VŠEOBECNÁ FAKULTNÍ NEMOCNICE V PRAZE

1. LÉKAŘSKÁ FAKULTA Univerzita Karlova

Studie BOX

(Blood Pressure and Oxygenation Targets in Postresuscitation Care)

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Všeobecná fakultní nemocnice
a 1.LF UK
Praha

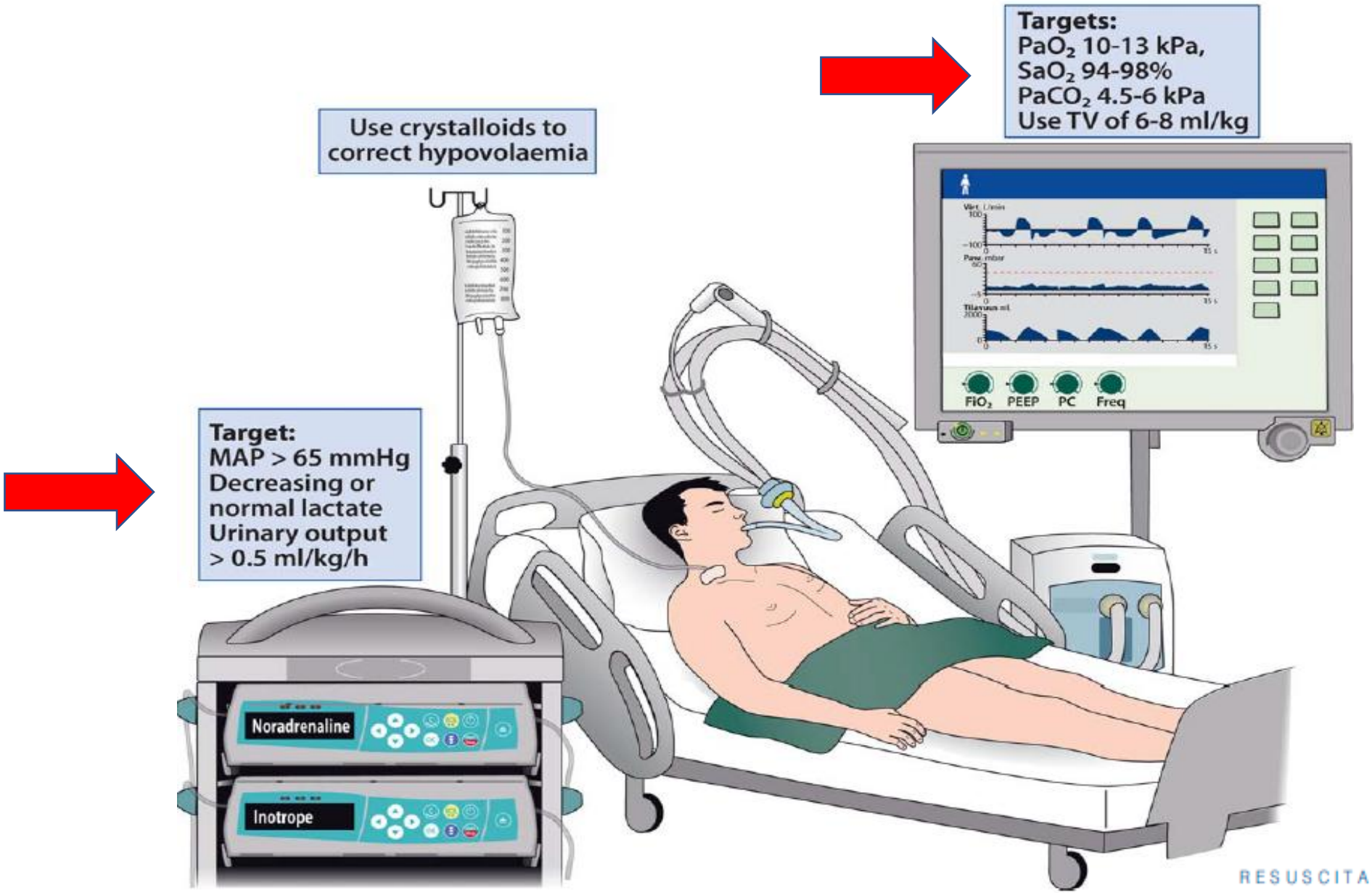
- Ischemicko-hypoxické poškození mozku je vedoucí příčinou úmrtí u OHCA
- Hypoxie a reperfúze jako sekundární zdroj poškození
- Observační i animální studie naznačují škodlivost hypoxémie i hyperoxémie
- 2 CRT neprokázaly rozdíl mezi nižší a vyšší oxygenací na přežití

- HOT-ICU: 2888 pacientů s akutním respiračním selháním : PaO2 8 kPa vs. 12 kPa- bez rozdílu v 90 denní mortalitě

Schjørring OL, Klitgaard TL, Perner A, et al. Lower or higher oxygenation targets for acute hypoxemic respiratory failure. N Engl J Med 2021; 384: 1301-11.

- ICU-ROX: 965 pacientů na UPV: SpO2 90-97% vs. bez specif. limitů- bez rozdílu dnů bez UPV do dne 28

Mackle D, Bellomo R, Bailey M, et al. Conservative oxygen therapy during mechanical ventilation in the ICU. N Engl J Med 2020; 382: 989-98.


Targets:
PaO2 10-13 kPa,
SaO2 94-98%
PaCO2 4.5-6 kPa
Use TV of 6-8 ml/kg
Use crystalloids to correct hypovolaemia
Target:
MAP > 65 mmHg
Decreasing or normal lactate
Urinary output > 0.5 ml/kg/h
FiO2
PEEP
PC
Freq
Noradrenaline
Inotrope

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Resuscitation
journal homepage: www.elsevier.com/locate/resuscitation
EUROPEAN RESUSCITATION COUNCIL

European Resuscitation Council and European Society of Intensive Care Medicine Guidelines 2021: Post-resuscitation care☆

Control of oxygenation

- After ROSC, use 100% (or maximum available) inspired oxygen until the arterial oxygen saturation or the partial pressure of arterial oxygen can be measured reliably.
- After ROSC, once SpO_2 can be measured reliably or arterial blood gas values are obtained, titrate the inspired oxygen to achieve an arterial oxygen saturation of 94–98% or arterial partial pressure of oxygen (PaO_2) of 10–13 kPa or 75–100 mmHg (Fig. 3).
- Avoid hypoxaemia ($PaO_2 < 8$ kPa or 60 mmHg) following ROSC.
- Avoid hyperoxaemia following ROSC.

Control of ventilation

- Obtain an arterial blood gas and use end tidal CO_2 in mechanically ventilated patients.
- In patients requiring mechanical ventilation after ROSC, adjust ventilation to target a normal arterial partial pressure of carbon dioxide ($PaCO_2$) i.e. 4.5–6.0 kPa or 35–45 mmHg.
- In patients treated with targeted temperature management (TTM) monitor $PaCO_2$ frequently as hypocapnia may occur.
- During TTM and lower temperatures use consistently either a temperature or non-temperature corrected approach for measuring blood gas values.
- Use a lung protective ventilation strategy aiming for a tidal volume of 6–8 mL kg^{-1} ideal body weight.

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

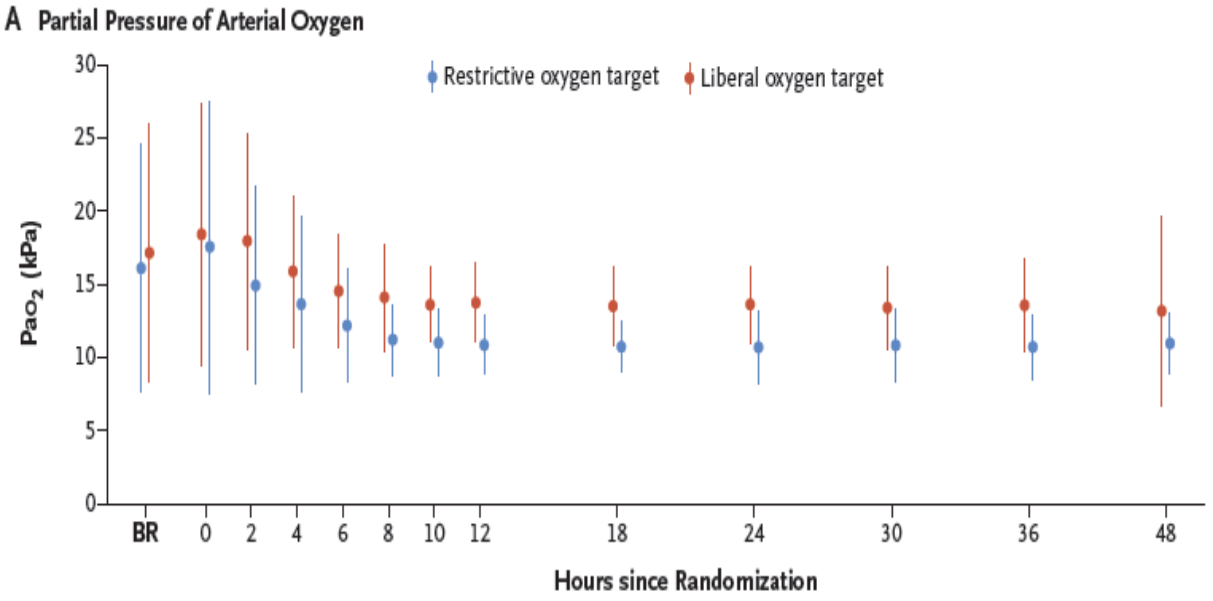
Oxygen Targets in Comatose Survivors of Cardiac Arrest

H. Schmidt, J. Kjaergaard, C. Hassager, S. Mølstrøm, J. Grand, B. Borregaard, L.E. Roelsgaard Obling, S. Venø, L. Sarkisian, D. Mamaev, L.O. Jensen, B. Nyholm, D.E. Høfsten, J. Josiassen, J.H. Thomsen, J.J. Thune, M.G. Lindholm, M.A. Stengaard Meyer, M. Winther-Jensen, M. Sørensen, M. Frydland, R.P. Beske, R. Frikke-Schmidt, S. Wiberg, S. Boesgaard, V. Lind Jørgensen, and J.E. Møller

- CRT 2x2 factorial design
- Comatose OHCA patients 1:1, TTM 36, MV 24 h at least
- Restrictive oxygen target (PaO2 9-10kPa)-FiO2 0,3 vs. liberal oxygen target (PaO2 13-14kPa)-FiO2 0,6.
- 789 patients (394 vs. 395)
- Primary outcome: composite of death from any cause or hospital discharge CPC 3,4 to D90
- Secondary outcomes: NSE at H48, death from any cause, cognitive ability scores and CPC at day 90

Table 1. Characteristics of the Patients at Baseline.*

Characteristic	Restrictive Oxygen Target (N=394)	Liberal Oxygen Target (N=395)
Age — yr		
Mean	62±13	63±14
Range	20–89	18–90
Male sex — no. (%)	325 (82.5)	312 (79.0)
Medical history — no./total no. (%)		
Hypertension	179/394 (45.4)	183/393 (46.6)
Diabetes	53/394 (13.5)	57/395 (14.4)
Myocardial infarction	89/393 (22.6)	83/394 (21.1)
Atrial fibrillation	56/391 (14.3)	71/394 (18.0)
Heart failure	58/393 (14.8)	79/394 (20.1)
Chronic obstructive pulmonary disease	29/392 (7.4)	34/394 (8.6)
Stroke	32/393 (8.1)	27/395 (6.8)
Chronic kidney disease	19/393 (4.8)	20/395 (5.1)
Renal-replacement therapy	1/393 (0.3)	3/395 (0.8)
Out-of-hospital cardiac arrest		
Features — no./total no. (%)		
Shockable rhythm	334/393 (85.0)	333/394 (84.5)
Pulseless electrical activity	15/393 (3.8)	20/394 (5.1)
Witnessed asystole	15/393 (3.8)	15/394 (3.8)
Witnessed arrest	333/394 (84.5)	339/394 (86.0)
Bystander cardiopulmonary resuscitation	346/388 (89.2)	333/388 (85.8)
First defibrillation by automated external defibrillator	79/386 (20.5)	103/390 (26.4)
Time until return of spontaneous circulation — min†	21±13	21±14
Findings and procedures at hospital arrival‡		
pH	7.21±0.12	7.21±0.13
Lactate — mmol/liter	5.8±3.7	5.9±4.0
Partial pressure of arterial oxygen — kPa	16.1±8.5	17.1±8.8
Immediate coronary angiography — no. (%)	363 (92.1)	359 (90.9)
Percutaneous coronary intervention — no. (%)	159 (40.4)	177 (44.8)



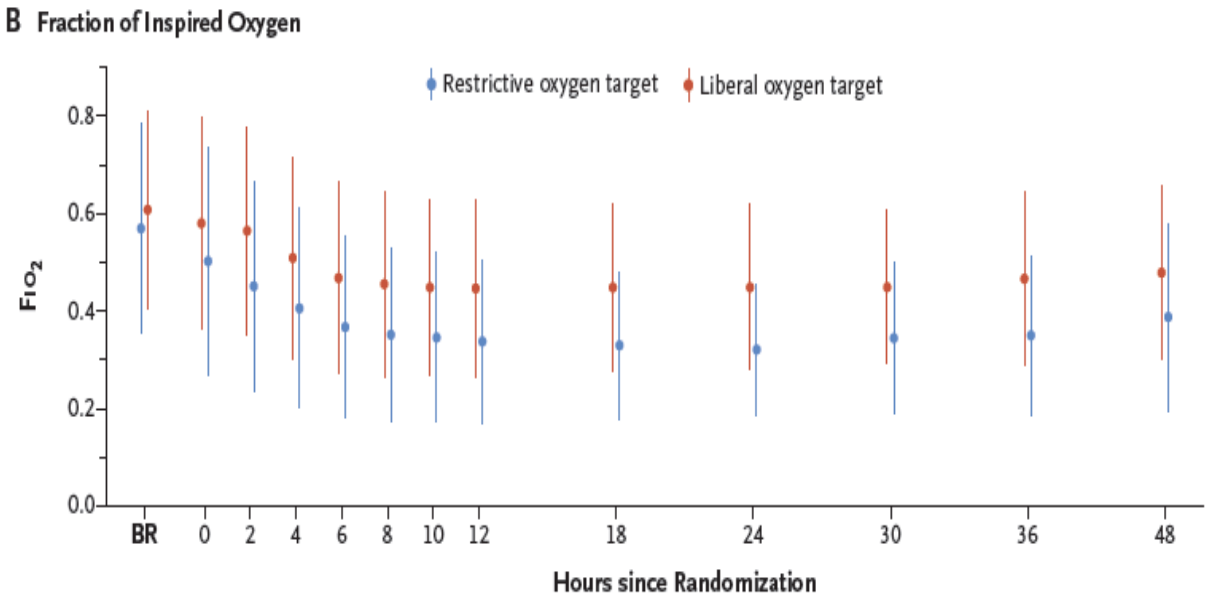


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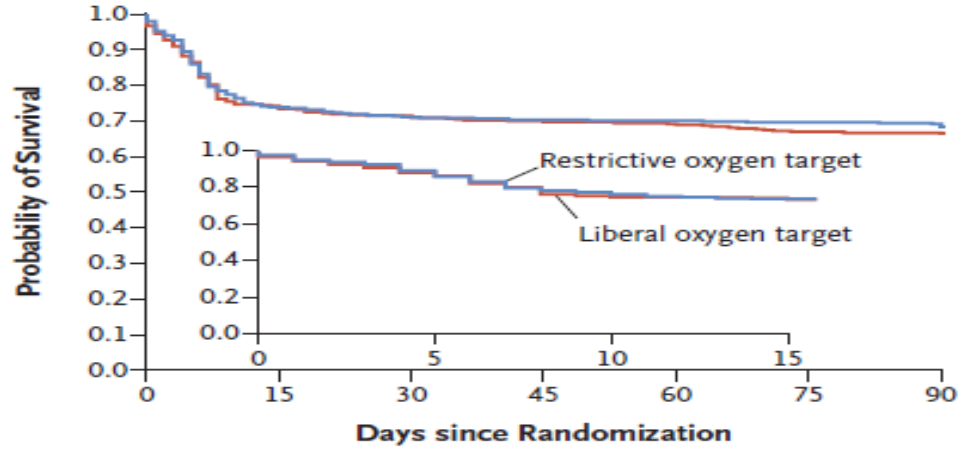
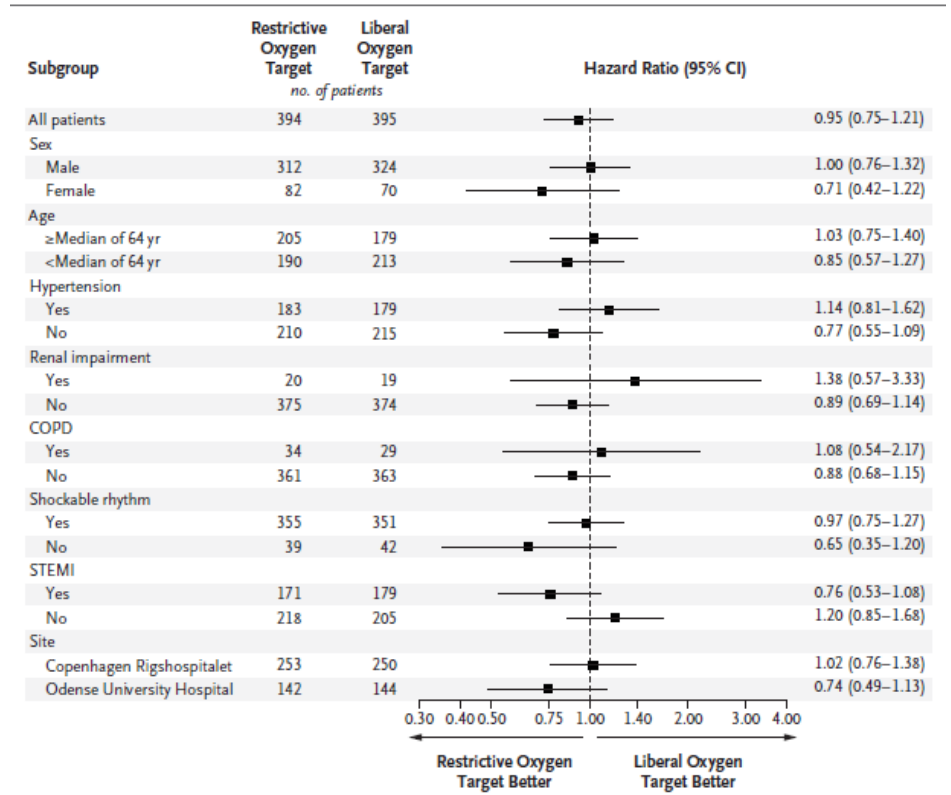
Table 2. Primary and Secondary Outcomes and Adverse Events.*

Variable	Restrictive Oxygen Target (N=394)	Liberal Oxygen Target (N=395)	Treatment Effect (95% CI)†	P Value
Primary outcome				
Death from any cause or CPC 3 or 4 at discharge — no. (%)‡	126 (32.0)	134 (33.9)	0.95 (0.75–1.21)	0.69
Secondary outcomes				
Death from any cause at 90 days — no. (%)	113 (28.7)	123 (31.1)	0.93 (0.72–1.20)	
Acute kidney injury with renal-replacement therapy — no. (%)	34 (8.6)	47 (11.9)	0.85 (0.69–1.03)	
Median CPC at 90 days (IQR)‡	1 (1–5)	1 (1–5)		
Median score on modified Rankin scale at 90 days (IQR)§	2 (0–6)	1 (0–6)		
Median score on Montreal Cognitive Assessment at 90 days (IQR)¶	27 (24–29)	27 (24–28)		
Median neuron-specific enolase at 48 hr (IQR) — μg/liter‖	17 (11–36)	18 (11–34)		
Adverse events — no. (%)				
Infection**	103 (26.1)	109 (27.6)	0.96 (0.82–1.13)	0.65
Arrhythmia††	57 (14.5)	52 (13.2)	1.06 (0.86–1.30)	0.60
Bleeding				
Any	82 (20.8)	92 (23.3)	0.93 (0.79–1.10)	0.40
Uncontrolled bleeding‡‡	17 (4.3)	21 (5.3)	0.90 (0.67–1.21)	0.62
Acute kidney injury with renal-replacement therapy	34 (8.6)	47 (11.9)	0.85 (0.69–1.03)	0.13
Electrolyte disorder§§	32 (8.1)	25 (6.3)	1.15 (0.85–1.56)	0.33
Metabolic disorder¶¶	34 (8.6)	28 (7.1)	1.12 (0.84–1.48)	0.42
Seizure‖‖	81 (20.6)	83 (21.0)	0.99 (0.83–1.17)	0.14



No. at Risk

Restrictive target	394	290	279	276	275	273	271
Liberal target	395	292	281	275	272	263	262



Conclusions

- Restrictive vs. liberal oxygenation strategy in oxygenation by comatose OHCA patients resulted in a similar incidence of death or severe disability or coma.

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Blood-Pressure Targets in Comatose Survivors of Cardiac Arrest

J. Kjaergaard, J.E. Møller, H. Schmidt, J. Grand, S. Mølstrøm, B. Borregaard, S. Venø, L. Sarkisian, D. Mamaev, L.O. Jensen, B. Nyholm, D.E. Høfsten, J. Josiassen, J.H. Thomsen, J.J. Thune, L.E.R. Obling, M.G. Lindholm, M. Frydland, M.A.S. Meyer, M. Winther-Jensen, R.P. Beske, R. Frikke-Schmidt, S. Wiberg, S. Boesgaard, S.A. Madsen, V.L. Jørgensen, and C. Hassager

- CRT 2x2 factorial design
- Comatose OHCA patients 1:1, TTM 36
- key exclusions: unwitnessed asystole or IC bleeding or stroke
- MAP: 63 mm Hg vs. MAP 77 mm Hg
- 789 patients (393 vs. 396)
- Blinded calibration of MAP devices (70 mm Hg for all, but real +/- 10%)
- MAP maintained with fluids to CVP 10 mm Hg, norepinephrine and the addition dopamine if needed
- Primary outcome: composite of death from any cause or hospital discharge CPC 3,4 to D90
- Secondary outcomes: NSE at H48, death from any cause, cognitive ability scores and CPC at day 90

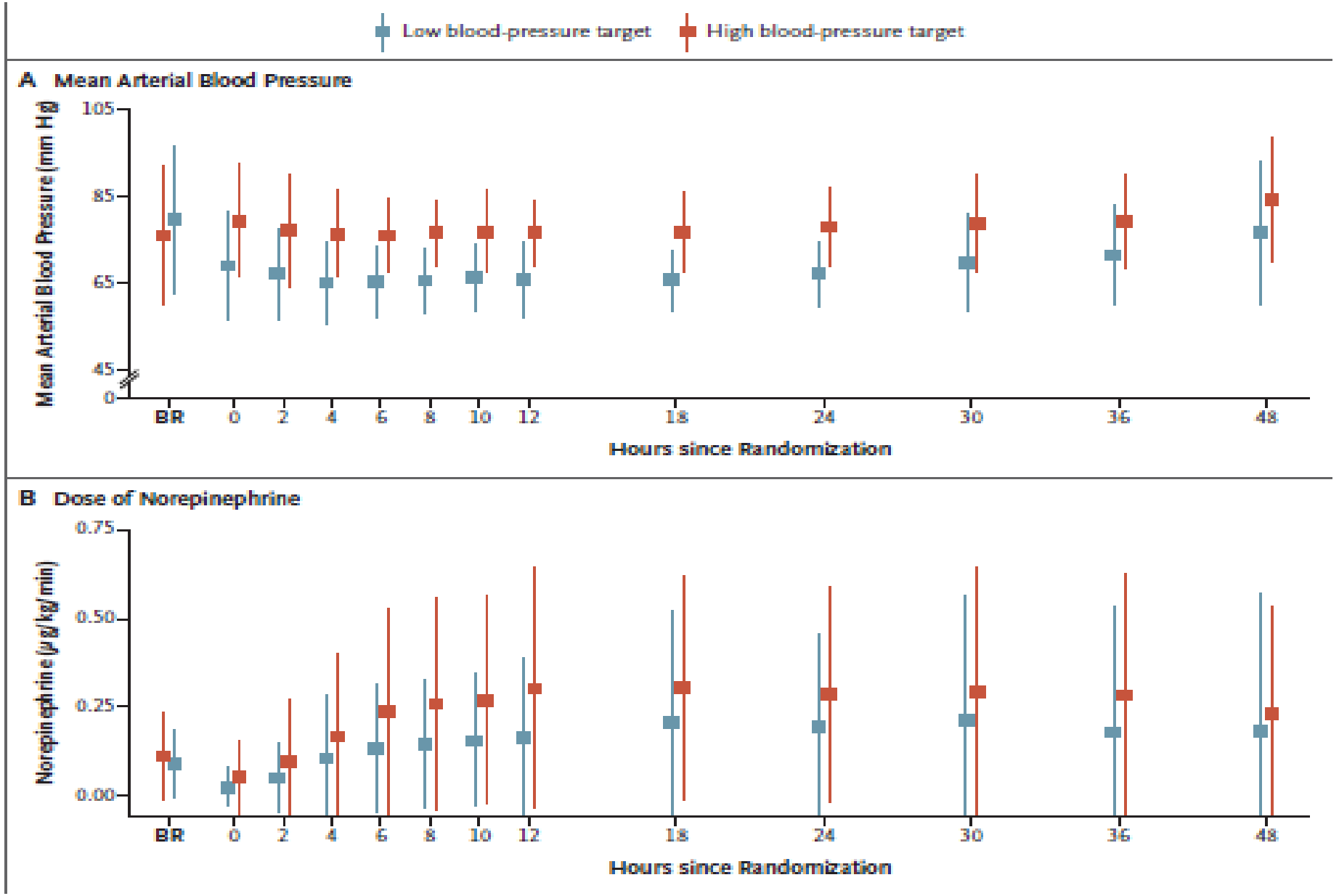
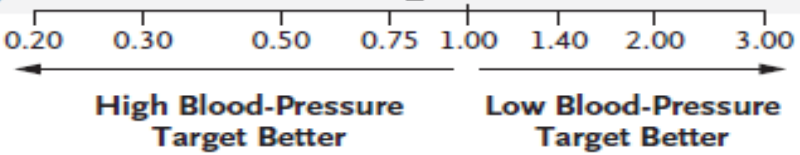

Low blood-pressure target
High blood-pressure target
A Mean Arterial Blood Pressure
Mean Arterial Blood Pressure (mm Hg)
105
85
65
45
0
BR
0
2
4
6
8
10
12
18
24
30
36
48
Hours since Randomization
B Dose of Norepinephrine
Norepinephrine (μg/kg/min)
0.75
0.50
0.25
0.00
BR
0
2
4
6
8
10
12
18
24
30
36
48
Hours since Randomization

Table 2. Outcomes and Adverse Events.*

Outcome or Event	High Blood-Pressure Target (N=393)	Low Blood-Pressure Target (N=396)	Hazard Ratio (95% CI)	P Value
Primary outcome				
Death from any cause or CPC of 3 or 4 at discharge within 90 days — no. (%)†	133 (34)	127 (32)	1.08 (0.84–1.37)	0.56
Secondary outcomes				
Death from any cause within 90 days — no. (%)	122 (31)	114 (29)	1.13 (0.88–1.46)	
Acute kidney injury with renal-replacement therapy — no. (%)	41 (10)	40 (10)	1.03 (0.66–1.59)	
Median CPC at 3 months (IQR)†	1 (1–5)	1 (1–5)		
Median modified Rankin scale score at 3 months (IQR)‡	1 (0–6)	1 (0–6)		
Median Montreal Cognitive Assessment score, per protocol (IQR)§	20 (15–27)	21 (15–27)		
Median Montreal Cognitive Assessment score at 3 months, post hoc (IQR)§	27 (24–29)	26 (24–29)		
Median neuron-specific enolase level at 48 hours (IQR) — μg/liter¶	18 (11–37)	18 (11–34)		
			Relative Risk (95% CI)	
Serious adverse events — no. (%)				
Infection‖	102 (26)	110 (28)	0.96 (0.82–1.11)	0.56
Arrhythmia**	59 (15)	50 (13)	1.10 (0.79–1.38)	0.33
Any bleeding††	82 (21)	92 (23)	0.93 (0.79–1.10)	0.43
Uncontrolled bleeding††	22 (6)	16 (4)	0.85 (0.64–1.13)	0.31
Electrolyte disorder‡‡	23 (6)	34 (9)	0.82 (0.66–1.04)	0.13
Metabolic disorder§§	31 (8)	31 (8)	1.00 (0.77–1.30)	0.98
Seizure¶¶	76 (19)	88 (22)	0.92 (0.78–1.08)	0.32

Subgroup	High Blood-Pressure Target	Low Blood-Pressure Target	Hazard Ratio (95% CI)
	no. of patients		
Overall	393	396	1.08 (0.84–1.37)
Sex			
Male	316	320	1.08 (0.82–1.43)
Female	76	76	1.08 (0.64–1.82)
Age			
At or above median of 64 yr	185	199	1.05 (0.77–1.44)
Below median of 64 yr	206	197	1.21 (0.81–1.80)
Hypertension			
Yes	176	186	1.15 (0.81–1.62)
No	215	210	1.01 (0.71–1.42)
Renal impairment			
Yes	22	17	0.95 (0.39–2.30)
No	371	378	1.09 (0.85–1.41)
COPD			
Yes	30	33	0.48 (0.23–0.99)
No	362	362	1.19 (0.92–1.55)
Shockable rhythm			
Yes	356	350	1.11 (0.85–1.45)
No	35	46	1.21 (0.66–2.22)
STEMI			
Yes	172	178	0.95 (0.66–1.37)
No	219	204	1.27 (0.90–1.78)
Site			
Copenhagen University Hospital Rigshospitalet	250	253	1.25 (0.92–1.69)
Odense University Hospital	143	143	0.82 (0.54–1.25)



Conclusions

- Targeting a mean arterial blood pressure of 77 mm Hg or 63 mm Hg in patients who had been resuscitated did not result in significantly different percentage of patients dying or having severe disability or coma.