRS) of tissue oxygen saturation is claimed to be a surrogate marker for global cerebral perfusion. Increasingly, NIRS target-based therapy has been used during cardiac surgery in the hope of decreasing the incidence of adverse neurological outcome.

OBJECTIVES: We report NIRS values for some common vegetables and faculty at a world-class medical institution.

DESIGN: Observational nonblinded study.

SETTING: Single tertiary care institution and local urban vegetable market.

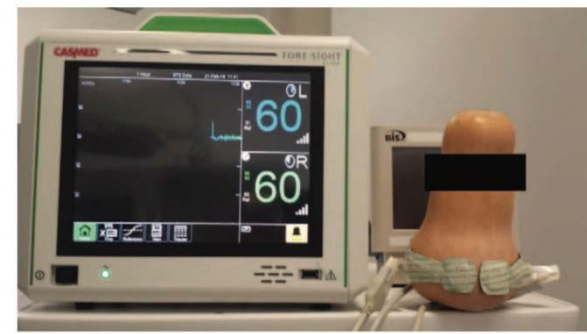
PARTICIPANTS: Five yams (*Dioscorea cayenensis*), five courgettes (*Cucurbita pepo*) and five butternut squashes (*Cucurbita moschata*) were studied. Five cardiothoracic surgeons and anaesthesiologists were the control group.

INTERVENTIONS: None.

MAIN OUTCOME MEASURES: NIRS value of each species.

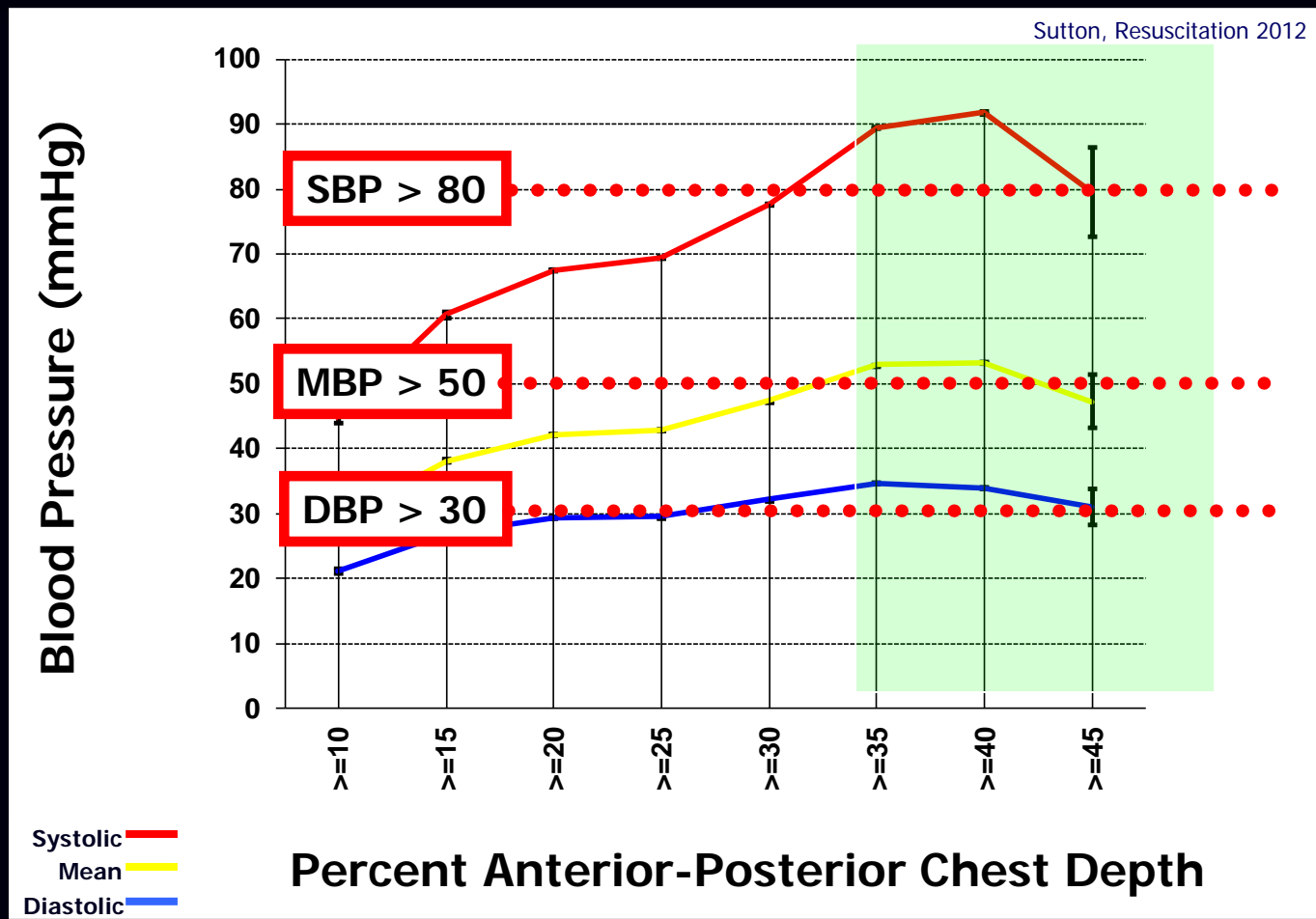
RESULTS: Mean NIRS value for the control group was 71% [95% confidence interval (CI) 68 to 74] and was similar to that of the yellow squashes [75% (95% CI 74 to 76)]. These values were significantly greater than the NIRS measurements of both the butternut squash and yam [63% (95% CI 62 to 64) and 64% (95% CI 63 to 65), respectively, $P < 0.01$].

CONCLUSION: Commonly eaten vegetables have NIRS measurements similar to those seen in healthy humans.



Experimental setup. A butternut squash is being studied. The oximetry probes are applied transversely at the widest level. The optical sensors are affixed side to side with the light emitting diodes positioned laterally. A portion of the subject was obscured to ensure anonymity.

Push Hard = Better Pediatric BPs



Clinical Paper

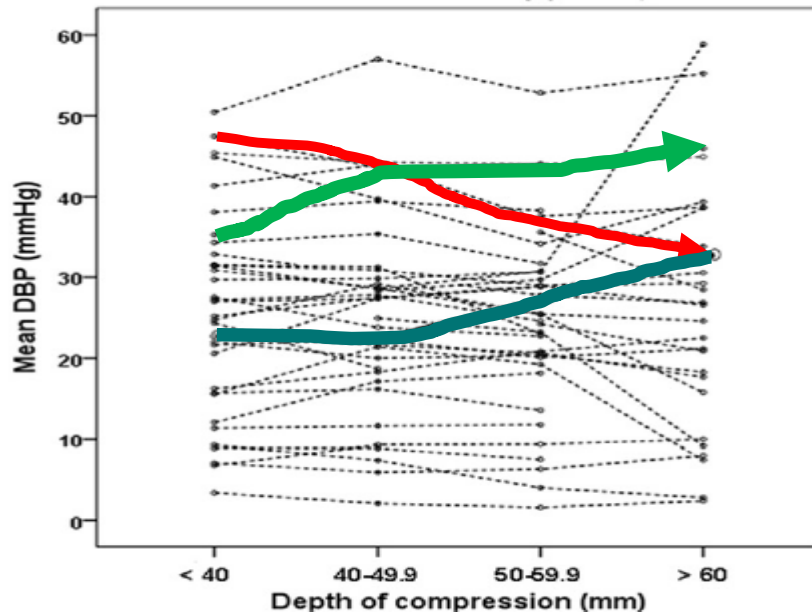
Resuscitation. 2015 Nov;96:163-9.

Simultaneous beat-to-beat assessment of arterial blood pressure and quality of cardiopulmonary resuscitation in out-of-hospital and in-hospital settings[☆]



Marko Sainio^{a,b,*}, Sanna Hoppu^a, Heini Huhtala^c, Joar Eilevstjønn^d, Klaus T. Olkkola^e, Jyrki Tenhunen^{a,f}

Femoral and radial artery patient, n=39



OHCA and IHCA
39 Patients
~42000 Compressions
Substantial heterogeneity

	Femoral artery recording n = 24	Radial artery recording n = 15
Male, No. (%)	18 (75)	10 (67)
Age, mean (SD), y	65.5 (18)	64.1 (17)
Location of arrest, No.		
IHCA	20	15
OHCA	4	0
Time from CA to EMS or MET arrival, median (IQR), min	2 (0, 3)	1 (0, 2)
Interval from CA to ABP measure, median (IQR), min	13 (9, 18)	4 (3, 10)

A 2013 Consensus Statement from the AHA recommended which of the following physiologic CPR quality targets*:

A. Diastolic blood pressure $> 30\text{mmHg}$

B. Coronary Perfusion Pressure $> 20\text{mmHg}$

C. $\text{ETCO}_2 > 10\text{mmHg}$

D. NIRs $> 50\%$

*Based on almost NO pediatric data

AHA Consensus Statement

CPR Quality: Improving Cardiac Resuscitation Outcomes Both Inside and Outside the Hospital

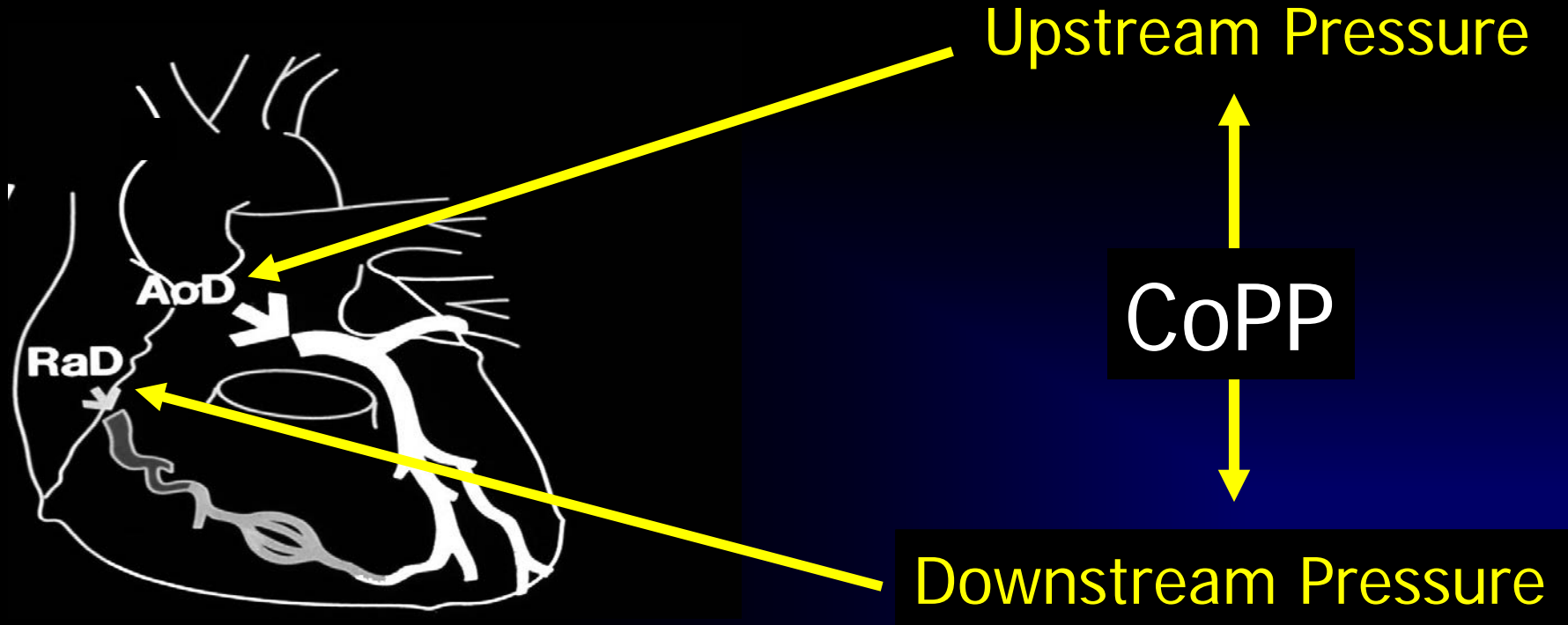
A Consensus Statement From the American Heart Association

Endorsed by the American College of Emergency Physicians

- **Monitor the patient's response to the resuscitation effort**
 - **Coronary perfusion pressure > 20mmHg**
 - **Diastolic pressure > 25mmHg**
 - **End Tidal Carbon Dioxide > 20mmHg**

Coronary Perfusion Pressure (CoPP)

Pressure gradient that drives myocardial blood flow



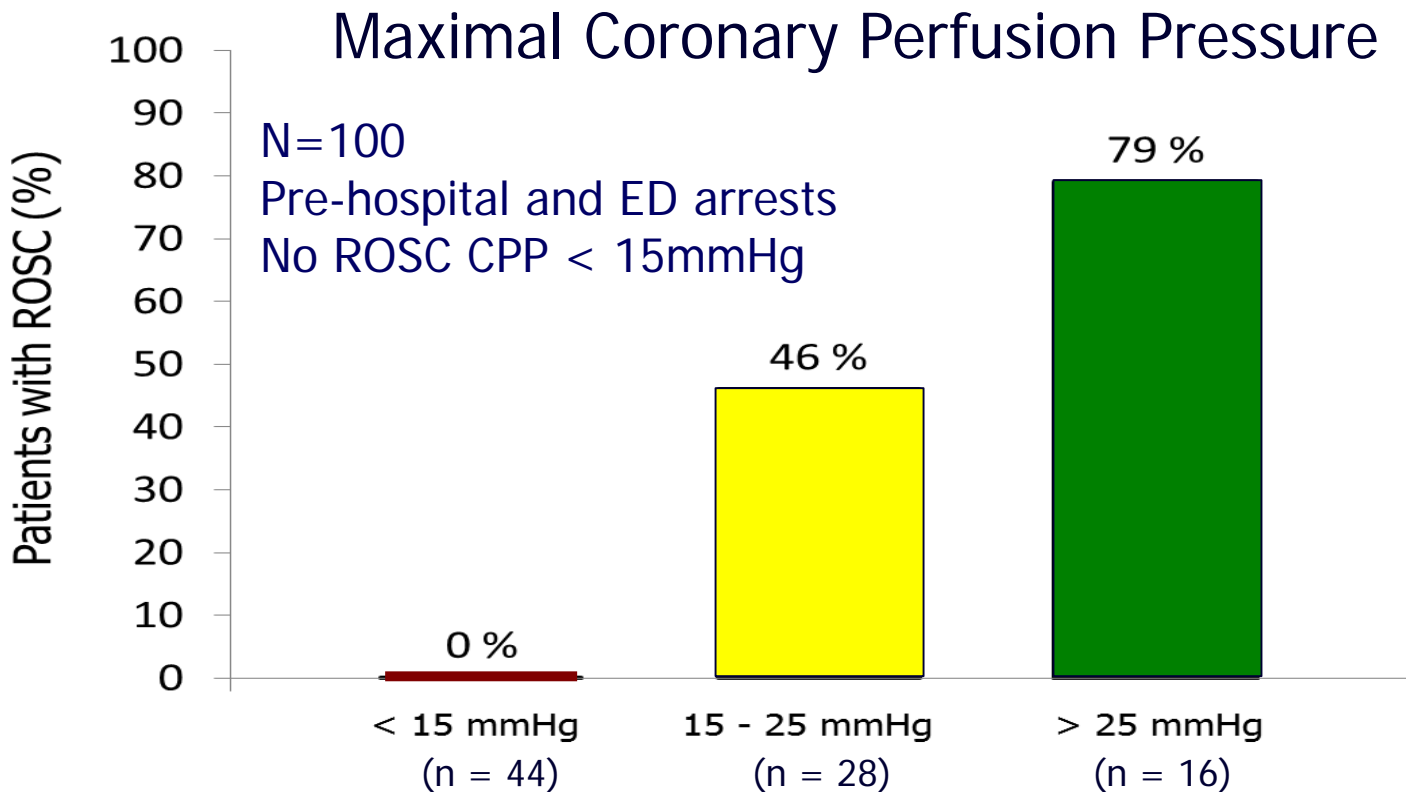
What are the right «goals» to target?

“ One... presses deep in the heart region

Effectiveness Measured
by Monitoring
Patient Response

Maas, Berlin Klin Wochenschr 1892

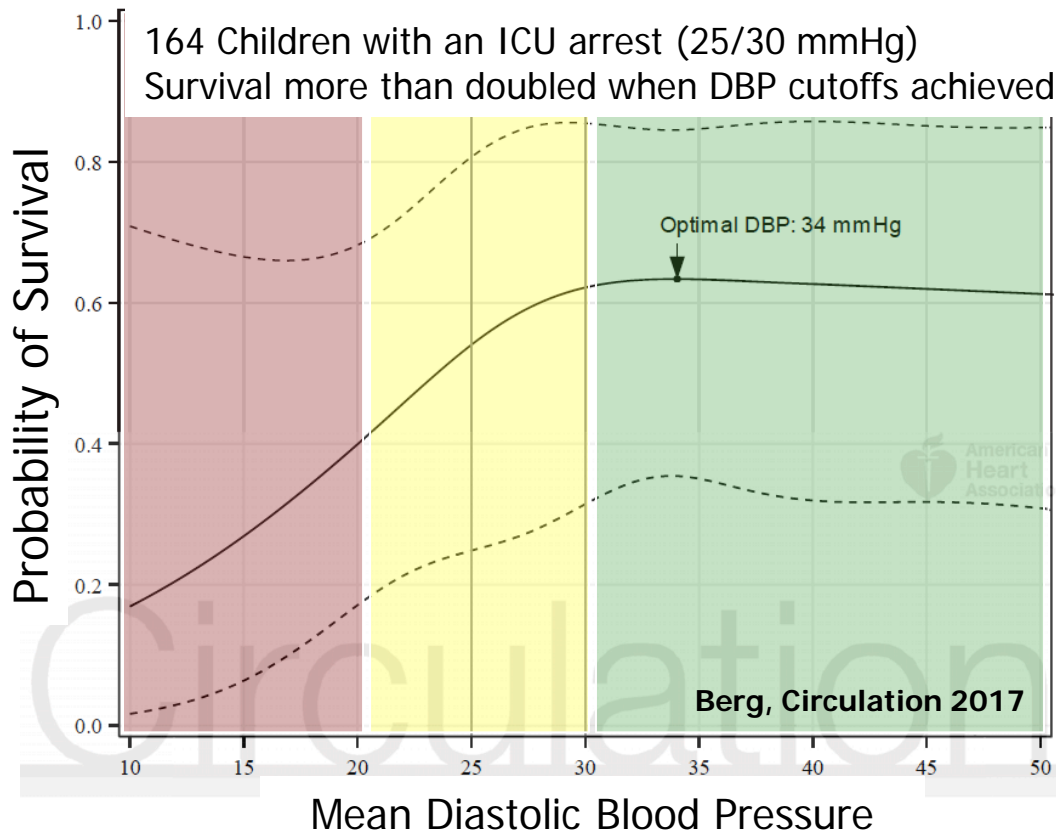
CoPP Higher in Patients with ROSC



Among these markers of CPR quality, which one has been associated with improved survival to hospital discharge with favorable neurological outcome after pediatric cardiac arrest?

- A. Chest compression rate 100-120 per minute
- B. DBP \geq 25mmHg in infants, \geq 30mmHg in older children
- C. ETCO₂ during CPR \geq 20mmHg
- D. Depth of compression > 50 mm

DBP Higher in Kids Who Survive



Hemodynamic-Directed Training Tools

Collaboration
with Biomedical Engineers

Monitoring and Titrating
to a Clinical Endpoint
makes sense to Clinical
Care Providers

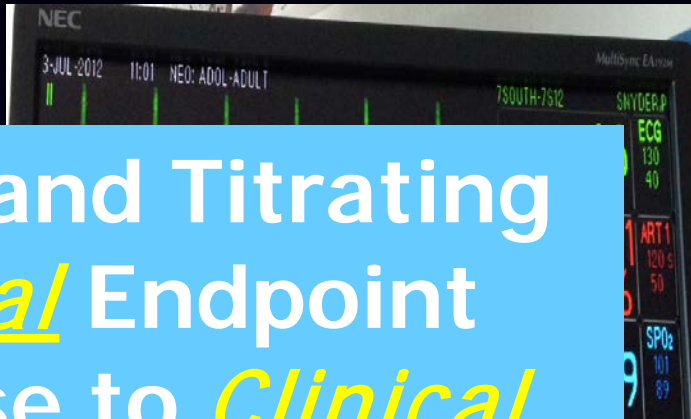


TABLE 3. Multivariable Model Adjusted for Clustering on Subject
Wolfe, PEC 2015

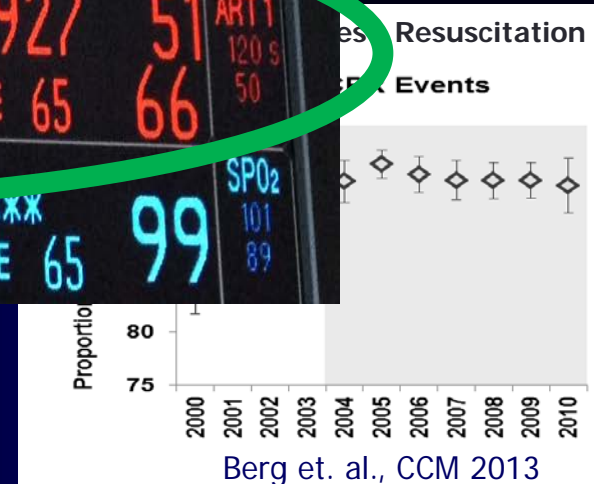
	OR	95% CI	P ^a
Acquisition			
Posttraining	5.2	1.3–21.2	0.02
Retention ^a			
12 h	4.4	1.3–14.9	0.018
3 mo	4.1	1.2–13.9	0.023



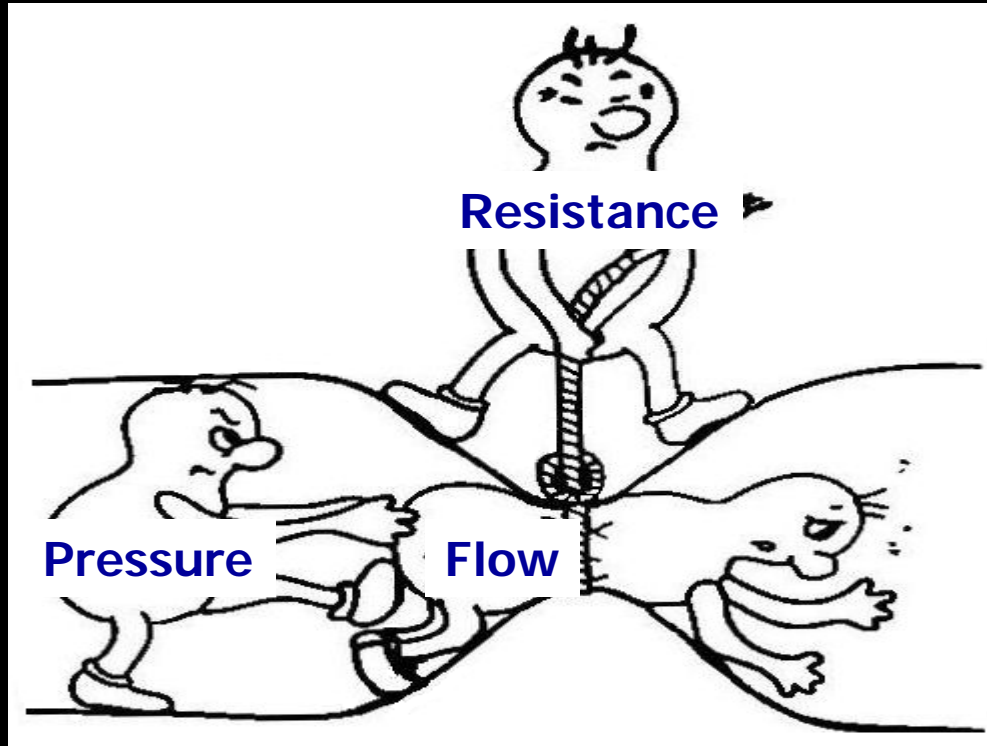
In-Hospital CPR \approx Out-of-Hospital CPR



JUST LOOK UP!



Pressure \neq Flow



Expired CO₂ (ETCO₂) Represents Flow

Blood flows out to the body



Gas exchange in the tissues:
CO₂ is picked up

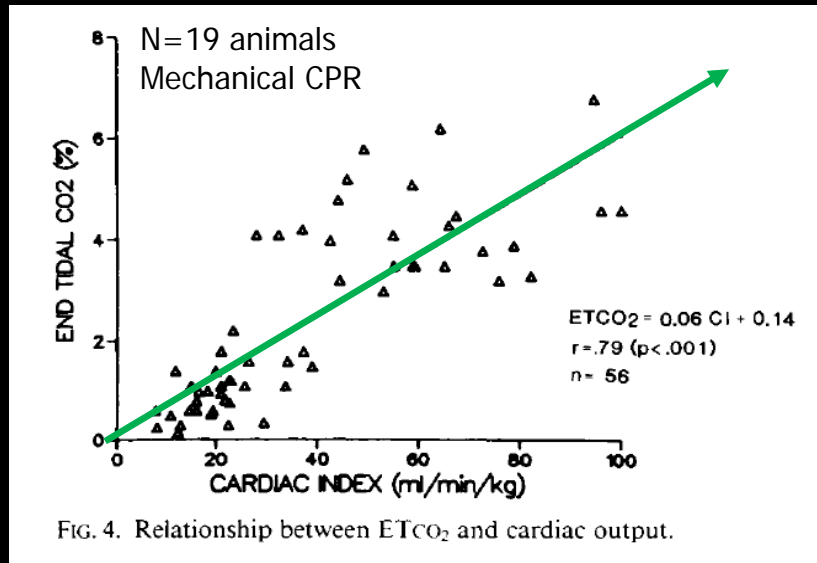


Better CCs
Move more blood

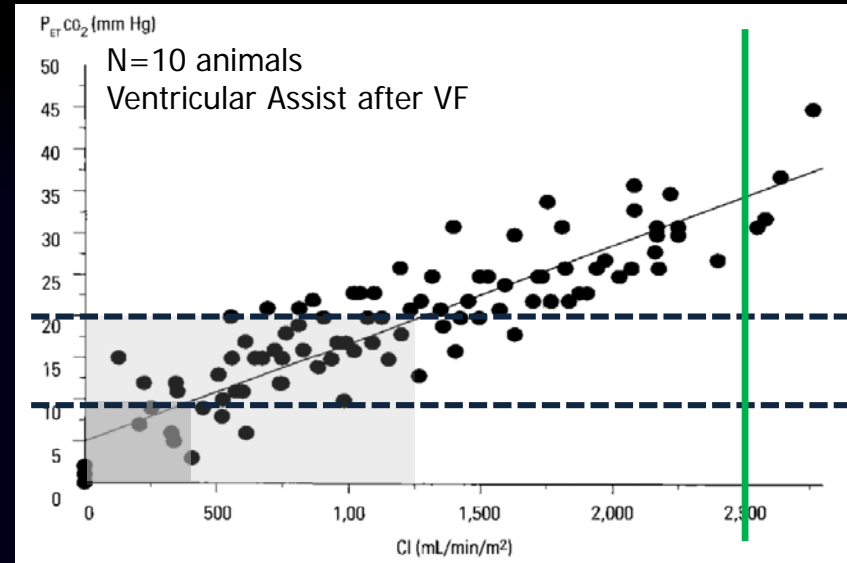


Higher ETCO₂

Translational Evidence: End-Tidal CO₂ is Proportional to Cardiac Output

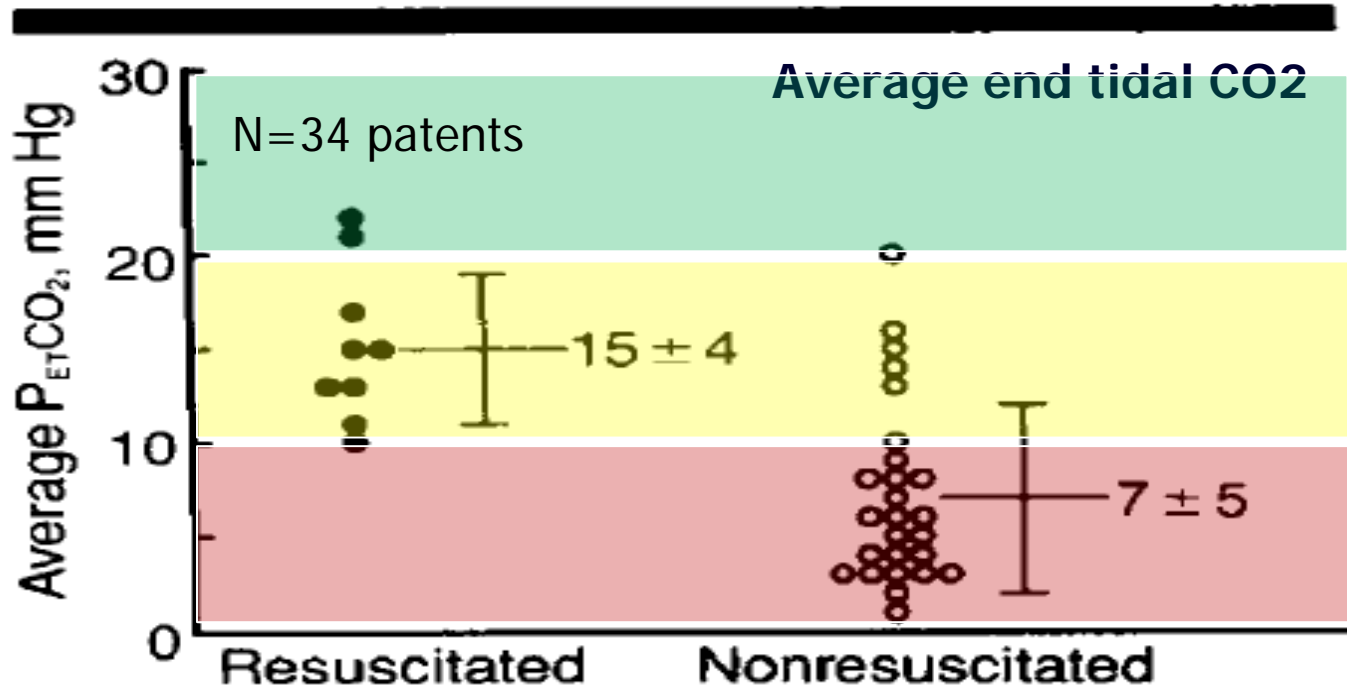


Weil, Crit Care Med 1985



Idris, Ann Emerg Med 1994

ETCO₂ in Adult IHCA / OHCA





Clinical Paper

[Resuscitation](#). 2015 Apr;89:149-54.

Quantitative relationship between end-tidal carbon dioxide and CPR quality during both in-hospital and out-of-hospital cardiac arrest[☆]



Kelsey R. Sheak^a, Douglas J. Wiebe^b, Marion Leary^a, Saeed Babaeizadeh^d,
Trevor C. Yuen^c, Dana Zive^f, Pamela C. Owens^e, Dana P. Edelson^c, Mohamud R. Daya^f,
Ahamed H. Idris^e, Benjamin S. Abella^{a,*}

583 cardiac arrest events (both OHCA and IHCA)
~30,000 chest compressions analyzed

Table 4

Assessment of overall case resuscitation characteristics by clinical outcomes.

	ROSC	No ROSC	<i>p</i> -Value	Survival to discharge	No survival to discharge	<i>p</i> -Value
Rate (cpm)	109.0 ± 8.4	110.0 ± 9.7	NS	110.0 ± 7.6	109.6 ± 9.4	NS
Depth (mm)	44.5 ± 8.0	43.8 ± 8.3	NS	44.9 ± 7.7	44.0 ± 8.4	NS
ETCO ₂ (mmHg)	34.5 ± 4.5	37.1 ± 13.7	<.001	38.3 ± 13.2	37.1 ± 15.3	<.001

All values are means ± standard deviation. cpm, compressions per minute; NS, not significant.

No Signal During Pediatric CPR

Multicenter study of 43 intubated children (HLHS excluded)
Primary evaluation: AHA target of 20mmHg

	ROSC \geq 20 min		Survival to Hospital Discharge	
	Relative Risk (95% CI)	P-value	Relative Risk (95% CI)	P-value
Mean ETCO ₂ (mmHg) over the first ten minutes	1.01 (0.99, 1.03)	0.605	0.99 (0.95, 1.04)	0.782
Mean ETCO ₂ over the first ten minutes > 20 mmHg	1.32 (0.89, 1.95)	0.162	0.92 (0.41, 2.08)	0.839
Mean ETCO ₂ over the first ten minutes > 25 mmHg	1.02 (0.72, 1.45)	0.899	0.86 (0.36, 2.06)	0.728
Mean ETCO ₂ over the first ten minutes > 30 mmHg	1.05 (0.64, 1.74)	0.848	0.86 (0.24, 3.06)	0.818
Mean ETCO ₂ categories		0.237		0.988
< 20 mmHg	Reference		Reference	
20 - < 25 mmHg	1.56 (1.01, 2.42)		1.03 (0.36, 2.93)	
25 - < 30 mmHg	1.17 (0.72, 1.92)		0.88 (0.29, 2.63)	
\geq 30 mmHg	1.26 (0.72, 2.19)		0.84 (0.22, 2.99)	
All ETCO ₂ < 10 mmHg	0.71 (0.25, 2.00)	0.520	0.60 (0.11, 3.39)	0.562
All ETCO ₂ < 15 mmHg	0.88 (0.55, 1.41)	0.593	1.17 (0.45, 3.02)	0.748
All ETCO ₂ < 20 mmHg	1.03 (0.70, 1.50)	0.886	1.28 (0.55, 3.00)	0.563

A Sudden Increase in Partial Pressure End-Tidal Carbon Dioxide at the Moment of Return of Spontaneous Circulation

Pokorná 2010

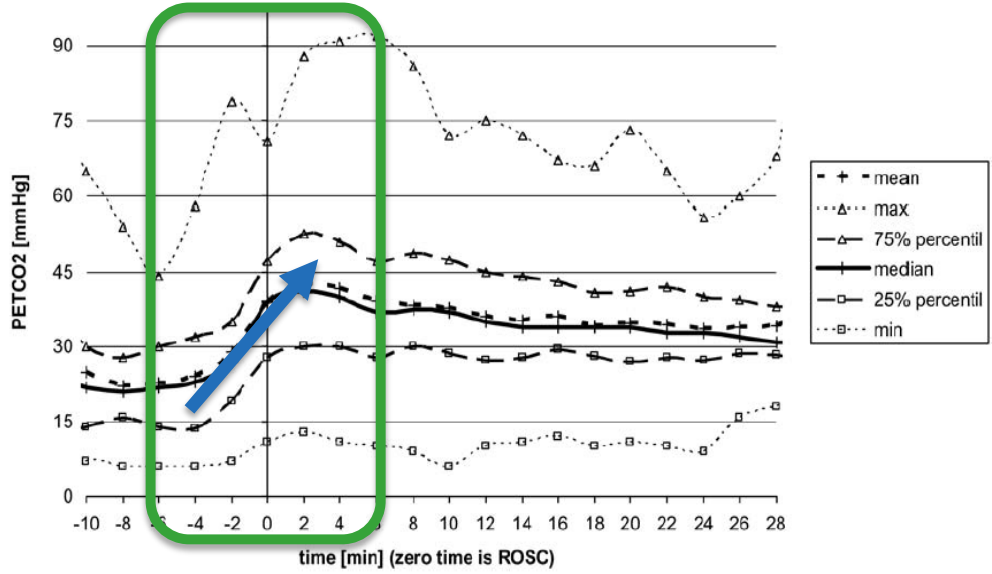
Out-of-hospital cardiac arrest

Adults (n=108)

2 Groups

- 59 with single episode of ROSC
- 49 with no signs of ROSC

ROSC = pulse

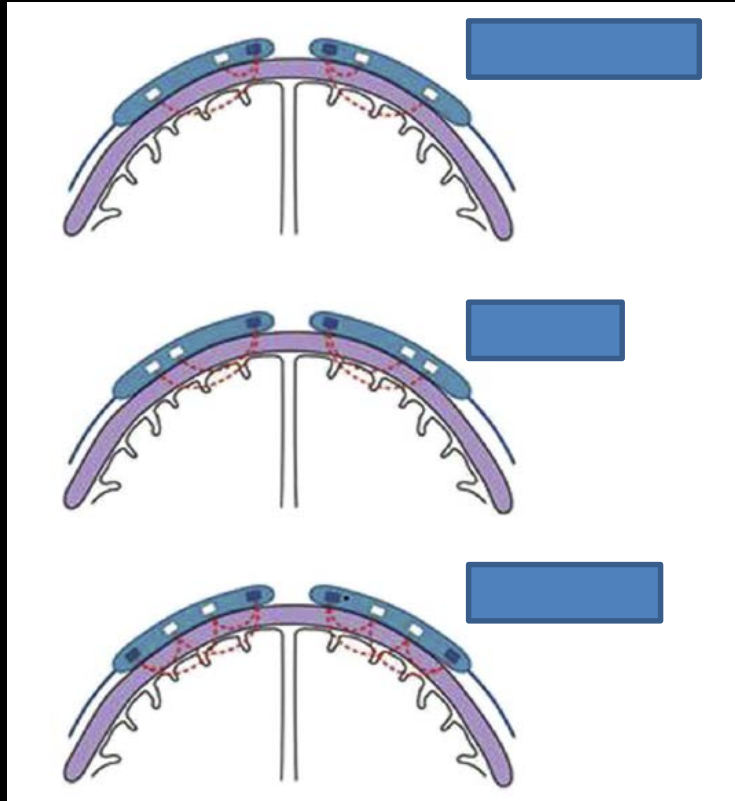


ETCO₂ ~10mmHg higher after ROSC (27 vs. 37)

End-tidal carbon dioxide monitoring during CPR may be unreliable in the following clinical circumstances:

- A. Leak around invasive airways
- B. Vasopressor administration
- C. Sodium bicarbonate administration
- D. All of the above

Cerebral Oxygen Saturation: NIRS



Non-invasive

Subtle differences

emitters, detectors

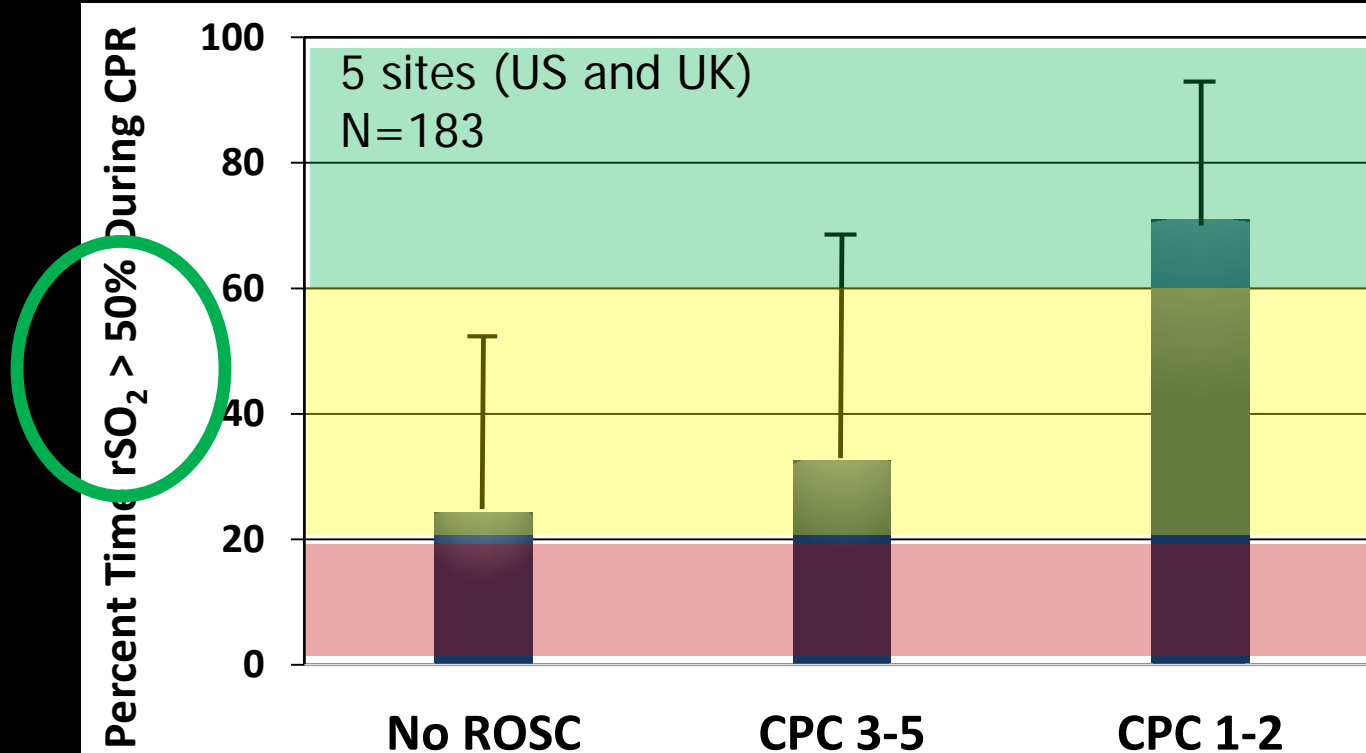
lowest detectable values

ambient light sensitivity

Can measure CPR quality when
pulsatile flow is not present

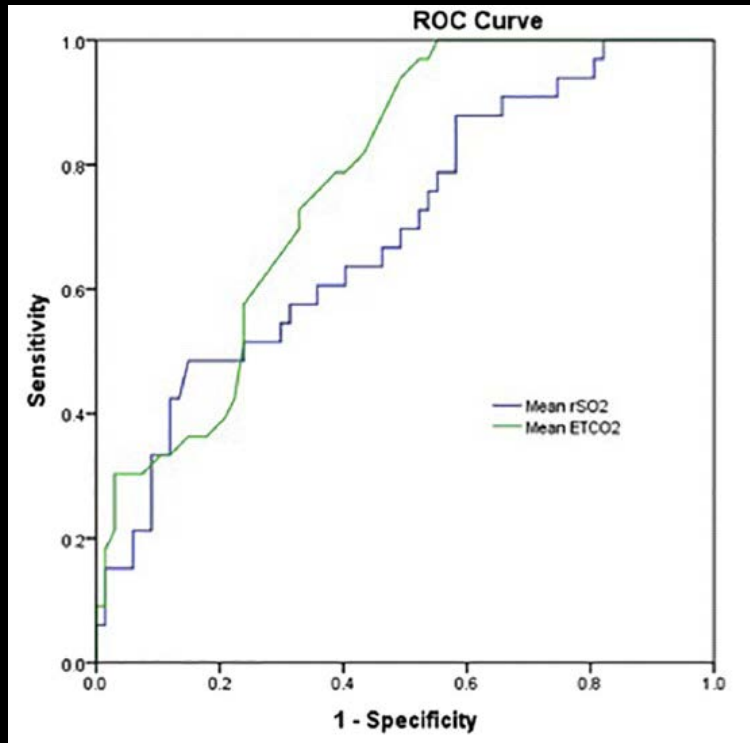
Cerebral Oximetry During Cardiac Arrest: A Multicenter Study of Neurologic Outcomes and Survival*

Parnia, CCM 2016



Cerebral oximetry versus end tidal CO₂ in predicting ROSC after cardiac arrest

Adam J. Singer, MD^{a,*}, Robert T. Nguyen, MD, MPH^b, Shreyas T. Ravishankar, MD^b,
Elinor Randi Schoenfeld, PhD^c, Henry C. Thode Jr, PhD^a, Mark C. Henry, MD^a, Sam Parnia, MD, PhD^b



ED patients with OHCA (n=100)

AUCs were similar (~0.7)

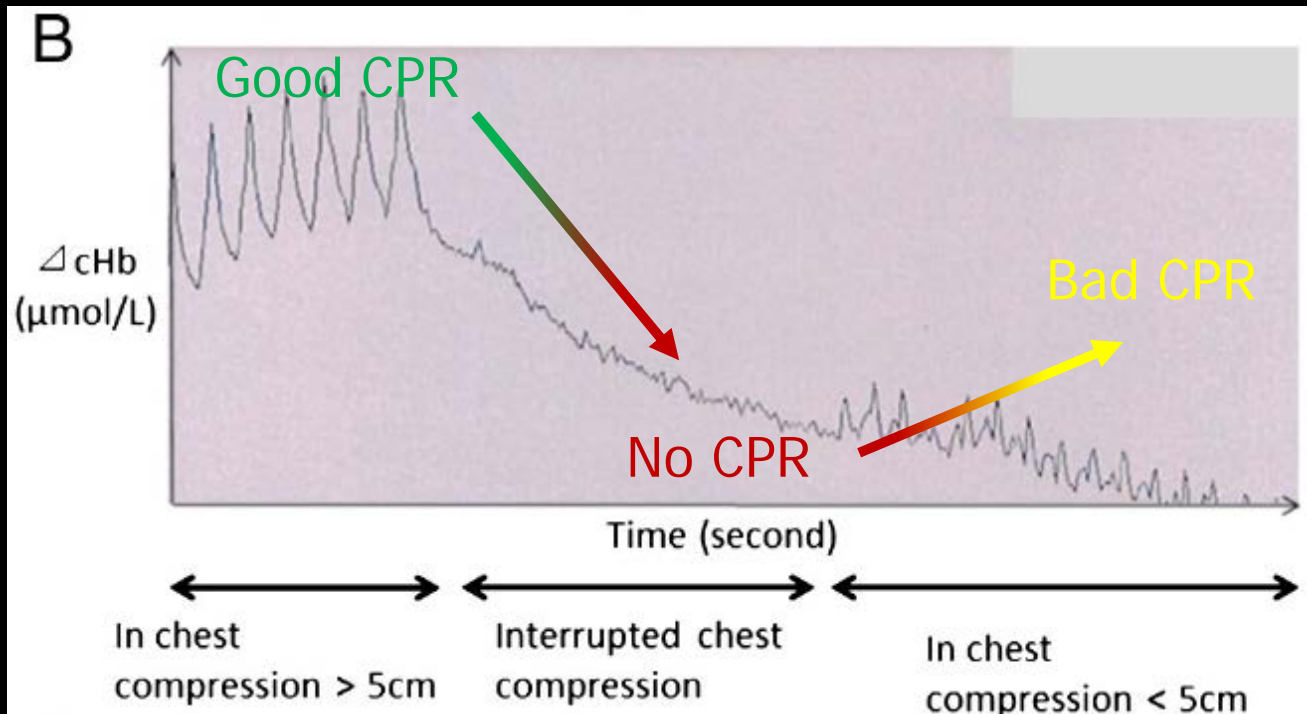
Poor correlation

ETCO₂ more sensitive

rSO₂ more specific

A new method to detect cerebral blood flow waveform in synchrony with chest compression by near-infrared spectroscopy during CPR

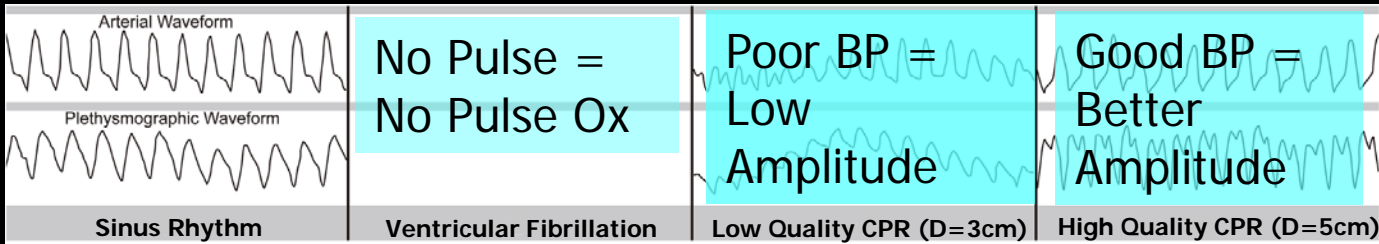
Yasuaki Koyama, MD*, Takafumi Wada, MD, Brandon D. Lohman, MD, Yuka Takamatsu, MD, Junichi Matsumoto, MD, Shigeki Fujitani, MD, Yasuhiko Taira, MD



Pulse Oximetry: A Non-Invasive, Novel Marker for the Quality of Chest Compressions in Porcine Models of Cardiac Arrest

Jun Xu¹, Chen Li², Liangliang Zheng³, Fei Han⁴, Yan Li¹, Joseph Walline⁵, Yangyang Fu¹, Dongqi Yao¹, Xiaocui Zhang⁴, Hui Zhang¹, Huadong Zhu¹, Shubin Guo¹, Zhong Wang⁶, Xuezhong Yu^{1*}

PLOS ONE | DOI:10.1371/journal.pone.0139707 October 20, 2015



		Low Quality (3cm)	High Quality (5cm)	t/U	P
HR (bpm)	3min	104±6	104±5	0.251	0.803
	6min	103±3	103±3	0.245	0.808
	9min	103±3	103±2	0.532	0.599
P _{ET} CO ₂ (mmHg)	3min	12±4	19±4	-4.830	<0.001
	6min	13±4	19±4	-3.948	<0.001
	9min	12±4	18±4	-4.690	<0.001
CPP (mmHg)	3min	14.6±9.8	25.0±17.5	-2.146	0.040
	6min	14±10	21±5	-2.301	0.028
	9min	15±10	21±5	-2.221	0.034
Amp (PVA)	3min	70±62	189±129	-3.317	0.003
	6min	71±63	194±132	-3.379	0.003
	9min	79±81	188±119	-3.081	0.005
AUC (PVPG)	3min	2215±852	3191±556	-3.872	0.001
	6min	2211±781	3193±517	-4.231	<0.001
	9min	2022±665	3067±522	-5.001	<0.001

Can we alter our resuscitation technique to improve outcomes?

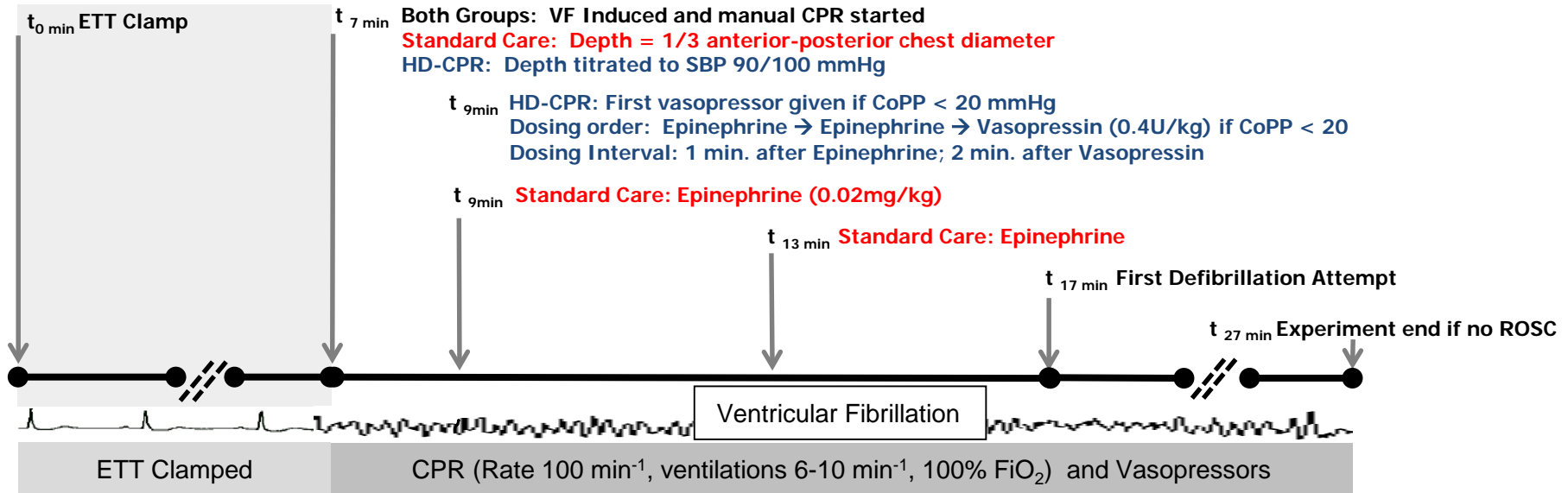
A translational perspective



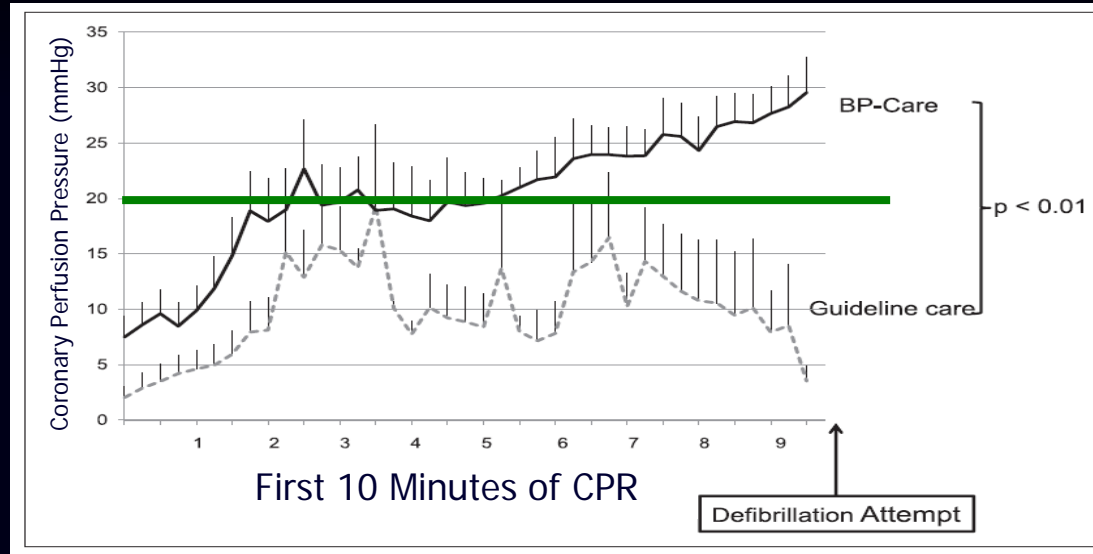
Hemodynamic-Directed CPR (HD-CPR)

Asphyxial Period

CPR Period



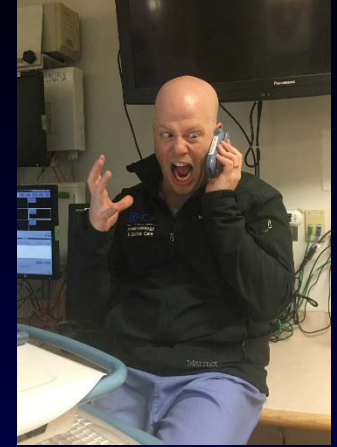
Asphyxia-Associated Cardiac Arrest



	Depth 51 (n=10)	CPP-20 (n=10)	p
Survival [n (%)]			
45 Minute ICU Survival	1 (10)	9 (90)	p = 0.001
24 Hour Survival	0 (0)	8 (80)	p = 0.001
Good Neurological Outcome	0 (0)	7 (70)	p = 0.003

What's next?

Pediatric asphyxia model
Adult asphyxia model
Adult VF model



But what about a progressive shock state?

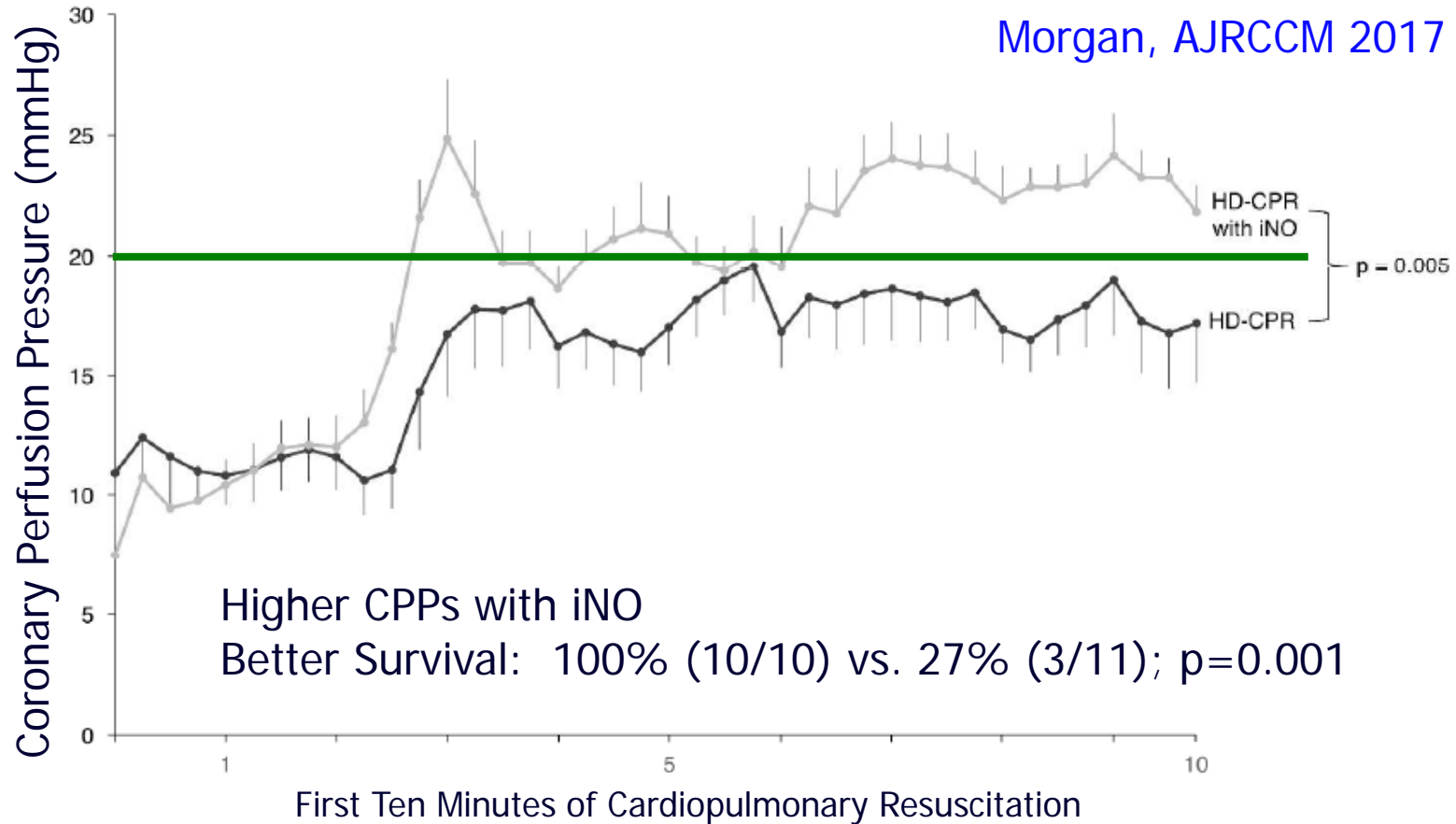
LPS model

The first 3 animals with HD-CPR died

Pulmonary HTN key physiologic roadblock

Shock Associated Cardiac Arrest

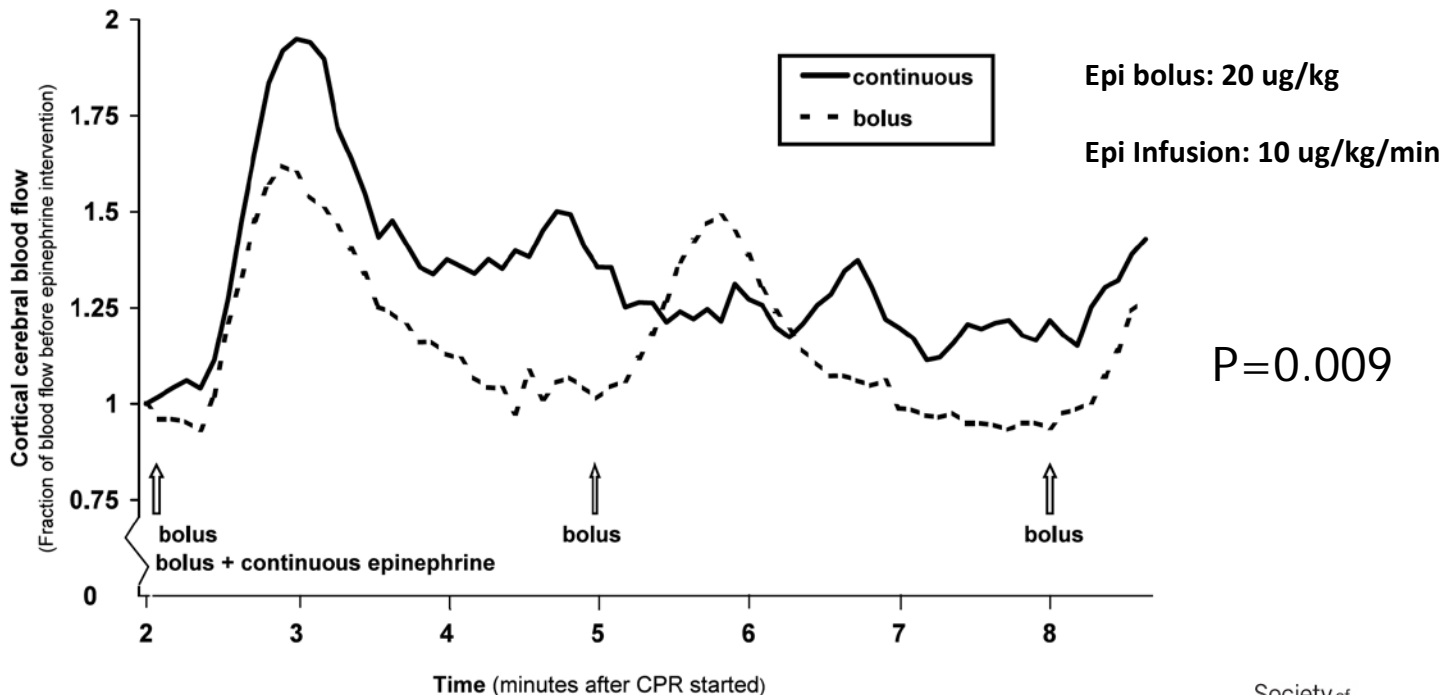
Morgan, AJRCCM 2017



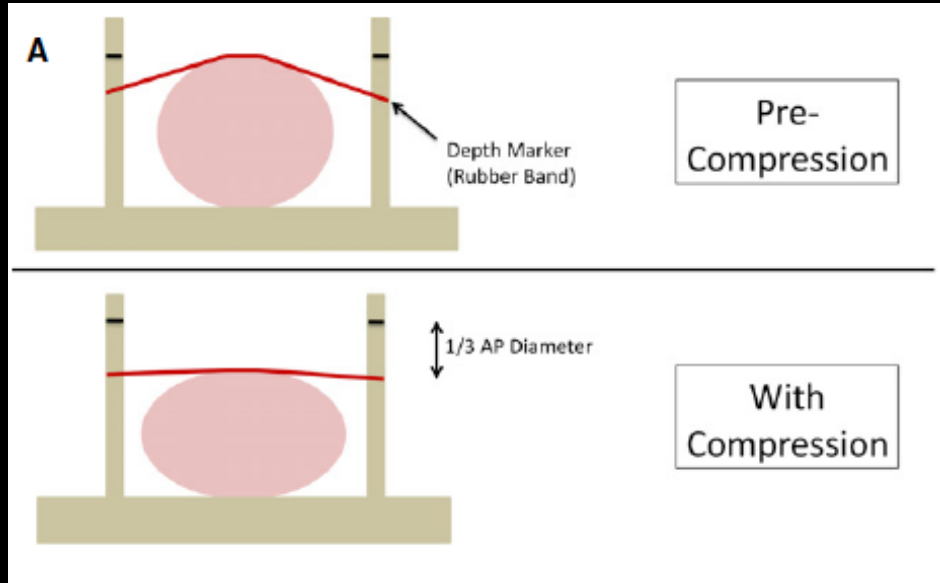
Bolus vs. Bolus + Continuous Epinephrine During CPR

N=24 animals
Laser Doppler CBF

Johansson Resuscitation 2003

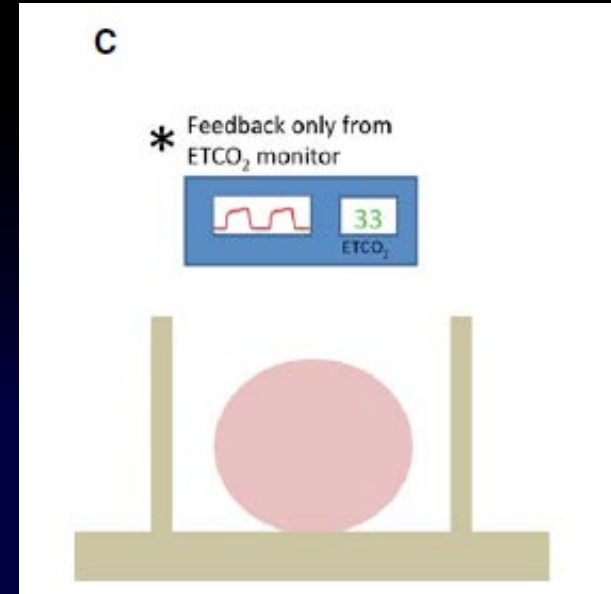


End Tidal CO₂ Guided Cardiopulmonary Resuscitation



Feedback optimized

VS



ETCO₂ Guided

Experimental Timeline

20 minutes of asphyxia

CPR, standard vs. ETCO₂-guided

↑
-20 minutes:
Begin 20 minutes
asphyxia (ETT
clamped).

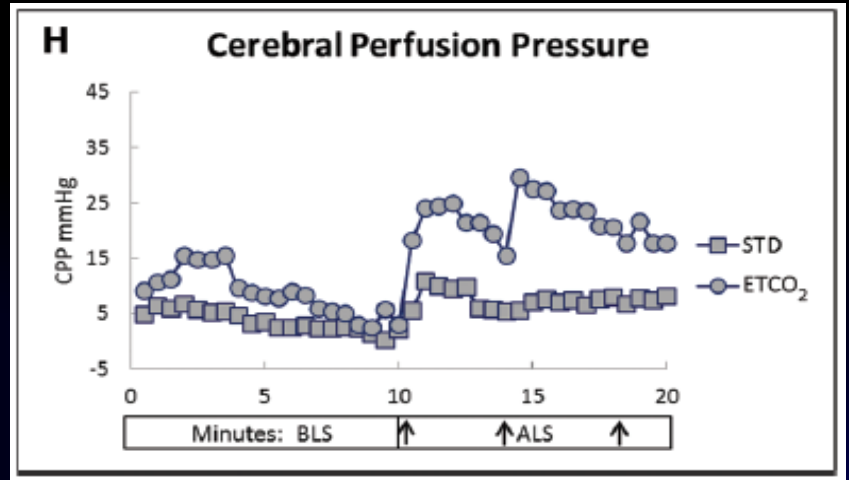
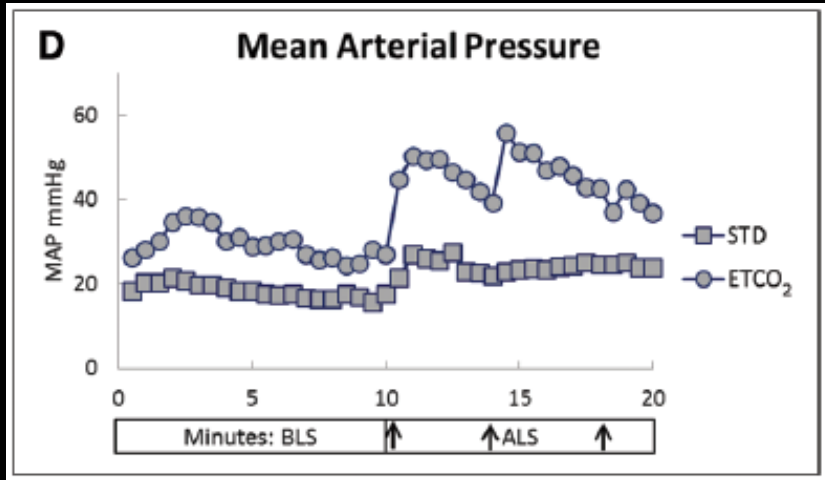
↑
-6 minutes:
Induce
fibrillation
(asphyxia
continues).

↑
0 minutes:
Begin 10 min BLS
(chest compressions
and ventilation).

↑
10 minutes:
Begin 10 min ALS
(BLS plus
epinephrine
every 4 min and
defibrillation
every 2 min).

↑
20 minutes:
If no ROSC then non-
survivor. If ROSC during
ALS then additional 20
min observation for
continuance of ROSC
without intervention.

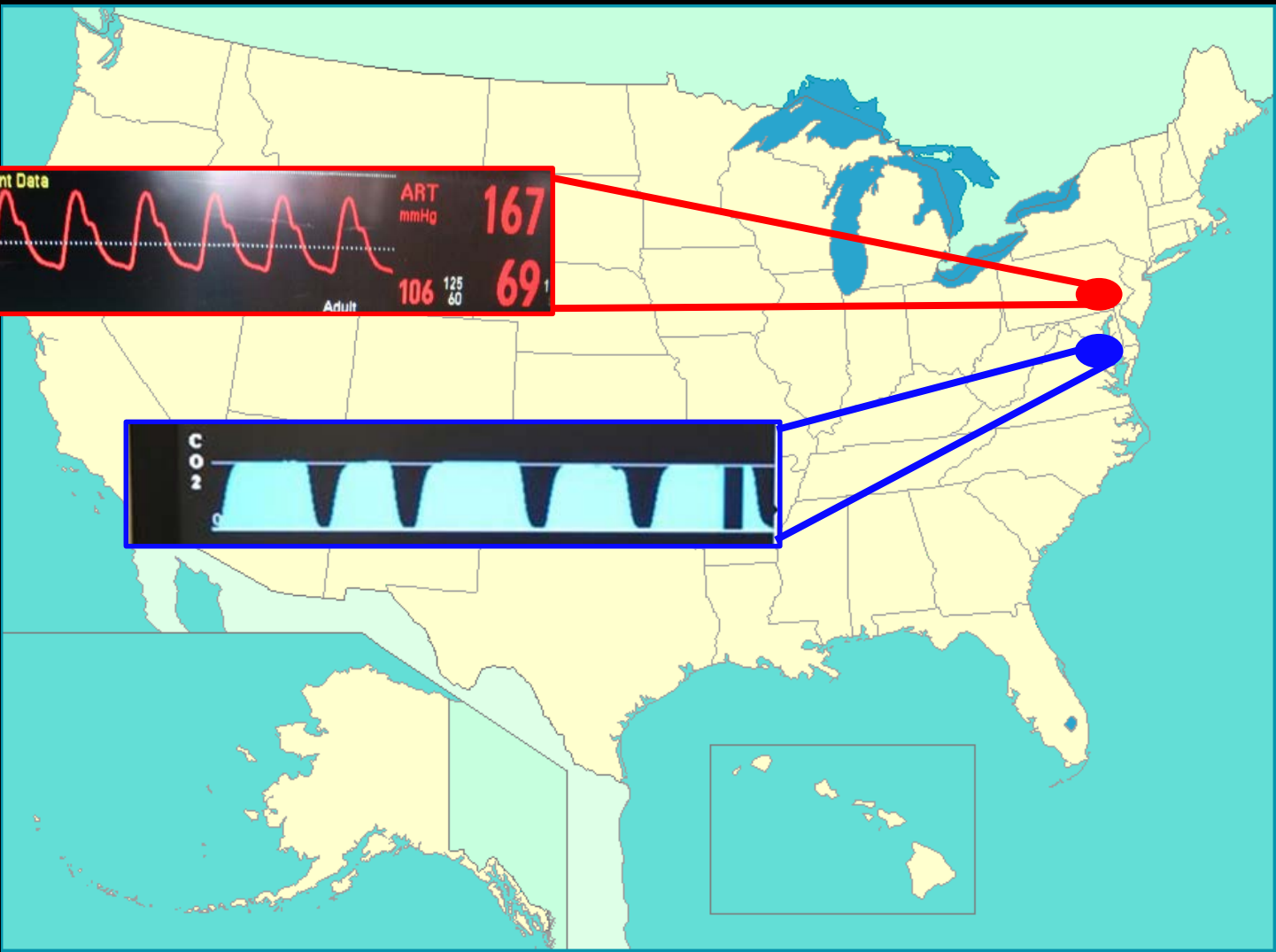
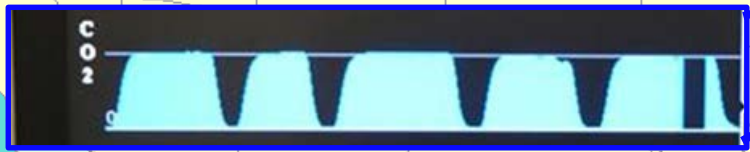
End Tidal CO₂ Guided CPR: Neonatal Asphyxial Arrest



Variables	End-Tidal Co ₂ Group	Standard Group	<i>p</i>
Outcome results			
Successful ROSC, <i>n</i> (%)	7/14 (50)	2/14 (14)	0.04

So if you had to pick...





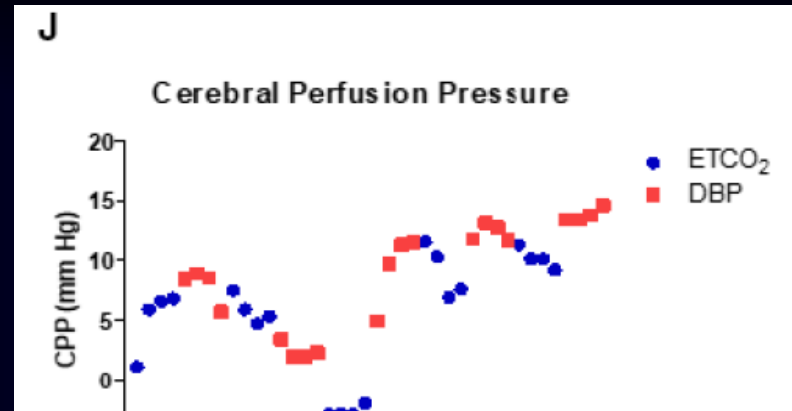
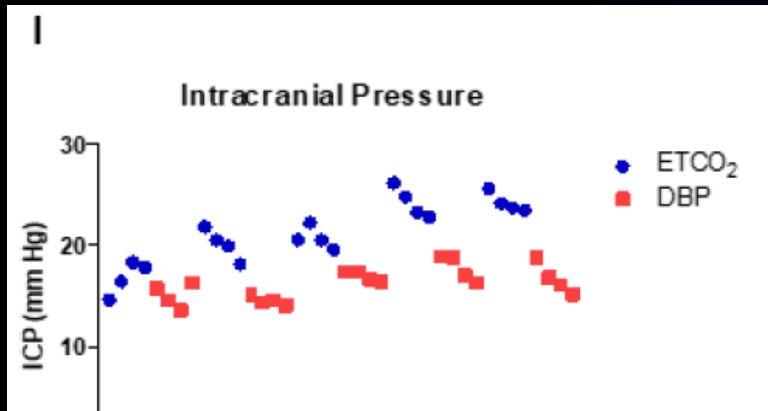
Pilot Study to Compare the Use of End-Tidal Carbon Dioxide–Guided and Diastolic Blood Pressure–Guided Chest Compression Delivery in a Swine Model of Neonatal Asphyxial Cardiac Arrest

JAHA, 2018

Caitlin E. O'Brien, MD, MPH; Michael Reyes, BA; Polan T. Santos, MD; Sophia E. Heitmiller, MHS; Ewa Kulikowicz, MS; Sapna R. Kudchadkar, MD, PhD; Jennifer K. Lee, MD; Elizabeth A. Hunt, MD, MPH, PhD; Raymond C. Koehler, PhD; Donald H. Shaffner, MD

End-tidal

DBP



Method specific physiologic changes



ELSEVIER

Contents lists available at ScienceDirect

Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation



EUROPEAN
RESUSCITATION
COUNCIL

Experimental paper

Morgan 2016

A quantitative comparison of physiologic indicators of cardiopulmonary resuscitation quality: Diastolic blood pressure versus end-tidal carbon dioxide[☆]

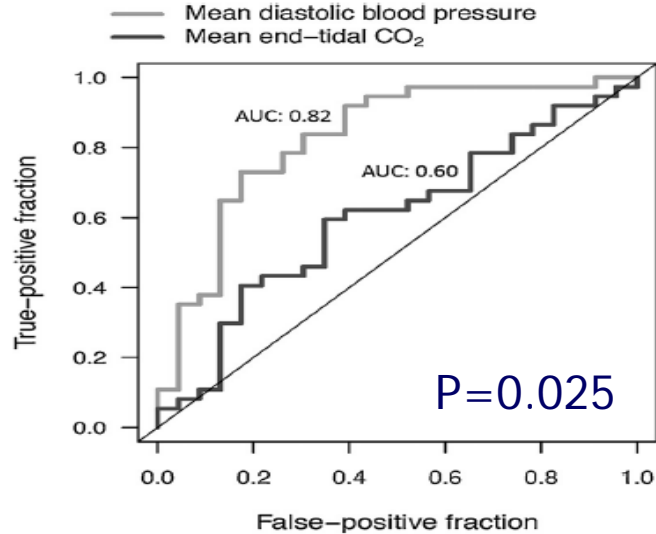
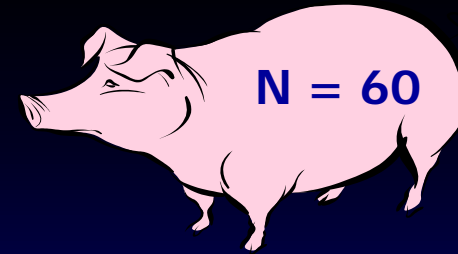



Fig. 3. Receiver operating characteristic curves evaluating the ability of diastolic blood pressure and end-tidal carbon dioxide to discriminate between survivors and non-survivors. Area under the curve (AUC) of DBP: 0.82, 95% CI: (0.70, 0.93). AUC of ETCO₂: 0.60, 95% CI: (0.45, 0.74).



DBP performed better than ETCO₂
 True across all models
 asphyxia
 VF

Optimal DBP target: ~34mmHg


The technique is not broadly implemented...



Contents lists available at [ScienceDirect](#)


Resuscitation

journal homepage: www.elsevier.com/locate/resuscitation



Clinical paper

Physiologic monitoring of CPR quality during adult cardiac arrest: A propensity-matched cohort study[☆]



Robert M. Sutton^{a,*}, Benjamin French^b, Peter A. Meaney^a, Alexis A. Topjian^a,
Christopher S. Parshuram^c, Dana P. Edelson^d, Stephen Schexnayder^e, Benjamin S. Abella^f,
Raina M. Merchant^f, Melania Bembea^g, Robert. A. Berg^a, Vinay M. Nadkarni^a, for the
American Heart Association's Get With The Guidelines–Resuscitation Investigators

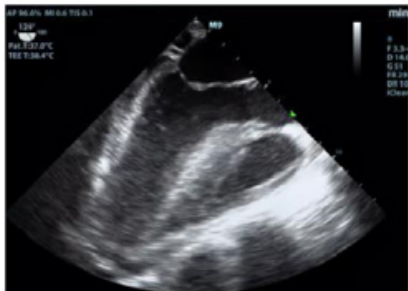
- 4% used ETCO₂
- 30% used diastolic pressure
- Event survival increased more than 20% when physiology was used

Evaluation of out-of-hospital cardiac arrest using transesophageal echocardiography in the emergency department



Felipe Teran^{a,b,*}, Anthony J. Dean^a, Claire Centeno^b,
Nova L. Panebianco^a, Amy J. Zeidan^c, Wilma Chan^a,
Benjamin S. Abella^{a,b}

MELAX**



LV, LA and RV chambers
LV Outflow Tract
Aortic root
Mitral and Aortic Valves

Determination of area of maximal compression (AMC) during CPR

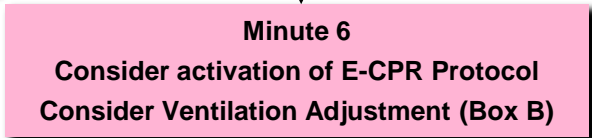
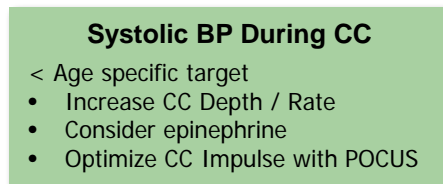
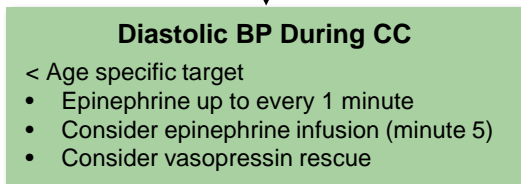
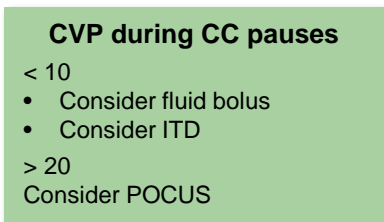
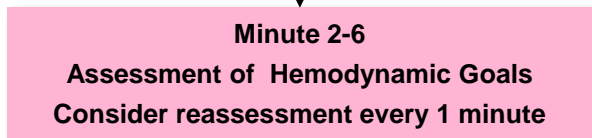
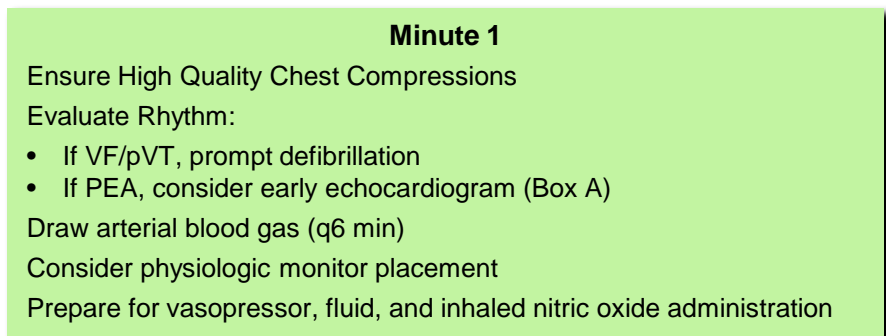
9 / 17 cases with AMC over LV outflow tract
TEE used to reposition to appropriate AMC

Disclaimer

The interpretation of the literature / opinions rendered by me do not necessarily reflect the official policy or position of the American Heart Association or its volunteers, the Children's Hospital of Philadelphia, the University of Pennsylvania, or anyone else for that matter.

Please direct complaints to Dr. Robert A. Berg, Division Chief, bergra@chop.edu

A Card for Your Pocket: 2030?



Details

High Quality CPR Mechanics

- Depth: > 1/3 AP Chest Depth
- Rate: 100-120/min
- Ensure full chest recoil
- Minimize interruptions

Diastolic BP Targets

- ≥ 25mmHg in infants
- ≥ 30mmHg in children > 1 year

Systolic BP Targets

- ≥ 60mmHg in infants
- ≥ 80mmHg in children > 1 year

Epinephrine

- Bolus: 0.01 mg/kg
- Infusion: 0.001 mg/kg/min

Vasopressin Rescue / Replacement

- Consider 0.4 units/kg/dose:
- after 2nd epinephrine dose
- high probability of PHTN

Box A: POCUS

PEA:

- Treat pneumothoraces / effusions
- Sepsis / PHTN: Consider iNO 80ppm
- If high probability of PE, consider tPA

Box B: Ventilation

Respiratory etiology and BP at goal:

- Consider ventilation rate increase

Adult Goal-Directed CPR Algorithm

Univ. of Michigan Emergency Department

1. Standard ACLS (quality CPR, rhythm check, shock VF/VT, Epi 1mg IV/IO q5min)

2. Place Advanced Airway & Attach Waveform Capnography

ENTER
PATHWAY
If ETCO₂
<20mmHg

Optimize Chest Compressions

Switch to LUCAS-2^A

Add Res-Q Pod^B

Switch to CARDIO-PUMP

EXIT
PATHWAY
If ETCO₂
>20mmHg

- A. May switch to LUCAS-2 regardless of ETCO₂
B. REMOVE Res-Q Pod after ROSC or ECPR started

3. Place Right Femoral Arterial + Venous 5Fr Catheters & transduce arterial BP

ENTER
PATHWAY
If DBP
<35mmHg

Start Epinephrine Infusion: 1 mcg/kg/min, continue until ROC

+

Epi 1mg q5min^C, until DBP>35 +/- Vasopressin 40u, x1 only^D

EXIT
PATHWAY
If DBP
>35mmHg

- C. May titrate Epi pushes to achieve DBP>35
D. May substitute Vasopressin for one Epi dose

Conclusions

- Physiologic-directed CPR is not a new concept
- Decades of experimental evidence
- Targeting underlying pathophysiology is key
 - More than just BP or end tidal or regional saturation
- Human trials are needed to obtain the evidence necessary to support widespread implementation

It's why we do what we do!



If not us, who?

THANK YOU

Personalizing Resuscitation with Physiologic-Directed CPR

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Chair: Resuscitation Committee at The Children's Hospital of Philadelphia

Medical Lead: Preventing Codes Outside the ICU

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March 16th, 2019





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