ADVANCED**CPR**
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THE SCIENCE OF HEAD UP CPR
BIBLIOGRAPHY

This bibliography lists peer-reviewed articles related to the concept and implementation of HEAD UP POSITION CPR.

1. Bachista K Moore J, Labarère J, Crowe R, Emanuleson L, Lick C, Debaty G, Holley J, Quinn R, Scheppke K, Pepe P. **Survival for Nonshockable Cardiac Arrests Treated With Noninvasive Circulatory Ajuncts and Head/Thorax Elevation.** *Critical Care Medicine* 2024;52(2):170-181, doi:DOI: 10.1097/CCM.0000000000006055

Abstract

<u>Objectives:</u> *Cardiac arrests remain a leading cause of death worldwide. Most patients have nonshockable electrocardiographic presentations (asystole/pulseless electrical activity). Despite well-performed basic and advanced cardiopulmonary resuscitation (CPR) interventions, patients with these presentations have always faced unlikely chances of survival. The primary objective was to determine if, in addition to conventional CPR (C-CPR), expeditious application of noninvasive circulation-enhancing adjuncts, and then gradual elevation of head and thorax, would be associated with higher likelihoods of survival following out-of-hospital cardiac arrest (OHCA) with nonshockable presentations.*

<u>Design:</u> *Using a prospective observational study design (ClinicalTrials.gov NCT05588024), patient data from the national registry of emergency medical services (EMS) agencies deploying the CPR-enhancing adjuncts and automated head/thorax-up positioning (AHUP-CPR) were compared with counterpart reference control patient data derived from the two National Institutes of Health clinical trials that closely monitored quality CPR performance. Beyond unadjusted comparisons, propensity score matching and matching of time to EMS-initiated CPR (TCPR) were used to assemble cohorts with corresponding best-fit distributions of the well-established characteristics associated with OHCA outcomes.*
<u>Setting:</u> *North American 9-1-1 EMS agencies.*

<u>Patients:</u> *Adult nontraumatic OHCA patients receiving 9-1-1 responses.*

<u>Interventions:</u> *In addition to C-CPR, study patients received the CPR adjuncts and AHUP (all U.S. Food and Drug Administration-cleared).*

<u>Measurements and main results:</u> The median TCPR for both AHUPCPR and C-CPR groups was 8 minutes. Median time to AHUP initiation was 11 minutes. Combining all patients irrespective of lengthier response intervals, the collective unadjusted likelihood of AHUP-CPR group survival to hospital discharge was 7.4% (28/380) vs. 3.1% (58/1,852) for C-CPR (odds ratio [OR], 2.46 [95% CI, 1.55–3.92]) and, after propensity score matching, 7.6% (27/353) vs. 2.8% (10/353) (OR, 2.84 [95% CI, 1.35–5.96]). Faster AHUP-CPR application markedly amplified odds of survival and neurologically favorable survival.

<u>Conclusions:</u> These findings indicate that, compared with C-CPR, there are strong associations between rapid AHUP-CPR treatment and greater likelihood of patient survival, as well as survival with good neurological function, in cases of nonshockable OHCA.

2. Pourzand P, Moore JC, Metzger A, Salverda B, Suresh M, Arango S, et al. **Hemodynamics, survival and neurological function with early versus delayed automated head-up CPR in a porcine model of prolonged cardiac arrest.** *Resuscitation.* 2023; doi: https://doi.org/10.1016/j.resuscitation.2023.110067.

Abstract

<u>Aim:</u> To determine if controlled head and thorax elevation, active compression-decompression cardiopulmonary resuscitation (CPR), and an impedance threshold device combined, termed automated head-up positioning CPR (AHUP-CPR), should be initiated early, as a basic (BLS) intervention, or later, as an advanced (ALS) intervention, in a severe porcine model of cardiac arrest.

<u>Methods:</u> Yorkshire pigs (n = 22) weighing 40 kg were anesthetized and ventilated. After 15 minutes of untreated ventricular fibrillation, pigs were randomized to AHUP-CPR for 25 minutes (BLS group) or conventional CPR for 10 minutes, followed by 15 minutes of AHUP-CPR (ALS group). Thereafter, epinephrine, amiodarone, and defibrillation were administered. Neurologic function, the primary endpoint, was assessed 24-hours later with a Neurological Deficit Score (NDS, 0 = normal and 260 = worst deficit score or death). Secondary outcomes included return of spontaneous circulation (ROSC), cumulative survival, hemodynamics and epinephrine responsivity. Data, expressed as mean ± standard deviation, were compared using Fisher's Exact, log-rank, Mann-Whitney U and unpaired t-tests.

<u>Results:</u> ROSC was achieved in 10/11 pigs with early AHUP-CPR versus 6/11 with delayed AHUP-CPR (p = 0.14), and cumulative 24-hour survival

was 45.5% versus 9.1%, respectively (p < 0.02). The NDS was 203 ± 80 with early AHUP-CPR versus 259 ± 3 with delayed AHUP-CPR (p = 0.035).
ETCO2, rSO2, and responsiveness to epinephrine were significantly higher in the early versus delayed AHUP-CPR.

Conclusion: When delivered early rather than late, AHUP-CPR resulted in significantly increased hemodynamics, 24-hour survival, and improved neurological function in pigs after prolonged cardiac arrest. Based on these findings, AHUP-CPR should be considered a BLS intervention.

3. Jaeger D, Kosmopoulos M, Voicu S, Kalra R, Gaisendrees C, Schlartenberg G, Bartos J, Yannopoulos D. **Cerebral hemodynamic effects of Head-up CPR in a porcine model**. *Resuscitation*. 2023;193. doi: https://doi.org/10.1016/j.resuscitation.2023.110039.

Abstract
Aim: To assess the hemodynamic effects of head elevation on cerebral perfusion during cardiopulmonary resuscitation (CPR) in a porcine model of cardiac arrest

Methods: VF was induced in eight 65kg pigs that were treated with CPR after five minutes of no flow. Mean arterial pressure (MAP) was measured at the descending thoracic aorta. Internal carotid artery blood flow (CBF) was measured with an ultrasound probe. Cerebral perfusion pressure (CerPP) was calculated in two ways (CerPPICAP and CerPPreported) using the same intracranial pressure (ICP) measurement. CePPreported was calculated as MAP-ICP. CerPPICAP was calculated by using intracranial arterial pressure (ICAP) – ICP. The animals were switched between head up (HUP) and supine (SUP) CPR every five minutes for a total of twenty minutes of resuscitation.

Results: MAP and coronary perfusion pressure measurements were similar in both CPR positions (p=0.36 and p=0.1, respectively). ICP was significantly lower in the HUP CPR group (14.7 ±1 mm Hg vs 26.9 ± 1 mm Hg, p<0.001) as was ICAP (30.1±2mm Hg vs 42.6± 1 mmHg, p<0.001). The proportional decrease in ICP and ICAP resulted in similar CerPPICAP comparing HUP and SUPCPR (p=0.7). CBF was significantly lower during HUPCPR when compared to SUPCPR (58.5± 3 ml/min vs 78±4 ml/min, p<0.001). A higher CerPPreported was found during the HUP compared to SUP-CPR, when MAP was used (36.6±2 mm Hg vs 23±2 mm Hg, p<0.001) without correcting for the hydrostatic pressure drop.

Conclusion: HUP did not affect cerebral perfusion pressure and it significantly decreased internal carotid blood flow.

4. *Moore JC, Bachista KM, Holley JE, Debaty GP, Lurie KG.* ***Head Up CPR is based upon the laws of physics****. Resuscitation 198 (2024) 110178. doi.org/10.1016/j.resuscitation.2024.110178*

Letter to editor in response to Jaeger et al.

Head Up (HUP) CPR, which includes controlled head and thorax elevation, active compression decompression (ACD) and/or automated CPR, and an impedance threshold device (ITD), utilizes gravity to lower intracranial pressure (ICP) and improve cerebral perfusion pressure (CerPP).[1]

Effective HUP-CPR uses these circulatory adjuncts to pump blood 'uphill.'1-4 HUP-CPR should be performed initially for ~2 minutes, with ~12cm of head elevation, to initiate drainage of blood from the head and thorax and prime the cardio-cerebral circuit.[4]Gradual elevation is then performed over another 2-minute period to maintain a perfusing aortic pressure while minimizing loss of pressure with elevation.[2,4] Ineffective HUP-CPR includes no priming period, elevating the head rapidly, performing conventional CPR with head elevation, and not using an ITD.[2,4]

Jaeger et al published a recent HUP-CPR animal study5 using a method of intracranial arterial pressure (ICAP) measurement: a 5F micromanometer-tipped catheter was inserted "as far as possible inside the cranium" without location confirmation. This method has not been described or validated. These 5F catheters can impede blood flow in smaller vessels. We observed signal dampening when unsuccessfully trying to replicate ICAP measurements. Jaeger reported during HUP-CPR, the CerPP measured using ICAP, was lower than previously reported. However, their own data suggests the ICAP measurement is unreliable, observing a baseline supine mean arterial pressure (MAP) in the thoracic aorta (78□2 mmHg) 19mmHg higher than the supine ICAP measurement (59□1 mmHg). When supine, these pressures should be similar or slightly higher in the high carotid or intracranial region. They hypothesize the differences observed in CerPP between HUP and supine positions are due to hydrostatic pressure differences, however with large differences seen even at baseline in the supine position, this hypothesis is questionable. The arterial tree is not a column of blood but a dynamic closed system, especially during CPR.

Further, Jaeger et al used a wedge to rapidly elevate to 30□ without mention of a priming phase and rapidly changed the CPR position every 5 minutes. Performance of HUP-CPR this way results in too rapid an elevation of the head and can lower aortic pressure. Our group cautioned not to perform HUP-CPR this way years ago, when we showed CerPP approaching nearly normal values with a priming phase *and gradual elevation over 2 minutes. Performing HUP-CPR as we recommend, takes a minimum of 4 minutes to fully elevate. When we studied a more rapid rise over <30 seconds, it took 7 minutes to reach 50% of baseline CerPP values versus 3 minutes with a 2-minute rise. Both groups achieved maximal CerPP values after 18 minutes of CPR.[4] It is unsurprising Jaeger observed inferior hemodynamics with how HUP-CPR was performed.*

Most importantly, CerPP is a number, and not a clinical outcome. This is why we have conducted previous studies showing improved cerebral blood flow and 24-hour neurological survival in animal models with HUP CPR.1,2 Initial human observational studies demonstrate a time sensitive association between initiation of HUP-CPR and survival.[3] HUP-CPR performed as previously studied continues to show great promise in the field of resuscitation.

References

1. Moore JC, Segal N, Lick MC, et al. Head and thorax elevation during active compression decompression cardiopulmonary resuscitation with an impedance threshold device improves cerebral perfusion in a swine model of prolonged cardiac arrest. Resuscitation. Aug 05 2017;doi:10.1016/j.resuscitation.2017.07.033

2. Moore JC, Salverda B, Rojas-Salvador C, Lick M, Debaty G, G Lurie K. Controlled sequential elevation of the head and thorax combined with active compression decompression cardiopulmonary resuscitation and an impedance threshold device improves neurological survival in a porcine model of cardiac arrest. Resuscitation. Jan 2021;158:220-227. doi:10.1016/j.resuscitation.2020.09.030

3. Bachista KM, Moore JC, Labarère J, et al. Survival for Nonshockable Cardiac Arrests Treated With Noninvasive Circulatory Adjuncts and Head/Thorax Elevation. Crit Care Med. Feb 01 2024;52(2):170-181. doi:10.1097/CCM.0000000000006055

4. Rojas-Salvador C, Moore JC, Salverda B, Lick M, Debaty G, Lurie KG. Effect of controlled sequential elevation timing of the head and thorax during cardiopulmonary resuscitation on cerebral perfusion pressures in a porcine model of cardiac arrest. Resuscitation. 04 2020;149:162-169. doi:10.1016/j.resuscitation.2019.12.011

5. Jaeger D, Kosmopoulos M, Voicu S, et al. Cerebral hemodynamic effects of head-up CPR in a porcine model. Resuscitation. Dec 2023;193:110039. doi:10.1016/j.resuscitation.2023.110039

5. *Moore JC. **Head-up cardiopulmonary resuscitation**. Current Opinions in Critical Care. 2023;29:155-161. doi:10.1097/MCC.0000000000001037.*

Abstract:

Purpose of review: The purpose of this review was to provide an overview of head-up (HUP) CPR physiology, relevant preclinical findings, and recent clinical literature.

Recent findings: Recent preclinical findings have demonstrated optimal hemodynamics and improved neurologically intact survival in animals receiving controlled head and thorax elevation with circulatory adjuncts. These findings are compared with animals in the supine position and/or receiving conventional CPR with the HUP position. There are few clinical studies of HUP CPR. However, recent studies have shown safety and feasibility of HUP CPR and improved near-infrared spectroscopy changes in patients with head and neck elevation. Additional observational studies have shown that HUP CPR performed with head and thorax elevation and circulatory adjuncts has a time-dependent association with survival to hospital discharge, survival with good neurological function, and return of spontaneous circulation.

Summary: HUP CPR is a new and novel therapy increasingly used in the prehospital setting and discussed in the resuscitation community. This review provides a relevant review of HUP CPR physiology and preclinical work, and recent clinical findings. Further clinical studies are needed to further explore the potential of HUP CPR.

6. Moore JC, Pepe P, Scheppke KE, et al. **Head and thorax elevation during cardiopulmonary resuscitation using circulatory adjuncts is associated with improved survival.** *Resuscitation*. 2022;179:9-17. doi: https://doi.org/10.1016/j.resuscitation.2022.07.039.

Abstract:

Background: Survival after out-of-hospital cardiac arrest (OHCA) remains poor. A physiologically distinct cardiopulmonary resuscitation (CPR) strategy consisting of (1) active compression-decompression CPR and/or automated CPR, (2) an impedance threshold device, and (3) automated controlled elevation of the head and thorax (ACE) has been shown to improve neurological survival significantly versus conventional (C) CPR in animal models. This resuscitation device combination, termed ACE-CPR, is now used clinically.

Objectives: To assess the probability of OHCA survival to hospital discharge after ACE-CPR versus C-CPR.

Methods: As part of a prospective registry study, 227 ACE-CPR OHCA patients were enrolled 04/2019–07/2020 from 6 pre-hospital systems in the United States. Individual C-CPR patient data (n = 5196) were obtained from three large published OHCA randomized controlled trials from high-performing pre-hospital systems. The primary study outcome was survival to hospital discharge. Secondary endpoints included return of spontaneous circulation (ROSC) and favorable neurological survival. Propensity-score matching with a 1:4 ratio was performed to account for imbalances in baseline characteristics.

Results: Irrespective of initial rhythm, ACE-CPR (n = 222) was associated with higher adjusted odds ratios (OR) of survival to hospital discharge relative to C-CPR (n = 860), when initiated in <11 min (3.28, 95 % confidence interval [CI], 1.55–6.92) and < 18 min (1.88, 95 % CI, 1.03–3.44) after the emergency call, respectively. Rapid use of ACE-CPR was also associated with higher probabilities of ROSC and favorable neurological survival.

Conclusions: Compared with C-CPR controls, rapid initiation of ACE-CPR was associated with a higher likelihood of survival to hospital discharge after OHCA.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Head up CPR, ACD-CPR, Active compression-decompression CPR, Impedance threshold device, ITD

7. Kim DW, Choi J, Won SH, et al. **A new variant position of head-up CPR may be associated with improvement in the measurements of cranial near-infrared spectrometry suggestive of an increase in cerebral blood flow in non-traumatic out-of-hospital cardiac arrest patients: A prospective interventional pilot study.** *Resuscitation*. 2022;175:159-66. doi: https://doi.org/10.1016/j.resuscitation.2022.03.032 .

Abstract:

Aim of the study: This study aimed to investigate the effect of the head-up position implemented during cardiopulmonary resuscitation (CPR) on cerebral blood flow (CBF) using near-infrared spectroscopy in out-of-hospital cardiac arrest patients.

Methods: Baseline characteristics (age, sex, cerebral performance category before cardiac arrest, witnessed cardiac arrest, bystander CPR, first monitored rhythm, no-flow time, prehospital low-flow time, CPR duration in the emergency department (ED), and reason for stopping CPR in the ED) were recorded. The changes of CBF were derived from the optical oscillation waveform measured by near-infrared spectroscopy in adult patients with out-of-hospital cardiac arrest by alternating head-up and supine positions at 4-minute intervals while performing

CPR. The CBF velocity according to the head position was also evaluated using the time derivative of the oscillation waveform.

Results: During the study period, 28 patients were enrolled. The median increase in CBF in the prefrontal area in the head-up position was 14.6% (Interquartile range, 8.8–65.0), more than that in the supine position. An increase in CBF was observed in the head-up position compared with the supine position in 83.3% of the patients included in the analysis.

Conclusion: CBF increased when the head-up position was used during CPR in non-traumatic out-of-hospital cardiac arrest patients.

Keywords: Cardiopulmonary resuscitation, Cerebral blood flow, Head up CPR

8. Moore J, Duval S, Lick C, et al. **Faster time to automated elevation of the head and thorax during cardiopulmonary resuscitation increases the probability of return of spontaneous circulation.** *Resuscitation*. 2021; 170:63-69. doi: https://doi.org/10.1016/j.resuscitation.2021.11.008

Abstract:
Objectives: Resuscitation in the Head Up position improves outcomes in animals treated with active compression decompression cardiopulmonary resuscitation and an impedance threshold device (ACD + ITD CPR). We assessed impact of time to deployment of an automated Head Up position(AHUP) based bundle of care after out-of-hospital cardiac arrest on return of spontaneous circulation (ROSC).

Methods: Observational data were analyzed from a patient registry. Patients received treatment with 1) ACD + and/or automated CPR 2) an ITD and 3) an AHUP device. Probability of ROSC (ROSCprob) from the 9-1-1 call to AHUP device placement was assessed with a restricted cubic spline model and linear regression.

Results: Of 11 sites, 6 recorded the interval from 9-1-1 to AHUP device (n = 227). ROSCprob for all rhythms was 34%(77/227). Median age (range) was 66 years (19-101) and 68% men. The ROSCprob for shockable rhythms was 47% (18/38). Minutes from 9-1-1 to AHUP device (median, range) varied between sites: 1) 6.4(4,15), 2) 8.0(5,19), 3) 9.9(4, 12), 4) 14.1(6, 36), 5) 15.9(6, 34), 6) 19.0(8, 38), (p = 0.0001). ROSCprob also varied; 1) 55.1%(16/29), 2) 60%(3/5), 3) 50%(3/6), 4) 22.7%(17/75), 5) 26.4%(9/34), and 6) 37.1%(29/78), (p = 0.019). For all rhythms between 4 and 12 min (n = 85), ROSCprob declined 5.6% for every minute elapsed (p = 0.024). For shockable rhythms, between 6 and 15 min (n = 23), ROSCprob declined 9.0% for every minute elapsed (p = 0.006).

Conclusions: Faster time to deployment of an AHUP based bundle of care is associated with higher incidence of ROSC. This must be considered when evaluating and implementing this bundle.

9. Duhem H, Moore J, Rojas-Salvador C, et al. **Improving post-cardiac arrest cerebral perfusion pressure by elevating the head and thorax.** *Resuscitation*. 2021; 159:45-53. DOI: https://doi.org/10.1016/j.resuscitation.2020.12.016

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

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

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

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

Keywords: Active compression-decompression CPR, Cardiac arrest, Cardiopulmonary resuscitation, Return of spontaneous circulation, Advanced cardiac life support, Cerebral perfusion pressure, Head Up CPR, Head and thorax elevation, Heart arrest, Impedance threshold device, Medical device, Patient positioning, Posture, Intracranial pressure

10. Huang CC, Chen KC, Lin ZY, et al. **The effect of the head-up position on cardiopulmonary resuscitation: a systematic review and meta-analysis.** *Critical Care*. 2021;25(376) doi: https://doi.org/10.1186/s13054-021-03797-x.

Abstract:
Objective: Experimental studies of head-up positioning (HUP) during cardiopulmonary resuscitation (CPR) have had some degree of conflicting published results. The current study aim was to analyze and reconcile those discrepancies in order to better clarify the effects of HUP CPR compared to conventional supine (SUP) CPR.

Methods: Three databases (PubMed, EMBASE and Cochrane Library) were searched comprehensively (from each respective database's inception to May 2021) for articles addressing HUP CPR. The primary outcome to be observed was cerebral perfusion pressure (CerPP), and secondary outcomes were mean intracranial pressure (ICP), mean arterial pressure (MAP), coronary perfusion pressure (CoPP) and frequencies of return of spontaneous circulation (ROSC).

Results: Seven key studies involving 131 animals were included for analysis. Compared to SUP CPR, CerPP (MD 10.37; 95% CI 7.11–13.64; $p < 0.01$; $I^2 = 58\%$) and CoPP (MD 7.56; 95% CI 1.84–13.27, $p = 0.01$; $I^2 = 75\%$) increased significantly with HUP CPR, while ICP (MD − 13.66; 95% CI − 18.6 to –8.71; $p < 0.01$; $I^2 = 96\%$) decreased significantly. Combining all study methodologies, there were no significant differences detected in MAP (MD − 1.63; 95% CI − 10.77–7.52; $p = 0.73$; $I^2 = 93\%$) or frequency of ROSC (RR 0.9; 95% CI 0.31–2.60; $p = 0.84$; $I^2 = 65\%$). However, in contrast to worse outcomes in studies using immediate elevation of the head in a reverse Trendelenburg position, study outcomes were significantly improved when HUP (head and chest only) was introduced in a steady, graduated manner following a brief period of basic CPR augmented by active compression–decompression (ACD) and impedance threshold (ITD) devices.

Conclusion: In experimental models, gradually elevating the head and chest following a brief interval of circulatory priming with ACD and ITD devices can enhance CoPP, lower ICP and improve CerPP significantly while maintaining MAP. This effect is immediate, remains sustained and is associated with improved outcomes.

Keywords: Head-up position, Cardiopulmonary resuscitation, Cerebral perfusion pressure

11. Moore JC, Salverda B, Rojas-Salvador C, et al. **Controlled sequential elevation of the head and thorax combined with active compression decompression cardiopumonary resuscitation and an impedance threshold device improves neurological survival in a porcine model of cardiac arrest.** *Resuscitation*. 2020a; 150-23-28 DOI: https://doi.org/10.1016/j.resuscitation.2020.09.030

Abstract:
Aim of the study: Controlled sequential elevation of the head and thorax (CSE) during active compression decompression (ACD) cardiopulmonary resuscitation (CPR) with an impedance threshold device (ITD) has been shown to increase cerebral perfusion pressure and cerebral blood flow in previous animal studies as compared to the traditional supine position. The potential for this novel bundled treatment strategy to improve survival with intact neurological function is unknown.

Methods: Female farm pigs were sedated, intubated, and anesthetized. Central arterial and venous access were continuously monitored. Regional brain tissue perfusion (CerO2) was also measured transcutaneous. Ventricular fibrillation (VF) was induced and untreated for 10 min. Pigs were randomized to (1) Conventional CPR (C-CPR) flat or (2) ACD + ITD CSE CPR that included 2 min of ACD + ITD with the head and heart first elevated 10 and 8 cm, and then gradual elevation over 2 min to 22 and 9 cm, respectively. After 19 min of CPR, pigs were defibrillated and recovered. A veterinarian blinded to the intervention assessed cerebral performance category (CPC) at 24 h. A neurologically intact outcome was defined as a CPC score of 1 or 2. Categorical outcomes were analyzed by Fisher's exact test and continuous outcomes with an unpaired student's t-test.

Results: In 16 animals, return of spontaneous circulation rate was 8/8 (100%) with ACD + ITD CSE and 3/8 (25%) for C-CPR (p = 0.026). For the primary outcome of neurologically intact survival, 6/8 (75%) pigs had a CPC score 1 or 2 with ACD + ITD CSE versus 1/8 (12.5%) with C-CPR (p = 0.04). Coronary perfusion pressure (mmHg, mean _ SD) was higher with CSE at 18 min (41 _ 24 versus 10 _ 5, p = 0.004). rSO2 (%, mean _ SD) and ETCO2 (mmHg, mean _ SD) values were higher at 18 min with CSE (32 _ 9 versus 17 _ 2, p = 0.01, and 55 mmHg _ 10 versus 21 mmHg _ 4, p < 0.001), respectively.

Conclusions: The novel bundled resuscitation approach of CSE with ACD + ITD CPR increased favorable neurological survival versus C-CPR in a swine model of cardiac arrest.

Keywords: Active compression_decompression CPR, Cardiac arrest, Cardiopulmonary resuscitation, Cerebral perfusion, Head Up CPR, Head and thorax elevation, Controlled sequential elevation, Impedance threshold device, Mechanical CPR

12. Pepe P, Aufderheide T, Lamhaut L, et al. **Rationale and Strategies for Development of an Optimal Bundle of Management for Cardiac Arrest.** *Critical Care Explorations*. 2020; 2:e0214. DOI: https://doi.org/10.1097/CCE.0000000000000214

Abstract:
Objectives: To construct a highly detailed yet practical, attainable roadmap for enhancing the likelihood of neurologically intact survival following sudden cardiac arrest.

Design, Setting, and Patients: Population-based outcomes following out-of-hospital cardiac arrest were collated for 10 U.S. counties in Alaska, California, Florida, Ohio, Minnesota, Utah, and Washington. The 10 identified emergency medical services systems were those that had recently reported significant improvements in neurologically intact survival after introducing a more comprehensive approach involving citizens, hospitals, and evolving strategies for incorporating technology-based, highly choreographed care and training. Detailed inventories of in-common elements were collated from the ten 9-1-1 agencies and assimilated. For reference, combined averaged outcomes for out-of-hospital cardiac arrest occurring January 1, 2017, to February 28, 2018, were compared with concurrent U.S. outcomes reported by the well-established Cardiac Arrest Registry to Enhance Survival.

Interventions: Most commonly, interventions and components from the ten 9-1-1 systems consistently included extensive public cardiopulmonary resuscitation training, 9-1-1 system-connected smart phone applications, expedited dispatcher procedures, cardiopulmonary resuscitation quality monitoring, mechanical cardiopulmonary resuscitation, devices for enhancing negative intrathoracic pressure regulation, extracorporeal membrane oxygenation protocols, body temperature management procedures, rapid cardiac angiography, and intensive involvement of medical directors, operational and quality assurance officers, and training staff.

Measurements and Main Results: Compared with Cardiac Arrest Registry to Enhance Survival (n = 78,704), the cohorts from the 10 emergency medical services agencies examined (n = 2,911) demonstrated significantly increased likelihoods of return of spontaneous circulation (mean 37.4% vs 31.5%; p < 0.001) and neurologically favorable hospital discharge, particularly after witnessed collapses involving bystander cardiopulmonary resuscitation and shockable cardiac rhythms (mean 10.7% vs 8.4%; p < 0.001; and 41.6% vs 29.2%; p < 0.001, respectively).

Conclusions: The likelihood of neurologically favorable survival following out-of-hospital cardiac arrest can improve substantially in communities that conscientiously and meticulously introduce a well-sequenced, highly choreographed, system-wide portfolio of both traditional and nonconventional approaches to training, technologies, and physiologic management. The commonalities found in the analyzed systems create a compelling case that other communities can also improve out-of-hospital cardiac arrest outcomes significantly by conscientiously exploring and adopting similar bundles of system organization and care.

Key Words: bundle of care; cardiac arrest; cardiopulmonary resuscitation; emergency medical services; resuscitation centers; sudden cardiac death survival

13. Moore J, Salverda B, Lick M, et al. **Controlled progressive elevation rather than an optimal angle maximizes cerebral perfusion pressure during head up CPR in a swine model of cardiac arrest.** *Resuscitation*. 2020b; 150:23-28. DOI: https://doi.org/10.1016/j.resuscitation.2020.02.023

Abstract:
Aim of the Study: Elevation of the head and thorax (HUP) during cardiopulmonary resuscitation (CPR) has been shown to double brain blood flow with increased cerebral perfusion pressures (CerPP) after active compression-decompression (ACD) CPR with an impedance threshold device (ITD). However, the optimal angle for HUP CPR is unknown.

Methods: In Study A, different angles were assessed (20°, 30°, 40°), each randomized over 5-min periods of ACD + ITD CPR, after 8 min of untreated ventricular fibrillation in an anesthetized swine model. Based upon Study A, Study B was performed, where animals were randomized to 1 of 2 sequences: 20°, 30 °, 40° or 40 °, 30 °, 20° with a similar protocol. The primary endpoint was CerPP for both studies.

Results: In Study A, no optimal HUP angle was observed in 18 pigs. CerPPs for 30° and 40° (mmHg, mean±SD) were equivalent (44 ±22 and 47 ± 26, p = 0.18). However, CerPP appeared higher when 40° HUP was performed during the last 5-min of CPR, suggestive of a sequence effect. For Study B, after 17 min of CPR, CerPP (mmHg) were higher with the 20°, 30°, 40° sequence: 60 ± 17 versus 33 ±18 (p = 0.035).

Conclusions: No optimal HUP CPR angle was observed. However, controlled progressive elevation of the head and thorax during CPR is more beneficial than an absolute angle or height to maximize CerPP. Further studies are needed to determine the optimal rate of rise during HUP ACD + ITD CPR.

Keywords: Active compression-decompression CPR, Cardiac arrest, Cardiopulmonary resuscitation, Cerebral perfusion, Head up CPR, Head and thorax elevation, Impedance threshold device, Mechanical CPR

14. Elphinstone, A. and Laws, S. **Does 'heads-up' cardiopulmonary resuscitation improve outcomes for patients in out-of-hospital cardiac arrest? A systematic review.** *British Paramedic Journal*. 2020;4(4):16-24 DOI: https://doi.org/10.29045/14784726.2020.12.4.4.16

Abstract:
Introduction: Survival rates for patients in out-of-hospital cardiac arrest have remained around 10% in the United Kingdom for the past seven years. If outcomes are to be improved, research into new methods of advanced life support is required. One such method may be 'heads-up' cardiopulmonary resuscitation.

Methods: A systematic review of literature exploring heads-up cardiopulmonary resuscitation was conducted in an attempt to identify its effects on survival to discharge and neurological outcome.

Results: A comprehensive search of CINAHL, MEDLINE and Google Scholar was undertaken. Six papers were classed as sufficiently relevant for inclusion. Included studies were generally of low quality and none studied the effect of heads-up cardiopulmonary resuscitation on out-of-hospital cardiac arrest patients. Animal studies identified a significant reduction in intracranial pressure and increase in cerebral and coronary perfusion pressure for use of augmented heads-up cardiopulmonary resuscitation in the porcine model of cardiac arrest.

Conclusion: Further research is required to analyse the effects and potential benefits of augmented heads-up cardiopulmonary resuscitation in out-of-hospital cardiac arrest.

Keywords: cardiopulmonary resuscitation; heads-up positioning; out-of-hospital cardiac arrest

15. Holley J, Moore J, Jacobs M, et al. **Supraglottic airway devices variably develop negative intrathoracic pressures: A prospective cross-over study of cardiopulmonary resuscitation in human cadavers.** *Resuscitation* 2020; 148:32-38. DOI: https://doi.org/10.1016/j.resuscitation.2019.12.022

Abstract:
Aim of the study: Negative intrathoracic pressure (ITP) during the decompression phase of cardiopulmonary resuscitation (CPR) is essential to refill the heart, increase cardiac output, maintain cerebral and coronary perfusion pressures, and improve survival. In order to generate negative ITP, an airway seal is necessary. We tested the hypothesis that some supraglottic airway (SGA) devices do not seal the airway as well the standard endotracheal tube (ETT).

Methods: Airway pressures (AP) were measured as a surrogate for ITP in seven recently deceased human cadavers of varying body habitus. Conventional manual, automated, and active compression-decompression CPR were performed with and without an impedance threshold device (ITD) in supine and Head Up positions. Positive pressure ventilation was delivered by an ETT and 5 SGA devices tested in a randomized order in this prospective cross-over designed study. The primary outcome was comparisons of decompression AP between all groups.

Results: An ITD was required to generate significantly lower negative ITP during the decompression phase of all methods of CPR. SGAs varied in their ability to support negative ITP.

Conclusion: In a human cadaver model, the ability to generate negative intrathoracic pressures varied with different SGAs and an ITD regardless of the body position or CPR method. Differences in SGAs devices should be strongly considered when trying to optimize cardiac arrest outcomes, as some SGAs do not consistently develop a seal or negative intrathoracic pressure with multiple different CPR methods and devices.

Keywords: Supraglottic airway, Cardiac arrest, CPR, Intrathoracic pressure, Endotrachael tube, Airway, ITD, Impedence threshhold device, ACD, Active compression decompression CPR, HeadsUp CPR, Airway seal

16. Rojas-Salvador C, Moore J, Salverda B, et al. **Effect of controlled sequential elevation timing of the head and thorax during cardiopulmonary resuscitation on cerebral perfusion pressures in a porcine model of cardiac arrest.** *Resuscitation*. 2020; 149:162-169. DOI: https://doi.org/10.1016/j.resuscitation.2019.12.011

Abstract

Aim: Controlled sequential elevation of the head and thorax (CSE) during active compression _decompression (ACD) CPR with an impedance threshold device (ITD) augments cerebral (CerPP) and coronary (CorPP) perfusion pressures. The optimal CSE is unknown.

Methods: After 8 minutes of untreated VF, 40 kg anesthetized female pigs were positioned on a customized head and thorax elevation device (CED). After 2 min of automated ACD + ITD-16 CPR to 'prime the system', 12 pigs were randomized to CSE to the highest CED position over 4-min or 10-min. The primary outcome was CerPP after 7 minutes of CPR. Secondarily, 24-sec (without a priming step) and 2-min CSE times were similarly tested (n = 6 group) in a non-randomized order. Values expressed as mean ±SD.

Results: After 7 min of CPR, CerPPs were significantly higher in the 4-min vs 10-min CSE groups (53 ±14.4 vs 38.5 ±3.6 mmHg respectively, p = 0.03) whereas CorPP trended higher. The 4-min CSE group achieved 50% of baseline (50% BL) CerPP faster than the 10-min group (2.5 ±1.2 vs 6 ±3.1 minutes, p = 0.03). CerPP values in the 2-min and 4-min CSE groups were significantly higher than in the 24-sec group. With CSE, CerPPs and CorPPs increased over time in all groups.

Conclusions: By optimizing controlled sequential elevation timing, CerPP values achieved 50% of baseline within less than 2.5 minutes and >80% of baseline after 7 minutes of CPR. This novel CPR approach rapidly restored CerPPs to near normal values non-invasively and without vasopressors.

Keywords: Active compression _decompression CPR, Cardiac arrest, Cardiopulmonary resuscitation, Cerebral perfusion pressure, Coronary perfusion pressure, Head Up CPR, Head and thorax elevation, Impedance threshold device, Medical device, Patient positioning

17. Pepe P, Scheppke K, Antevy P, et al. **Confirming the clinical safety and feasibility of a bundled methodology to improve cardiopulmonary resuscitation involving a head-up/torso-up chest compression technique.** *Critical Care Medicine*. 2019; 47(3):449-455. DOI: https://doi.org/10.1097/CCM.0000000000003608

Abstract:
Objectives: Combined with devices that enhance venous return out of the brain and into the thorax, preclinical outcomes are improved significantly using a synergistic bundled approach involving mild elevation of the head and chest during cardiopulmonary resuscitation. The objective here was to confirm clinical safety/feasibility of this bundled approach including use of mechanical cardiopulmonary resuscitation provided at a head-up angle.

Design: Quarterly tracking of the frequency of successful resuscitation before, during, and after the clinical introduction of a bundled head-up/torso-up cardiopulmonary resuscitation strategy.

Setting: 9-1-1 response system for a culturally diverse, geographically expansive, populous jurisdiction.

Patients: All 2,322 consecutive out-of-hospital cardiac arrest cases (all presenting cardiac rhythms) were followed over 3.5 years (January 1, 2014, to June 30, 2017).

Interventions: In 2014, 9-1-1 crews used LUCAS (Physio-Control Corporation, Redmond, WA) mechanical cardiopulmonary resuscitation and impedance threshold devices for out-of-hospital cardiac arrest. After April 2015, they also 1) applied oxygen but deferred positive pressure ventilation several minutes, 2) solidified a pit-crew approach for rapid LUCAS placement, and 3) subsequently placed the patient in a reverse Trendelenburg position (~20°).

Measurements and Main Results: No problems were observed with head-up/torso-up positioning (n = 1,489), but resuscitation rates rose significantly during the transition period (April to June 2015) with an ensuing sustained doubling of those rates over the next 2 years (mean, 34.22%; range, 29.76–39.42%; n = 1,356 vs 17.87%; range, 14.81–20.13%, for 806 patients treated prior to the transition; p < 0.0001). Outcomes improved across all subgroups. Response intervals, clinical presentations and indications for attempting resuscitation remained unchanged. Resuscitation rates in 2015–2017 remained proportional to neurologically intact survival (~35–40%) wherever tracked.

<u>Conclusions</u>: The head-up/torso-up cardiopulmonary resuscitation bundle was feasible and associated with an immediate, steady rise in resuscitation rates during implementation followed by a sustained doubling of the number of out-of-hospital cardiac arrest patients being resuscitated. These findings make a compelling case that this bundled technique will improve out-of-hospital cardiac arrest outcomes significantly in other clinical evaluations.

<u>Key Words</u>: cardiac arrest; cardiopulmonary resuscitation; emergency medical services; head-up CPR; impedance threshold device; sudden death

18. Park Y, Hong K, Shin S, et al. **Worsened survival in the head-up tilt position cardiopulmonary resuscitation in a porcine cardiac arrest model.** Clinical and Experimental Emergency Medicine. 2019; 6(3):250-256. DOI: https://doi.org/10.15441/ceem.18.060

    Abstract:
    <u>Objective</u>: Head elevation at an angle of 30° during cardiopulmonary resuscitation (CPR) was hemodynamically beneficial compared to supine position in a previous porcine cardiac arrest experimental study. However, survival benefit of head-up elevation during CPR has not been clarified. This study aimed to assess the effect of head-up tilt position during CPR on 24-hour survival in a porcine cardiac arrest experimental model.

    <u>Methods</u>: This was a randomized experimental trial using female farm pigs (n=18, 42±3 kg) sedated, intubated, and paralyzed on a tilting surgical table. After surgical preparation, 15 minutes of untreated ventricular fibrillation was induced. Then, 6 minutes of basic life support was performed in a position randomly assigned to either head-up tilt at 30° or supine with a mechanical CPR device, LUCAS-2, and an impedance threshold device, followed by 20 minutes of advanced cardiac life support in the same position. Primary outcome was 24-hour survival, analyzed by Fisher exact test.

    <u>Results</u>: In the 8 pigs from the head-up tilt position group, one showed return of spontaneous circulation (ROSC); all eight pigs expired within 24 hours. In the eight pigs from the supine position group, six had the ROSC; six pigs survived for 24 hours and two expired. The head-up position group showed lower 24-hour survival rate and lower ROSC rate than supine position group (P<0.01).

Conclusion: The use of head-up tilt position with 30 degrees during CPR showed lower 24-hour survival than the supine position.

Keywords: Heart arrest; Cardiopulmonary resuscitation; Animal experimentation

19. Moore J, Segal N, Debaty G, Lurie K. **"The Do's and Don'ts" of Head Up CPR: Lessons learned from the Animal Laboratory**. Letter to the editor. *Resuscitation*. 2018;129:e6-e7

We read with interest the recent article by Putzer et al, where swine were randomized to either the supine position (SUP) or a head and thorax elevation position (HUP) for 20 min of standard mechanical cardiopulmonary resuscitation (CPR) [1]. The mean calculated Cerebral Perfusion Pressures (CerPP) although significantly higher in the HUP group, were below 4 mmHg and only 7% of the baseline CerPP for the HUP group [1]. These low CerPP values are generally incompatible with life. CPR adjuncts to improve hemodynamics such as the Impedance Threshold Device (ITD) and Active Compression-Decompression (ACD) CPR were not used, different from prior published HUP CPR studies [2–4]. The hemodynamics observed by Putzer et al were markedly lower than HUP CPR studies performed previously with these circulatory enhancement devices, where CerPP was observed up to 50–60% of baseline with HUP ACD+ITD CPR [3,4]. It is therefore not surprising that Putzer et al did not find improved cerebral NIRS readings or cerebral metabolism with HUP CPR. These low CerPP values are consistent with previous work comparing SUP and HUP with standard CPR only [3].

The benefit of HUP CPR is predicated on the fact that in order to pump blood 'uphill' to the brain, some sort of circulatory enhancement is needed above and beyond that achieved with standard CPR. This is a fundamental requirement of HUP CPR. Using the ITD alone or ACD+ITD CPR, HUP CPR in swine has been shown to (1) Reduce intracranial pressure, (2) Reduce the potential for a concussion with every compression, and (3) Increase cerebral and to a lesser degree coronary perfusion pressures, (4) Effectively double cerebral blood flow [2–4].

Other lessons learned include that CPR should be started in the SUP position before elevation of the head to 'prime' the cardio-cerebral circuit, as the optimal head and heart elevation height or angle is likely dependent upon the amount of forward blood flow. Rapid elevation of the head to the HUP position may be dangerous as the aortic pressure can decline due to gravity [5]. Thus, CPR should *not be interrupted when the head is elevated. Additionally, a whole-body HUP position over the long term may be dangerous as blood eventually flows to the feet due to gravity over time [1,2,5].*

The clinical potential for HUP CPR is significant. However, like any other new discovery and approach, we must temper our enthusiasm with the realities of implementing a new concept. Without devices to augment the circulation, control the amount and speed of HUP elevation, and if using an automated CPR device, maintain alignment with the chest and ensure stability during elevation, HUP CPR may not be helpful and could be harmful.

Knowledge of the physiology behind these "Do's and Don'ts" is critical to the development of HUP CPR. Moreover, realization of HUP CPR requires implementing this new physiologic construct into established systems-based approaches to cardiac arrest care. There are no silver bullets in resuscitation; simply elevating the head during CPR will not improve neurological outcomes.

20. Putzer G MJ, Helbok R, Mair P. **Reply to "The Do's and Don'ts" of Head Up CPR: Lessons learned from the Animal Laboratory**. Letter to the Editor. *Resuscitation*. 2018;129:e8.

We appreciate the comments from Moore et al. regarding our manuscript comparing the effect of a head-up position (HUP) versus a standard supine position (SUP) during basic life support cardiopulmonary resuscitation (BLS CPR) on cerebral oxygenation and metabolism. We are aware about the fact that most previous HUP CPR studies used an impedance threshold device (ITD) in combination with active compression-decompression (ACD) CPR, which influence intrathoracic pressure, preload and afterload and thereby systemic and cerebral haemodynamics. In contrast to the statement of Moore and colleagues, we used an ACD device (LUCAS2 , Physio Control, Redmond, WA, USA) which is well described in the methods section of the manuscript [1]. In addition, it is important to understand that the primary focus of our study was to investigate whether a higher cerebral perfusion pressure (CPP), as achieved during HUP CPR, would translate into improved brain tissue oxygenation and metabolism. Interestingly, our data suggest that increased CPP may not necessarily lead to better oxygen delivery to brain cells. In other words, pressure does not equal flow. This is a well-known principle derived from microcirculation re- search from bench to bedside: a mean arterial pressure regarded as normal does not necessarily translate into microvascular perfusion and tissue oxygenation in critically ill patients [2–4]. We agree with Moore at al. that CPP values obtained in the current study (11.2 ± 9.5 in the HUP vs. 1.0 ± 9.2 mmHg in the SUP group (p = 0.045) after 5 *min and 3.4 ± 6.4 vs.−3.8 ± 2.8mmHg (p=0.023) after 20min of BLS CPR) were too low and were not compatible with life. Future studies should evaluate the effect of HUP in conjunction with an ITD or during advanced life support (ALS) where higher CPP values can be obtained. Still, our study highlights the importance of a multimodal neuromoni- toring approach when investigating the effect of specific CPR inter- ventions on the brain: it is important to understand that CPP is a cal- culated variable (CPP = mean arterial pressure – intracranial pressure) and cannot simply be used as surrogate parameter for cerebral blood flow and cerebral oxygen delivery in patients after cardiac arrest. Therefore we strongly recommend that future studies investigating the effect of specific CPR interventions on brain haemodynamics should include online monitoring tools to measure brain tissue oxygenation and if feasible brain metabolism. This is important to better define the lowest level of CPP in these severely injured patients/animals during BLS and ALS CPR.*

There is no silver bullet in resuscitation; however, our research should aim at crystallizing a bundle of surrogate parameters for effective CPR in terms of brain resuscitation which could help in improving outcome after cardiac arrest.

21. Moore J, Holley J, Segal N, et al. **Consistent head up cardiopulmonary resuscitation haemodynamics are observed across porcine and human cadaver translational models.** *Resuscitation*. 2018; 132:133-139. DOI: https://doi.org/10.1016/j.resuscitation.2018.04.009

Abstract:
Aim: The objectives were: 1) replicate key elements of Head Up (HUP) cardiopulmonary resuscitation (CPR) physiology in a traditional swine model of ventricular fibrillation (VF), 2) compare HUP CPR physiology in pig cadavers (PC) to the VF model 3) develop a new human cadaver (HC) CPR model, and 4) assess HUP CPR in HC.

Methods: Nine female pigs were intubated, and anesthetized. Venous, arterial, and intracranial access were obtained. After 6 min of VF, CPR was performed for 2 min epochs as follows: Standard (S)-CPR supine (SUP), Active compression decompression (ACD) CPR+impedance threshold device (ITD-16) CPR SUP, then ACD+ITD HUP CPR. The same sequence was performed in PC 3 h later. In 9 HC, similar vascular and intracranial access were obtained and CPR performed for 1 min epochs using the same sequence as above.

Results: The mean cerebral perfusion pressure (CerPP, mmHg) was 14.5 ± 6 for ACD+ITD SUP and 28.7 ± 10 for ACD+ITD HUP (p=.007) in VF, −3.6 ± 5 for ACD+ITD

SUP and 7.8 ± 9 for ACD+ITD HUP (p=.007) in PC, and 1.3 ± 4 for ACD+ITD SUP and 11.3 ± 5 for ACD+ITD HUP (p=.007) in HC. Mean systolic and diastolic intracranial pressures (ICP) (mmHg) were significantly lower in the ACD+ITD HUP group versus the ACD+ITD SUP group in all three CPR models.

Conclusion: HUP CPR decreased ICP while increasing CerPP in pigs in VF as well as in PC and HC CPR models. This first-time demonstration of HUP CPR physiology in humans provides important implications for future resuscitation research and treatment.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Impedance threshold, device, Active compression decompression CPR, Cerebral perfusion, Swine, Human cadaver, Head up CPR

22. Putzer G, Braun P, Martini J, et al. **Effects of head-up vs. supine CPR on cerebral oxygenation and cerebral metabolism – a prospective, randomized porcine study.** *Resuscitation*. 2018; 128:51-55. DOI: https://doi.org/10.1016/j.resuscitation.2018.04.038

Abstract:
Background: Recent studies have shown that during cardiopulmonary resuscitation (CPR) head-up position (HUP) as compared to standard supine position (SUP) decreases intracranial pressure (ICP) and increases cerebral perfusion pressure (CPP). The impact of this manoeuvre on brain oxygenation and metabolism is not clear. We therefore investigated HUP as compared to SUP during basic life support (BLS) CPR for their effect on brain oxygenation and metabolism.

Methods: Twenty pigs were anaesthetized and instrumented. After 8 min of cardiac arrest (CA) pigs were randomized to either HUP or SUP and resuscitated mechanically for 20 min. Mean arterial pressure (MAP), ICP, CPP, cerebral regional oxygen saturation (rSO2) and brain tissue oxygen tension (PbtO2) were measured at baseline, after CA and every 5 min during CPR. Cerebral venous oxygen saturation (ScvO2) was measured at baseline, after CA and after 20 min of CPR. Cerebral microdialysis parameters, e.g. lactate/pyruvate ratio (L/P ratio) were taken at baseline and the end of the experiment.

Results: ICP was significantly lower in HUP compared to SUP animals after 5 min (18.0 ±4.5 vs. 24.1 ±5.2 mmHg; p=0.033) and 20 min (12.0 ±3.4 vs. 17.8 ±4.3 mmHg; p=0.023) of CPR. Accordingly, CPP was significantly higher in the HUP group after 5 min (11.2 ±9.5 vs. 1.0 ±9.2 mmHg; p=0.045) and 20 min (3.4 ±6.4 vs.−3.8 ±2.8 mmHg; p=0.023) of CPR. However, no difference was found in rSO2, PbtO2, ScvO2 and L/P ratio between groups after 20 min of CPR.

Conclusion: In this animal model of BLS CPR, HUP as compared to SUP did not improve cerebral oxygenation or metabolism.

Keywords: Animals, Blood pressure, Cardiac arrest, Cardiopulmonary resuscitation, Cerebral cortex/metabolism, Heart arrest/therapy, Microdialysis/methods, Near infrared spectroscopy, oxygen/blood oxygen/metabolism, Pigs

23. Moore J, Segal N, Lick M, et al. **Head and thorax elevation during active compression decompression cardiopulmonary resuscitation with an impedance threshold device improves cerebral perfusion in a swine model of prolonged cardiac arrest.** *Resuscitation*. 2017; 121:195-200. DOI: http://dx.doi.org/10.1016/j.resuscitation.2017.07.033

Abstract:
Aim of the study: As most cardiopulmonary resuscitation (CPR) efforts last longer than 15 min, the aim of this study was to compare brain blood flow between the Head Up (HUP) and supine (SUP) body positions during a prolonged CPR effort of 15 min, using active compression-decompression (ACD) CPR and impedance threshold device (ITD) in a swine model of cardiac arrest.

Methods: Ventricular fibrillation (VF) was induced in anesthetized pigs. After 8 min of untreated VF followed by 2 min of ACD-CPR + ITD in the SUP position, pigs were randomized to 18 min of continuous ACD-CPR + ITD in either a 30° HUP or SUP position. Microspheres were injected before VF and then 5 and 15 min after start of CPR.

Results: The mean blood flow (ml/min/g, mean ± SD) to the brain after 15 min of CPR was 0.42 ± 0.05 in the HUP group (n = 8) and 0.21 ± 0.04 SUP (n = 10), respectively, (p < 0.01). The HUP group also had statistically significantly lower intracranial pressures and higher calculated cerebral perfusion pressures after 5, 15, 19 (before adrenaline) and 20 (after adrenaline) minutes of HUT versus SUP CPR.

Conclusions: After prolonged ACD-CPR + ITD in the HUP position, brain blood flow was 2-fold higher versus the SUP position. These positive findings provide strong *pre-clinical support to proceed with a clinical evaluation of elevation of the head and thorax during ACD-CPR + ITD in humans in cardiac arrest.*

Keywords: Active compression decompression CPR, Cardiac arrest, Cardiopulmonary resuscitation, Cerebral perfusion, Impedance threshold device, Head and thorax elevation, Head up CPR, Mechanical CPR, Resuscitation

24. Kim T, Shin SD, Song KJ, et al. **The effect of resuscitation position on cerebral and coronary perfusion pressure during mechanical cardiopulmonary resuscitation in porcine cardiac arrest model.** *Resuscitation*. 2017; 113:101-107. DOI: https://doi.org/10.1016/j.resuscitation.2017.02.008

Abstract:
Objective: Automated cardiopulmonary resuscitation (CPR) devices can be used during transport in a smallQ7spaces (e.g. an elevator) to reduce the length of stretcher and via body position change. It is unknown whether patient position is associated with the optimal cerebral (CePP) and coronary (CoPP) perfusion pressure.

Methods: This study utilized a randomized experimental design and anesthetized, intubated and paralyzed female pigs (n = 12) (mean 42, SD 3 kg) on a customized tilt table. After 6 min of untreated ventricular fibrillation, mechanical CPR with Lucas-2 (L-CPR) and an impedance threshold device (ITD) was performed for 3 min in 0° supine position. L-CPR + ITD was then performed for 5 min in a position randomly assigned to either (1) head-up tilt (HUT) at one of three angles (30°, 45°, or 60°) or (2) head-down tilt (HDT) at one of three angles (30°, 45°, or 60°) and at (3) supine position between HUT and HDT positions. 4 Pigs we reassigned to each angle of HUT or HDT position and 12 pigs were assigned to supine position. CePPs and CoPPs were measured and compared using MIXED procedure with pig as a random effect among angles and compared between angles with Tukey post-hoc analysis.

Results: Baseline hemodynamic parameters were similar among pigs. From HDT to HUT by angle of elevation, mean aortic pressures and intracranial pressures significantly decreased. With 60°, 45°, 30° head-down, 0° (supine), and 30°, 45°, 60° head-up positioning, mean (SD) CePPs increased consistently as follows: 2.4(0.4), 9.3(1.6), 16.5(1.6), 27.0(1.5), 35.1(0.4), 39.4(0.6), and 39.9(0.3) mmHg, respectively. CoPPs were followings according to same angle: 12.9(2.5), 13.3(2.5), 12.8(0.4), 18.1(0.7), 30.3(0.4), 24.1(0.6), and 26.5(0.9) mmHg, respectively. The CePPs were peak at HUT(45°) and HUT(60°), but CoPP was peak in HUT(30°) and higher than HUT(45°) and HUT(60°).

Conclusions: Cerebral perfusion pressure during L-CPR + ITD were similar and highest in the HUT(45° and 60°) positions whereas the peak coronary perfusion pressure was observed with HUT(30°).

Keywords: *Cardiopulmonary resuscitation, Cerebral perfusion pressure, Position, Swine*

25. Ryu H, Moore J, Yannopoulos D, et al. **The effect of head up cardiopulmonary resuscitation on cerebral and systemic hemodynamics. *Resuscitation.*** 2016; 102:29-34. DOI: http://dx.doi.org/10.1016/j.resuscitation.2016.01.033

Abstract:
Aim: Chest compressions during cardiopulmonary resuscitation (CPR) increase arterial and venous pressures, delivering simultaneous bidirectional high-pressure compression waves to the brain. We hypothesized that this may be detrimental and could be partially overcome by elevation of the head during CPR.

Measurements: Female Yorkshire farm pigs (n = 30) were sedated, intubated, anesthetized, and placed on a table able to elevate the head 30° (15 cm) (HUP) and the heart 10° (4 cm) or remain in the supine (SUP) flat position during CPR. After 8 minutes of untreated ventricular fibrillation and 2 minutes of SUP CPR, pigs were randomized to HUP or SUP CPR for 20 more minutes. In Group A, pigs were randomized after 2 minutes of flat automated conventional (C) CPR to HUP (n = 7) or SUP (n = 7) C-CPR. In Group B, pigs were randomized after 2 minutes of automated active compression decompression (ACD) CPR plus an impedance threshold device (ITD) SUP CPR to either HUP (n = 8) or SUP (n = 8).

Results: The primary outcome of the study was difference in CerPP (mmHg) between the HUP and SUP positions within groups. After 22 minutes of CPR, CerPP was 6 ± 3 mmHg in the HUP versus -5 ± 3 in the SUP (p = 0.016) in Group A, and 51 ± 8 versus 20 ± 5 (p = 0.006) in Group B. Coronary perfusion pressures after 22 minutes were HUP 6 ± 2 vs SUP 3 ± 2 (p = 0.283) in Group A and HUP 32 ± 5 vs SUP 19 ± 5, (p = 0.074) in Group B. In Group B, 6/8 pigs were resuscitated in both positions. No pigs were resuscitated in Group A.

Conclusions: The HUP position in both C-CPR and ACD + ITD CPR significantly improved CerPP. This simple maneuver has the potential to improve neurological outcomes after cardiac arrest.

Keywords: Cardiac Arrest, Cardiopulmonary resuscitation, Mechanical CPR, Impedance threshold device, Active compression decompression CPR, Cerebral perfusion

26. Lurie K, Nemergut E, Yannopoulos D, Sweeney M. The Physiology of Cardiopulmonary Resuscitation. *Anesthesia & Analgesia*. 2016; 122(3):767-783. DOI: http://doi.org/10.1213/ane.0000000000000926

Outcomes after cardiac arrest remain poor more than a half a century after closed chest cardiopulmonary resuscitation (CPR) was first described. This review article is focused on recent insights into the physiology of blood flow to the heart and brain during CPR. Over the past 20 years, a greater understanding of heart–brain–lung interactions has resulted in novel resuscitation methods and technologies that significantly improve outcomes from cardiac arrest. This article highlights the importance of attention to CPR quality, recent approaches to regulate intrathoracic pressure to improve cerebral and systemic perfusion, and ongoing research related to the ways to mitigate reperfusion injury during CPR. Taken together, these new approaches in adult and pediatric patients provide an innovative, physiologically based road map to increase survival and quality of life after cardiac arrest.

27. Debaty G, Shin S, Metzger A, et al. **Tilting for perfusion: head-up position during cardiopulmonary resuscitation improves brain flow in a porcine model of cardiac arrest.** *Resuscitation*. 2015; 87:38-43. DOI: http://dx.doi.org/10.1016/j.resuscitation.2014.11.019

Abstract:
Introduction: Cerebral perfusion is compromised during cardiopulmonary resuscitation (CPR). We hypothesized that beneficial effects of gravity on the venous circulation during CPR performed in the head-up tilt (HUT) position would improve cerebral perfusion compared with supine or head-down tilt (HDT).

Methods: Twenty-two pigs were sedated, intubated, anesthetized, paralyzed and placed on a tilt table. After 6 min of untreated ventricular fibrillation (VF) CPR was performed on 14 pigs for 3 min with an automated CPR device called LUCAS (L) plus an impedance threshold device (ITD), followed by 5 min of L-CPR + ITD at 0◦ _supine, 5 min at 30◦ _HUT, and then 5 min at 30◦ _HDT. Microspheres were used to measure organ blood flow in 8 pigs. L-CPR + ITD was performed on 8 additional pigs at 0◦, 20◦, 30◦, 40◦, and 50◦ _HUT.

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Results: Coronary perfusion pressure was 19 ±2 mmHg at 0◦ vs. 30 ±3 at 30◦ HUT (p < 0.001) and 10 ±3 at 30◦ HDT (p < 0.001). Cerebral perfusion pressure was 19 ±3 at 0◦ vs. 35 ±3 at 30◦ HUT (p < 0.001) and 4 ±4 at 30◦ HDT (p < 0.001). Brain–blood flow was 0.19 ±0.04 ml min−1 g−1 at 0◦ vs. 0.27 ±0.04 at 30◦ HUT (p = 0.01) and 0.14 ±0.06 at 30◦ HDT (p = 0.16). Heart blood flow was not significantly different between interventions. With 0, 10, 20, 30, 40 and 50◦ HUT, ICP values were 21 ±2, 16±2, 10 ±2, 5 ±2, 0 ±2, −5 ±2 respectively, (p < 0.001), CerPP increased linearly (p = 0.001), and CPP remained constant.

Conclusion: During CPR, HDT decreased brain flow whereas HUT significantly lowered ICP and improved cerebral perfusion. Further studies are warranted to explore this new resuscitation concept.

Keywords: Cardiac arrest, Cardiopulmonary resuscitation, Mechanical CPR, Impedance threshold device, Cerebral perfusion