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1 **Improving Post-Cardiac Arrest Cerebral Perfusion Pressure by Elevating the Head and**
2 **Thorax**

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28

29 **ABSTRACT**

30

31 **Aim:** The optimal head and thorax position *after* return of spontaneous circulation (ROSC)
32 following cardiac arrest (CA) is unknown. This study examined whether head and thorax
33 elevation post-ROSC is beneficial, in a porcine model.

34 **Methods:** Protocol A: 40kg anesthetized pigs were positioned flat, after 7.75 minutes of
35 untreated CA the heart and head were elevated 8 and 12 cm, respectively, above the horizontal
36 plane, automated active compression decompression (ACD) plus impedance threshold device
37 (ITD) CPR was started, and 2 minutes later the heart and head were elevated 10 and 22 cm,
38 respectively, over 2 minutes to the highest head up position (HUP). After 30 minutes of CPR
39 pigs were defibrillated and randomized 10 minutes later to four 5-minute epochs of HUP or
40 flat position. Multiple physiological parameters were measured. In Protocol B, after 6 minutes
41 of untreated VF, pigs received 6 minutes of conventional CPR flat, and after ROSC were
42 randomized HUP versus Flat as in Protocol A. The primary endpoint was cerebral perfusion
43 pressure (CerPP). Multivariate analysis-of-variance (MANOVA) for repeated measures was
44 used. Data were reported as mean± SD.

45 **Results:** In Protocol A, intracranial pressure (ICP) (mmHg) was significantly lower post-ROSC
46 with HUP (9.1±5.5) versus Flat (18.5±5.1) (p<0.001). Conversely, CerPP was higher with HUP
47 (62.5±19.9) versus Flat (53.2±19.1) (p=0.004), respectively. Protocol A and B results
48 comparing HUP versus Flat were similar.

49 **Conclusion:** Post-ROSC head and thorax elevation in a porcine model of cardiac arrest resulted
50 in higher CerPP and lower ICP values, regardless of VF duration or CPR method.

51

52

53 **IACUC Protocol Number: 19-09**

54

55

56 **KEYWORDS**

57 **Active compression-decompression CPR**

58 **Cardiac arrest**

59 **Cardiopulmonary Resuscitation**

60 **Return of spontaneous circulation**

61 **Advanced Cardiac Life Support**

62 **Cerebral perfusion pressure**

63 **Head Up CPR**

64 **Head and thorax elevation**

65 **Heart arrest**

66 **Impedance threshold device**

67 **Medical device**

68 **Patient positioning**

69 **Posture**

70 **Intracranial pressure**

71

72 **INTRODUCTION**

73 Elevation of the head and thorax (EHT) improves clinical outcomes in critically ill
74 patients with traumatic brain injury, heart failure, and respiratory distress¹⁻⁵. EHT helps to drain
75 venous blood from the brain, lower intracranial pressure (ICP), and improve multiple essential
76 physiological processes including oxygenation, transpulmonary flow, and circulation⁶⁻⁹.

77 Recent pre-clinical and clinical data have shown that the combination of gravity-assisted
78 active compression decompression (ACD), cardiopulmonary resuscitation (CPR) with an
79 impedance threshold device (ITD) improves cerebral perfusion pressures and neurologically-
80 intact survival rates after cardiac arrest (CA), especially when using controlled sequential
81 EHT¹⁰⁻¹⁴. This new approach does not work with conventional (C-) CPR, as forward flow is
82 too limited^{12,15}. However, when used with CPR techniques that augment circulation, EHT
83 harnesses gravity to enhance draining venous blood from the brain, lowers ICP, and improves
84 circulation to the brain, heart and other vital organs, and improves neurologically-intact survival
85 versus C-CPR in the Flat position.

86 While recent evidence supports a benefit of EHT during CPR, the optimal position *after*
87 return of spontaneous circulation (ROSC) remains unknown. Lower ICP and higher CerPP after
88 ROSC may decrease reperfusion injuries in the post arrest phase and thereby improve
89 outcome¹⁶. Herein we tested the hypothesis that EHT *after* ROSC would increase cerebral
90 perfusion pressure and lower ICP relative to the flat position, regardless of the duration of
91 cardiac arrest or method of CPR.

92

93 **METHODS**

94 The study was approved by the Institutional Animal Care and Use Committee of the
95 Hennepin Healthcare Research Institute (HHRI). A certified and licensed HHRI veterinarian

96 assured that animal care and the study protocol complied with the National Research Council
97 2011 Guidelines for the Care and Use of Laboratory Animals.

98

99 *Study design and measurements*

100 Study preparation and surgical techniques were performed as previously
101 described^{11,12,17}. Female Yorkshire farm pigs weighing ~40 kg were fasted overnight, received
102 intramuscular ketamine (1000 mg), and then 5% inhaled isoflurane. Animals were placed on a
103 customized elevation device (CED) CPR device as previously described¹⁴ and shown in
104 Supplemental Figure 1, capable of elevating the head and thorax to perform CPR as previously
105 described¹³, and then intubated with a 7.5 mm cuffed endotracheal tube (ETT), connected to an
106 anesthesia machine (Narkomed, North American Drager) and ventilated with a tidal volume of
107 10 mL/kg. Isoflurane was continued until 3 minutes prior to induction of ventricular fibrillation
108 (VF). End tidal carbon dioxide (ETCO₂) and transcutaneous oxygen saturation (SO₂) were
109 measured with a CO2SMO Plus (Novamatrix Systems). Respiratory rate and FiO₂ were titrated
110 to keep SO₂ > 92% and ETCO₂ between 37-43 mmHg. Intravenous (IV) access was then
111 obtained and pigs received normal saline during the preparatory phase to maintain a mean right
112 atrial pressure (RAP) between 7-10 mmHg. Animals received a 100 unit/kg bolus of
113 intravenous heparin every hour. Temperature was continuously measured via esophageal probe
114 and maintained between 37-38°C during the preparatory phase. Proximal airway pressure was
115 measured through the ETT with a differential pressure transducer (TSD160C, Biopac Systems,
116 Inc). RAP and aortic blood pressure (AoP) were measured using micromanometer-tipped
117 catheters (Mikro-Tip Transducer, Millar Instruments) placed using a femoral approach and
118 positioned in the right atrium and thoracic aorta at the level of the diaphragm, respectively.
119 Catheter placement was confirmed with fluoroscopy. An intracranial bolt was placed in a burr
120 hole in the skull to measure ICP with a micromanometer-tipped catheter. It was positioned

121 approximately 5 mm into cerebral cortex. To measure regional cerebral oximetry (rSO₂)
122 paediatric rSO₂ probes (SenSmart 8004CB, Nonin Medical, MN) were placed along a line
123 between the lateral canthus of each eye and the medial portion of the bottom of the ear. For
124 these analyses, rSO₂ values were used from the one of two probes that showed the greatest
125 change in rSO₂ pre-arrest to the end of the untreated VF period. Arterial blood gases (ABG)
126 and reference blood samples were analyzed using a Gem Premier 3000 device (Instrumentation
127 Laboratory, Lexington, MA). Surface electrocardiograms, ETCO₂, ICP, RAP, AoP,
128 intrathoracic pressure were continuously monitored and recorded (BioPac MP150; BioPac
129 Systems Inc) and then stored and analyzed using the BioPac Acqknowledge 4.2 software.

130

131 *Experimental protocols*

132 **Protocol A:**

133 The study protocol is shown in Figure 1a. VF was induced via direct current from a
134 pacing wire placed in the right ventricle as previously described^{11,12}. After 7.75 minutes the
135 CED was raised completely flat to the lowest elevation position. After 8 minutes of untreated
136 VF, ACD CPR was performed with an automatic piston device (Caztek Engineering, St. Paul,
137 MN)¹⁴. An ITD (ResQPOD-16, ZOLL Medical) was attached to the endotracheal tube at the
138 initiation of CPR. Manual positive pressure ventilation was delivered with a tidal volume of 10
139 mL/kg and a 30:2 compression:ventilation ratio, without oxygen to simulate basic life support
140 (BLS)^{13,18} and to prime the cardio-cerebral circuit. After 2 minutes of BLS ACD+ITD CPR in
141 the lowest CED position, ACD+ITD CPR (rate: 100/minute; depth 22% antero-postero
142 diameter; decompression force ~10 kg) was performed continuously with a 10:1
143 compression/ventilation ratio and the head and thorax were progressively elevated at a rate of
144 6 cm/minute over 2 minutes to the highest level of the CED was achieved, as previously
145 described¹⁴ (as shown in Supplemental Figure 1). After 30 minutes of CPR in this highest CED

146 position, 0.25 or 0.5 mg of epinephrine was administered intravenously if the decompression
147 phase arterial blood pressure was 20-30 mmHg, or <20 mmHg, respectively. IV amiodarone
148 (25 mg) was administered at that time. Animals were then defibrillated with up to three 200 J
149 biphasic shocks (X-series, ZOLL Medical). After ROSC, animals received isoflurane (1.0%).
150 The head and thorax were maintained at the highest CED level for 10 minutes before
151 randomization into one of the following sequences for 5-minutes epochs: Flat, head up at
152 highest CED position (HUP), Flat, HUP (group 1) or HUP, Flat, HUP, Flat (group 2). Pigs
153 completing the protocol were included in the study. They were then euthanized with an
154 intravenous injection of KCl.

155

156 **Protocol B:**

157 As outlined in Figure 1b, after 6 minutes of untreated VF, automated C-CPR was
158 performed in the supine and flat position, as previously described¹⁴ (and shown in Supplemental
159 Figure 1), at 100 compressions per minute, a depth of 22% of the antero-postero-diameter, full
160 passive chest recoil, and a 50% duty cycle. Manual positive pressure ventilation was performed
161 with room air with a 30:2 compression: ventilation ratio. After 6 minutes of CPR, epinephrine
162 and/or amiodarone were administered similarly to protocol A as well as defibrillation. If ROSC
163 was not achieved, additional CPR was performed using ACD+ITD and pigs were defibrillated
164 again. After ROSC, animals received isoflurane as in Protocol A. The head and thorax were
165 maintained flat for 10 minutes before randomization to one of two 5-minutes epoch sequences:
166 Flat, HUP, Flat, HUP (group 1) or HUP, Flat, HUP, Flat (group 2) as in Protocol A. At the end
167 of the protocol pigs were euthanized with intravenous KCl. As such, the post-ROSC
168 interventions for Protocols A and B were the same.

169

170

171

172

173 ***Statistical analysis***

174 Mean CerPP was the primary study endpoint. Secondary outcomes included mean AoP,
175 RAP, ICP, coronary perfusion pressure (CorPP), EtCO₂ and rSO₂. AoP, RAP, ICP, airway
176 pressures, heart rate, SpO₂ and rSO₂ were measured and then averaged during the last minute
177 of each 5-minutes epoch. CorPP was calculated as decompression phase, or diastolic, AoP
178 minus RAP. CerPP was calculated as mean aortic pressure (MAP) minus ICP.

179 We estimated that a sample size of 6 pigs would achieve 80% power to detect a mean
180 difference of 10 mmHg with an estimated standard deviation of 2 in CerPP between the HUP
181 and Flat ACD+ITD groups, with a significance level (alpha) of 0.05, using a two-sided t-test.

182 Data are expressed as mean \pm standard deviation. We fit multivariate analysis-of-
183 variance (MANOVA) with the repeated measures appearing as dependent variables and study
184 group and head position entered as main effects. A first-order interaction involving time and
185 head position was assessed for statistical significance. A paired t-test was also performed to
186 compare the first two 5-minutes epoch interventions and the second 5-minutes intervention. All
187 statistical tests were two-sided, and a p-value of <0.05 was required to reject the null hypothesis.
188 P-values for all secondary outcomes were adjusted for multiple comparisons using the
189 Bonferroni method. Statistical analysis was performed using the SPSS software (SPSS
190 Statistics, Version 24.0. Armonk, NY: IBM Corp).

191

192 **RESULTS**

193 *Protocol A*

194 ROSC was achieved in 7 out of 9 pigs. After 29 minutes of CPR, the mean CerPP and
195 CorPP were 36.2 \pm 24.4 and 25.3 \pm 29.6 mmHg for all 9 pigs. Arterial pH and lactates levels were

196 7.1±0.1 and 7.5±1.4 mmol/L. One pig had multiple broken ribs and a pneumothorax and did
197 not achieve ROSC and one had refractory VF without ROSC. Additionally, one pig was
198 profoundly hypotensive post-ROSC and died half way through the HUP/flat protocol.

199 Hemodynamic variables, arterial blood gas and serum lactate values for the 6 pigs that
200 survived the entire protocol are shown in Table 1. After 29 minutes of ACD+ITD HUP CPR
201 the mean CorPP and CerPP of the 6 survivors were 40.6±20.5 mmHg and 50.5±15.6 mmHg,
202 respectively. Arterial pH values were 7.1±0.1 and lactate levels were 6.9±1.9 mmol/L.

203 rSO₂ values were measured continuously in all 9 pigs. Prior to VF induction the mean
204 rSO₂ values were 73.9±3.1%. These values decreased to 57.8±4.4% just prior to CPR. Over 30
205 minutes of CPR rSO₂ increased to a maximal level of 63.1±5.8% and were 59.1±6.4% just prior
206 to defibrillation.

207 After 29 minutes of CPR, rSO₂ values were 61.8±5.1% in the 6/9 pigs with a sustained
208 ROSC versus 53.7±5.2% in the 3/9 pigs without ROSC or sustained ROSC. Arterial lactate and
209 pH values were 7.1±0.1 and 6.9±1.9mmol/L in the 6/9 pigs with a sustained ROSC versus
210 7.2±0.2 and 7.4±0.1mmol/L in the 3/9 pigs without ROSC or sustained ROSC, respectively.

211 Key post-ROSC outcomes are shown in Figures 3-5 and Table 1. For all 4 epochs
212 studied, ICP during HUP was 9.1±5.5mmHg and 18.6±5.1mmHg Flat (p<0.001). CerPP was
213 62.5±19.9mmHg HUP and 53.2±19.1mmHg Flat (p=0.004). As demonstrated in Figure 2, a
214 representative pressure tracing from one animal, changes in body position resulted in rapid
215 changes in ICP, RAP, CerPP, and rSO₂ and no change in AoP. Randomization order did not
216 alter the changes observed in the different positions. With a MANOVA, no significant first-
217 order interaction involving time and head position was observed for CerPP (P=0.46). CerPP
218 was 9.3±7.0 mmHg higher with HUP versus Flat corresponding to a 17.4% higher CerPP levels
219 (p=0.004, Supplementary Table 2) and did not differ according to time of measurement
220 (P=0.96) (Figures 3 and 4 and Table 1). ICP values were 9.5±1.8 mmHg lower with HUP

221 ($P<0.001$, Supplementary Table 2). Arterial lactate, rSO_2 , RAP and pH and transcutaneous
222 SaO_2 values were not significantly altered by the position of the head and thorax post-ROSC
223 when comparing values across all 4 epochs.

224 Outcomes were generally similar when data for the first two 5-minutes epoch
225 interventions were analysed separately, although differences between interventions were not
226 always statistically significant. Each time the head and thorax were elevated, RAP and ICP
227 decreased, and CerPP increased, as shown in Figure 4. More specifically, for the first two 5-
228 minute epoch interventions, CerPP increased with HUP 7.4 ± 7.3 mmHg (a relative 14% change)
229 ($p=0.07$), and ICP decreased 9.9 ± 1.8 mmHg (a relative 52% decrease) ($p<0.001$). However,
230 RAP values were significantly higher in the first two interventions (HUP/Flat) versus the
231 second HUP/Flat sequence ($P=0.029$), suggesting a real decrease in RAP over time. These
232 changes were reproducible, both in terms of the rate and magnitude of change when comparing
233 HUP versus Flat. In addition, rSO_2 values were higher with HUP versus Flat in 5/6 pigs (for
234 the last pig, values were equal) during epochs 1 and 2 (uncorrected $p=0.032$) but lost statistical
235 significance with the Bonferonni correction. Two pigs with a sustained ROSC and low SO_2
236 values throughout the experiment had severe lung injuries on necropsy.

237 Epinephrine was administered intravenously during the post-ROSC phase when the
238 MAP was less than 55 mmHg. In the 6 pigs with a sustained ROSC that completed the protocol,
239 epinephrine was required in 2/6 pigs to achieve ROSC and 3/6 for at least some portion of the
240 post-ROSC period. The average dose of epinephrine used post-ROSC was 0.11 ± 0.06
241 $\mu\text{g}/\text{kg}/\text{min}$. Use of epinephrine did not impact the changes in ICP, RAP, CerPP, MAP or rSO_2
242 observed with a change in body position post-ROSC (data in Supplement).

243

244 *Protocol B*

245 Protocol B results, shown in Table 1 and Figures 3 and 5, were generally similar to those
246 observed in Protocol A. ROSC was achieved in a total of 5/6 pigs after 6 minutes of untreated
247 VF and 6 minutes of standard CPR. Additional CPR with ACD+ITD was used in 1/6 pigs to
248 achieve ROSC after defibrillation following C-CPR failed. All 6 pigs were used in the post-
249 ROSC study. Epinephrine was required in 4/6 pigs to achieve ROSC and 1/6 for at least some
250 portion of the post-ROSC period. The dose of epinephrine used post-ROSC was 0.05
251 $\mu\text{g}/\text{kg}/\text{min}$. Use of epinephrine did not impact the changes in ICP, RAP, CerPP, MAP or rSO_2
252 observed with a change in body position post-ROSC (data in Supplement). Cerebral rSO_2 was
253 not measured in Protocol B due to lack of available functional sensors.

254 The CerPP, CorPP, and other key hemodynamic variables after 6 minutes of standard
255 CPR and prior to defibrillation are shown in Table 1. After 6 minutes of CPR, the mean CorPP
256 and CerPP were 19.3 ± 3.1 mmHg and 17.3 ± 4.1 mmHg, respectively

257 Key outcomes are shown in Figures 3 – 5 and Table 1. For all 4 epochs studied ICP
258 values during HUP were 11.0 ± 4.3 and 19.7 ± 3.0 Flat ($p < 0.001$) and CerPP was 80.4 ± 7.3 HUP
259 and 68.0 ± 6.2 Flat ($p = 0.001$). In MANOVA, no significant first-order interaction involving time
260 and head position was observed for CerPP ($p = 0.18$). CerPP was 12.5 ± 5.9 mmHg higher with
261 HUP versus Flat, corresponding to 18.3% higher CerPP levels ($p < 0.001$, Supplementary table
262 3) but did not differ according to time ($P = 0.96$) (Figure 3 – 5 and Table 1). ICP values were
263 8.7 ± 2.3 mmHg lower with HUP ($p < 0.001$)

264 Outcomes were similar when the data for the first two 5-minutes epoch interventions
265 were analysed separately. Each time the head and thorax were elevated RAP and ICP decreased
266 and CerPP increased, as shown in Figure 5. More specifically, for the first two 5-minutes epoch
267 interventions, CerPP increased with HUP 15.3 ± 6.2 mmHg (a relative 23.4% increase) ($p = 0.003$)
268 and ICP decreased 8.3 ± 2.4 mmHg (a relative 41% decrease) ($p < 0.01$). In contrast to Protocol A
269 results, there were no differences in RAP depending on the time of intervention.

270

271 **DISCUSSION**

272 The primary goal of this study was to use an animal model of cardiac arrest to determine
273 if elevation of the head and thorax after ROSC would be of hemodynamic benefit when
274 compared with the conventional approach of leaving the body in the flat horizontal plane. Using
275 a randomized controlled study design, we demonstrated that each time the head and thorax were
276 elevated 22 and 8 cm, respectively, CerPP increased and ICP decreased, with two different
277 methods of CPR and two different durations of untreated VF. MAP, on average, remained
278 constant with the gradual change in position. These new findings are supportive of a modest
279 elevation the head and thorax *after* ROSC to lower ICP and improve CerPP, as long as the MAP
280 is stable. The findings were similar for ACD+ITD CPR in the HUP position during resuscitation
281 for 29 minutes prior to defibrillation and for C-CPR in the flat position for a shorter duration of
282 VF and CPR. The overall observations are similar to what has been reported for the routine
283 treatment of traumatic brain injury¹⁹.

284 These investigations build upon recent studies demonstrating that controlled sequential
285 elevation of the head and thorax during ACD+ITD CPR was synergistic, with near
286 normalization of CerPP values after prolonged CPR and a 6-fold increase in neurologically-
287 intact survival in animals¹³. The natural question that arose from those studies was, should the
288 head and heart remain elevated post ROSC? Our results demonstrate that CerPP increased by
289 nearly 20% after ROSC after 30 minutes of ACD+ITD HUP CPR by maintaining HUP versus
290 lowering the pigs to a flat position. The impact of gravity was profound, immediate,
291 reproducible, and may be of significant clinical benefit. Each time the head and thorax were
292 elevated 22cm and 8 cm, respectively, from the horizontal plane, ICP decreased on average 10-
293 mmHg. In the setting of potential brain injury, a 10-mmHg reduction in ICP may be clinically
294 relevant²⁰. Improving cerebral perfusion in the early phase of ROSC may be of critical

295 importance to limit reperfusion injuries. This is supported by the observations from
296 experimental models suggesting that heart and brain injuries occur during the reperfusion phase
297 of cardiac arrest or within the few hours following resuscitation.¹⁸

298 This study was not designed to compare ACD+ITD CPR HUP versus C-CPR flat.
299 However, it is noteworthy that after 8 minutes of untreated VF and 29 minutes of ACD+ITD
300 HUP CPR the CerPP was markedly higher than after 6 minutes of untreated VF and 6 minutes
301 of C-CPR, consistently with previous reports^{12,21}. Overall, post-ROSC hemodynamic values
302 were higher both HUP and flat after C-CPR with the shorter VF and CPR times versus
303 ACD+ITD HUP CPR. In contrast to the ACD+ITD HUP CPR group, there was no change in
304 RAP with a change in body position post-ROSC in the C-CPR group.

305 Although no adverse effects of HUP were observed in this study, there is a theoretical
306 harm associated with HUP in the setting of significant hypotension, especially if the head is
307 elevated too rapidly or too high. In patients with traumatic brain injury, 30° HUP is routinely
308 used in the intensive care unit as it provides significant clinical benefit and improves clinical
309 outcomes, but only when the MAP with HUP is adequate to pump blood ‘uphill’¹⁹.

310 This study has some limitations. First brain blood flow was not directly measured, nor
311 were short term or long-term clinical outcomes. However, prior studies on head and thorax
312 elevation during CPR have shown a close relationship between blood flow, CerPP and coronary
313 perfusion pressure^{11, 22}. This linear relationship might be explained by the impairment of
314 cerebral blood flow autoregulation observed in patients after cardiac arrest²³. Second, our study
315 was powered to test the primary hypothesis but some of the differences in the secondary
316 endpoints did not achieve statistical significance.

317

318 **CONCLUSION**

319 The results from this animal study demonstrate that head and thorax elevation post-
320 ROSC significantly increased CerPP and lowers ICP, regardless of the method of CPR. These
321 preclinical data are a first step towards implementation of a new and simple post-resuscitation
322 intervention that may be synergistic with other head and thorax elevation manoeuvres during
323 CPR to improve neurological survival, by decreasing the likelihood of brain injury.

324

325

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404 **Table 1:** Haemodynamic measurements at baseline, at the end of CPR and in the post-ROSC
 405 period for the two study protocols. Values are mean (standard deviation). P values are
 406 comparing HUP vs Flat during post-ROSC for the whole experiment. All secondary outcome's
 407 P values are adjusted for multiple comparisons using the Bonferroni method.

408
 409

	Protocol A		All Interventions		
	At baseline	After 29min of CPR	Flat	HUP	P
Intrathoracic pressure	2.0 (0.2)	-2.4 (1.3)	1.8 (0.6)	1.5 (0.3)	.99
Mean arterial pressure	82.4 (8.9)	59.4 (17.2)	71.8 (15.2)	71.6 (15.6)	.99
Mean right atrial pressure	7.4 (1.8)	41.0 (10.2)	7.1 (2.0)	4.6 (1.3)	.54
Intracranial pressure	16.5 (0.9)	8.9 (3.8)	18.6 (5.1)	9.1 (5.5)	<.001
Cerebral perfusion pressure	65.9 (8.4)	50.5 (15.6)	53.2 (19.1)	62.5 (19.9)	.004
Coronary perfusion pressure	66.9 (9.2)	40.6 (20.5)	58.9 (14.7)	60.5 (15.1)	.99
Cerebral oximetry	74.8 (3.3)	61.8 (5.1)	61.0 (10.6)	63.2 (8.9)	.99
End-tidal CO ₂	39.4 (3.0)	34.3 (10.9)	22.9 (6.1)	20.4 (3.4)	.99
Oxygen saturation	95.6 (1.4)	82.2 (10.0)	73.0 (26.9)	73.9 (28.5)	.99
Heart rate	92.3 (12.1)	100.0 (0.0)	148.4 (28.0)	148.4 (16.3)	.99
Arterial pH	7.46 (0.03)	7.10 (0.08)	7.09 (0.13)	7.09 (0.14)	.99
Arterial lactate	0.9 (0.3)	6.9 (1.9)	8.3 (3.6)	8.3 (3.5)	.99

	Protocol B		All Interventions		
	At baseline	After 6min of CPR	Flat	HUP	P
Intrathoracic pressure	1.9 (0.2)	-0.8 (0.4)	1.8 (0.4)	1.4 (0.7)	.99
Mean arterial pressure	84.7 (7.8)	42.7 (6.9)	87.7 (8.4)	91.4 (10.4)	.56
Mean right atrial pressure	10.0 (1.5)	30.8 (7.0)	7.6 (2.3)	7.1 (2.6)	.99
Intracranial pressure	19.1 (1.9)	25.3 (4.3)	19.7 (3.0)	11.0 (4.3)	<.001
Cerebral perfusion pressure	65.6 (9.5)	17.3 (4.1)	68.0 (6.2)	80.4 (7.3)	<.001
Coronary perfusion pressure	66.0 (8.0)	19.3 (3.1)	72.2 (8.2)	75.7 (11.1)	.56
End-tidal CO ₂	37.6 (1.7)	4.6 (3.2)	35.8 (7.5)	31.4 (8.9)	.99
Heart rate	110.5 (19.6)	100.0 (0.0)	150.5 (32.6)	154.0 (35.2)	.99

410

411 **Figure Legends**

412

413 Figure 1

414 Figure 1a: Study outline for protocol A

415 Figure 1b: Study outline for protocol B

416

417 Figure 2

418 Representative haemodynamic tracings post-ROSC. ITP: Intrathoracic pressure, AoP: Aortic
419 pressure, RAP: Right atrial pressure, ICP: Intracranial pressure, CerPP: Cerebral perfusion
420 pressure.

421

422 Figure 3

423 Main haemodynamic parameters and cerebral oximetry of HUP versus Flat for the whole post-
424 ROSC period.

425

426 Figure 4

427 Main haemodynamic parameters and cerebral oximetry during the post-ROSC period in
428 Protocol A. (median, 25/75% percentiles, min/max) [mmHg].

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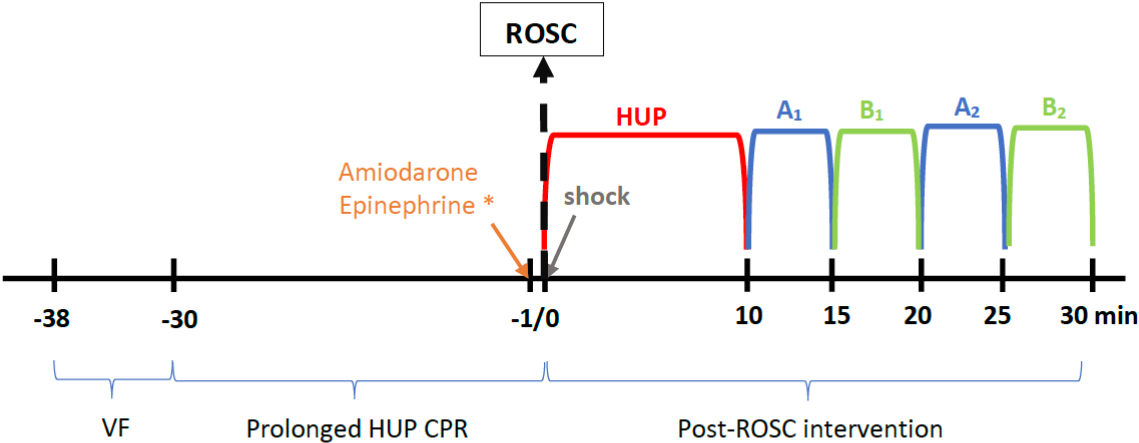
431 Figure 5

432 Main haemodynamic parameters and cerebral oximetry during the post-ROSC period in
433 Protocol B. (median, 25/75% percentiles, min/max) [mmHg].

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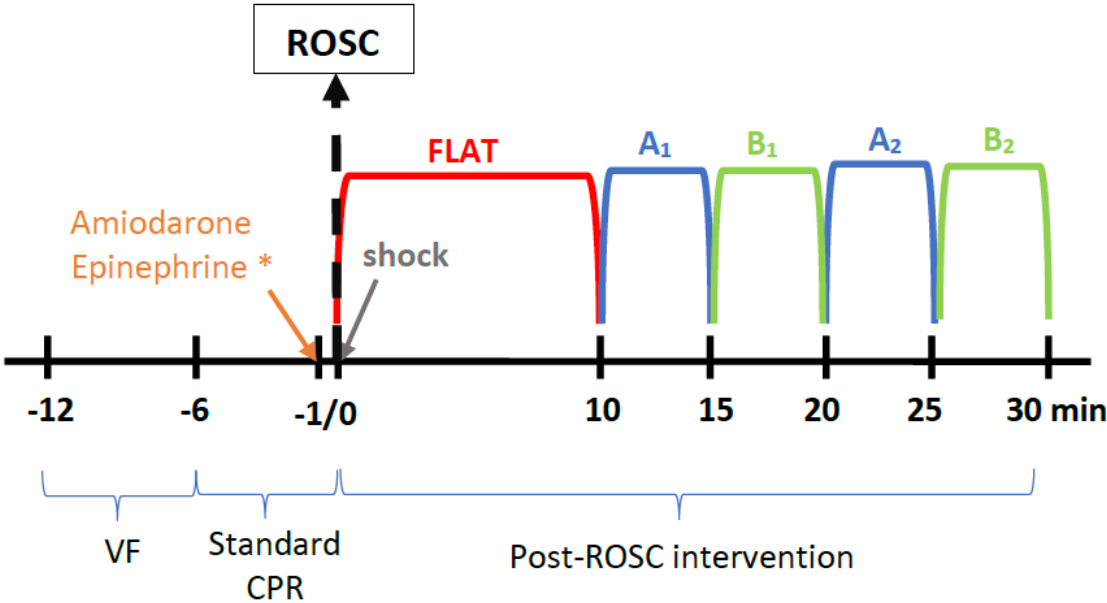
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Protocol A

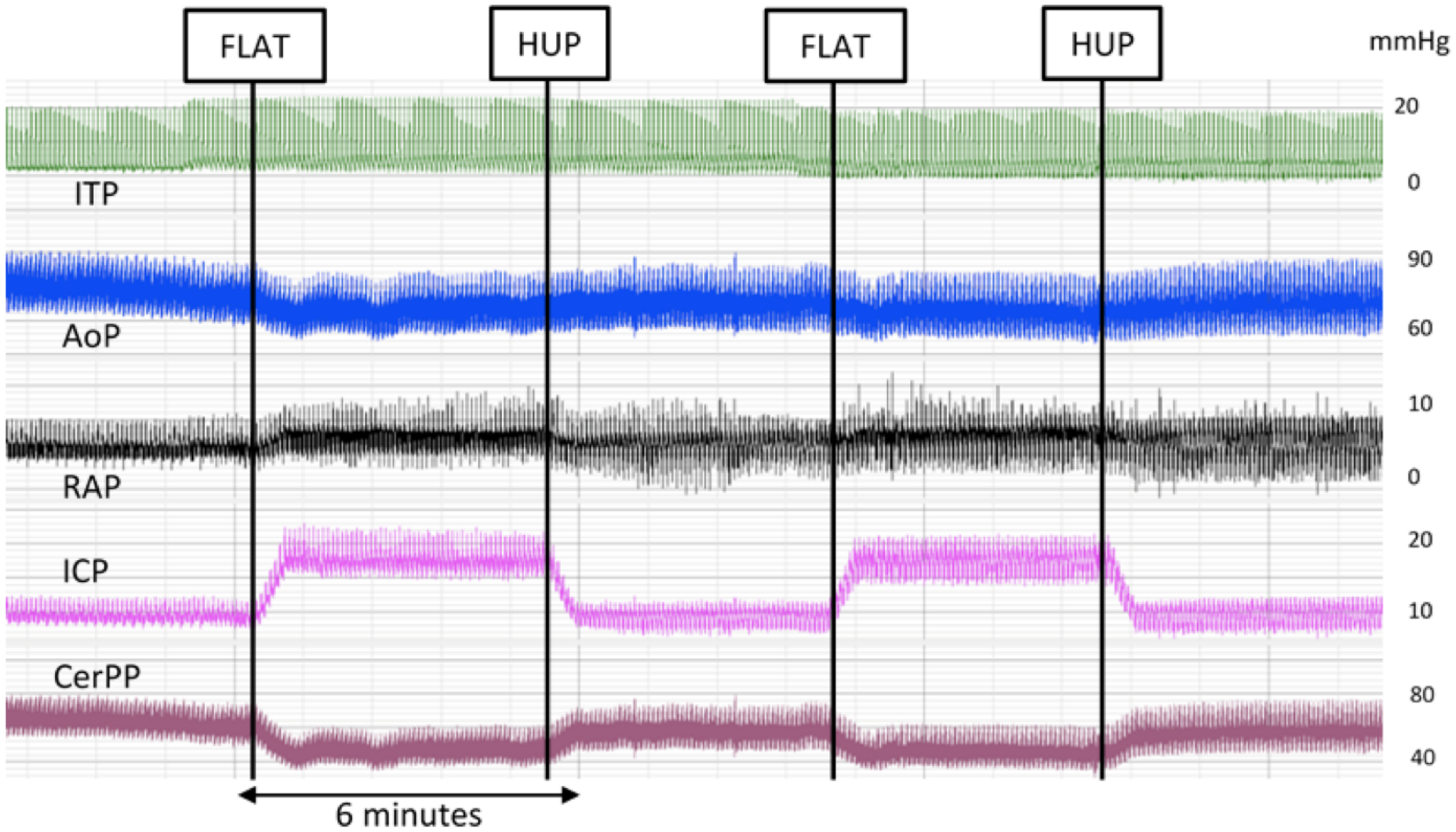


* If required
 A: First intervention (HUP or FLAT)
 B: Second intervention (HUP or FLAT)

Protocol B



* If required
 A: First intervention (HUP or FLAT)
 B: Second intervention (HUP or FLAT)



rSO2

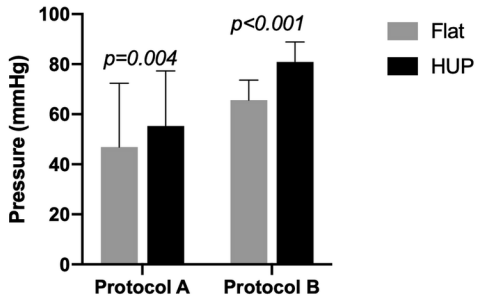
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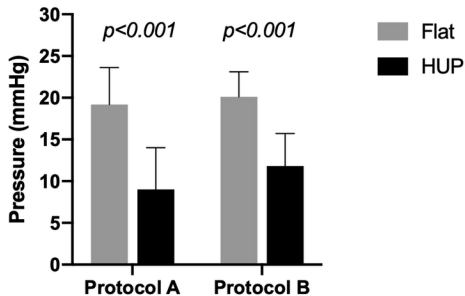
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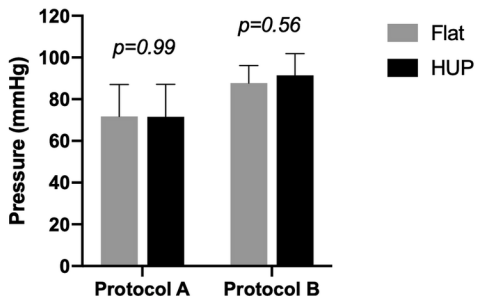
Cerebral perfusion pressure



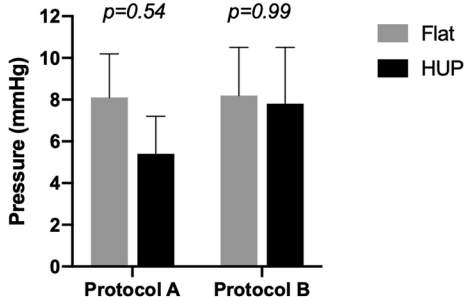
Intracranial pressure



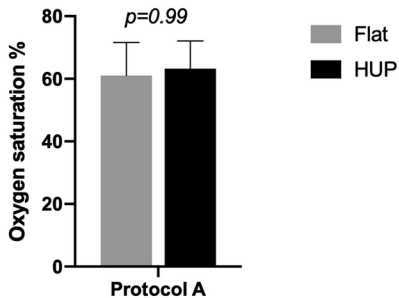
Aortic pressure



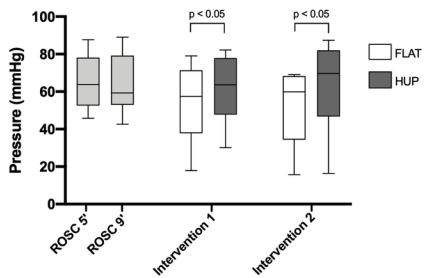
Right atrial pressure



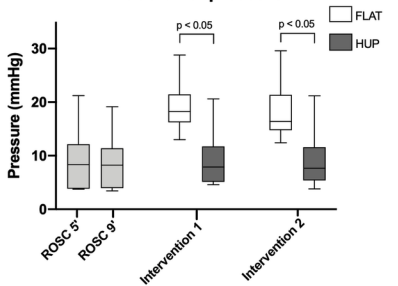
Cerebral oximetry



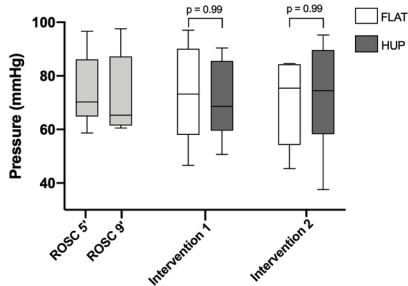
Cerebral perfusion pressure



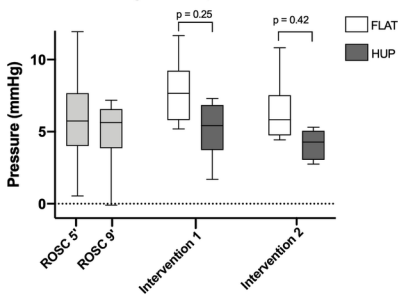
Intracranial pressure



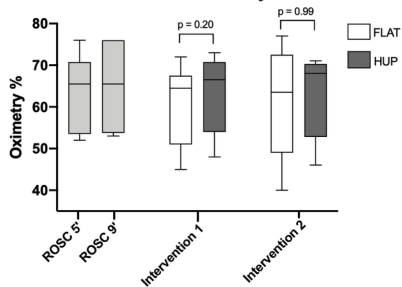
Aortic pressure



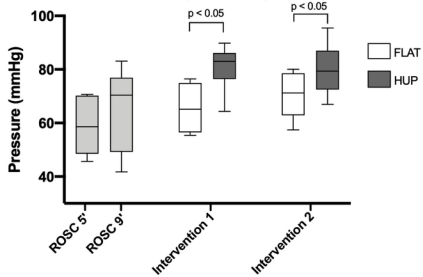
Right atrial pressure



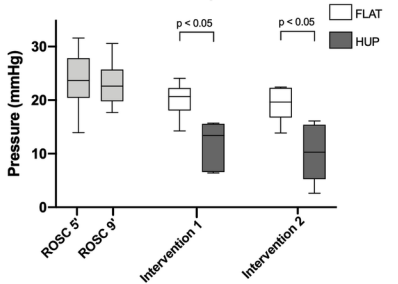
Cerebral oximetry



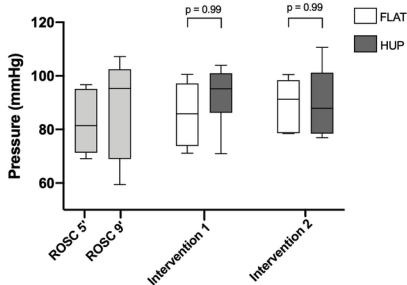
Cerebral perfusion pressure



Intracranial pressure



Aortic pressure



Right atrial pressure

