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ANNOTATED BIBLIOGRAPHY

This annotated bibliography provides an overview of current publications related to the ElevatedCPR™ Method, often reported in the literature as 'Elevated CPR,' 'Head Up CPR' or 'gravity assisted CPR.' It includes current research, commentary, and publications important to understanding the potential benefit and physiology of the ElevatedCPR Method, other key topics surrounding the ElevatedCPR Method, as well as publications reporting no potential benefit from Head Up Position CPR.

The following abbreviations are used throughout this document:
HUP: Head Up Position, **SUP**: Supine Position, **CPR**: Cardiopulmonary Resuscitation, **VF**: Ventricular Fibrillation, **S-CPR**: Standard CPR, **ACD**: Active Compression Decompression, **ITD**: Impedance Threshold Device, **CerPP**: Cerebral Perfusion Pressure, **CorPP**: Coronary Perfusion Pressure, **ICP**: Intracranial Pressure, **BLS**: Basic Life Support, **DACSE**: Device Assisted Controlled Sequential Elevation

I. **Physiology and Potential Benefits**

1. Debaty G, Shin S, Metzger A, Kim T, Ryu HH, Rees J, et al. Tilting for perfusion: head-up position during cardiopulmonary resuscitation improves brain flow in a porcine model of cardiac arrest. *Resuscitation*. 2015;87(2015):38-43.

   First research article (published online in 2014) comparing results of supine, whole body 30° head down or whole body 30° HUP CPR. Found that CPR performed with the LUCAS device, ITD, and HUP provides better CerPP, oxygenation, and cerebral blood flow compared to supine or whole body 30° head down.

2. Erich J. Heads-Up CPR: Can Elevating the Patient's Head Improve Outcomes? *EMSWorld*. 2015 (August):22-28.

   EMS article introducing concept of HUP-CPR to prehospital providers including highlighting early success of Palm Beach County with bundled care of HUP, ITD, ACD-CPR. PBC used a Pelican case to create a whole-body tilt. Authors and researchers caution against this full body tilt method because of possible dependent pooling in the lower extremities with prolonged resuscitation.

3. Ryu H, Moore J, Yannopoulos D, Lick M, McKnite S, Shin SD, et al. The Effect of Head Up Cardiopulmonary Resuscitation on Cerebral and Systemic Hemodynamics. *Resuscitation*. 2016;102:29-34.

Research showed that elevating head and shoulders during prolonged HUP ACD+ITD CPR but not during prolonged conventional standard CPR improves cerebral and coronary perfusion.

4. Kim T, Shin SD, Song KJ, Park YJ, Ryu HH, Debaty G, 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.

Examines both cerebral and coronary blood flow for supine, head up, and head down positions at various angles initially to optimize resuscitation. Found that HUP 30 degrees optimizes cerebral and coronary perfusion in this porcine model using LUCAS 2 and ITD.

5. Moore J, Segal N, Lick M, Dodd K, 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;2017(121):195-200. doi: http://dx.doi.org/10.1016/j.resuscitation.2017.07.033.

Research uses microspheres to measure blood flow to brain and other organs during prolonged (greater than 15 minutes) SUP and HUP ACD+ITD CPR. Showed doubling of blood flow to brain with HUP ACD+ITD CPR (head and shoulders raised) versus SUP CPR. Time to first gasp was also found to be shorter in the HUP ACD+ITD group. Gasping may be used as a clinical indicator of improved blood flow to the brain.

6. Powell J, Dearden, K, Grayson, S. Rialto's Resuscitation Toolkit. *Journal of Emergency Medical Services*. 2017 (December):28-34.

Prehospital journal article highlighting the bundle of care including HUP CPR and ITD used by Rialto California EMS to double survival rates in their community. To date, this data has not been presented in a peer-reviewed journal.

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

This research developed and validated a human cadaver model to assess the physiology of HUP CPR. It shows consistent, reproducible and significant decreases in ICP and rise in CerPP with HUP CPR across the VF porcine model, cadaveric porcine model and human cadaveric model. Standard and ACD CPR plus an ITD were studied in all three models.

8. Pepe P, Scheppke K, Antevy P, Crowe R, Millstone D, Coyle C, et al. (2019). 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, 47*(3), 449-455. doi:DOI: 10.1097/CCM.0000000000003608

Research examining human related factors of implementing a head/torso elevation for high quality CPR. The body was on a stretcher that was tilted upwards about 20 degrees. Study examined >2000 out of hospital cardiac arrest cases over three and half years for the safety and practical application of elevating the head and torso. They found a bundled care approach that included high quality manual CPR followed by CPR with the LUCAS 2.0, use of ITD, along with head and torso elevation to around 20° using a whole body head up tilt on a stretcher, had a synergistic effect. Survival to hospital alive rates nearly doubled from 18% to 34% for all patients. These results were maintained well beyond initial study effect period. Impact on survival to hospital discharge was not reported.

9. Lurie K, Lick C, Pepe P, Lamhaut L., Levy M, Price R, et al. (2019). State of the Future of the Science of Resuscitation. *Journal of Emergency Medical Services, March*(Supplement).

Supplement to JEMS recapping the Take Heart America Conference in Oakland, California in September 2018. Focused on current, cutting-edge science and implementation of such including HUP for CPR, supraglottic airways for resuscitation, ECMO, and high-performing Systems of Care.

10. Moore J Salverda B, Lick M, Rojas-Salvador C, Debaty 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 swine model of cardiac arrest. Presented at: American Heart Association Resuscitation Science Symposium; Nov 11, 2019; Philidelphia, PA. Circulation: American Heart Association; 2019.

Abstract/Poster presented at 2019 American Heart Association Resuscitation Science Symposium. Bundled resuscitation using ACD+ITD CPR with a controlled sequence increased neurologically-intact survival 6-fold versus standard CPR in a swine model of cardiac arrest. In addition, CerPP, CorPP, ETCO2, and cerebral oximetry were all significantly higher throughout the 19 minutes of CPR with device-assisted controlled sequential elevation of the head and thorax versus conventional standard CPR.

11. Rojas-Salvador N, Salverda. B, Moore J, Lick M, Debaty G, Lurie K. (2020). Regional cerebral tissue oxygenation correlates with aortic pressure, end tidal CO2, coronary perfusion pressure and neurological outcome in a swine model of cardiac arrest [Research Poster Presentation]. National Association of EMS Physicians Annual Conference, San Diego, CA.

Poster presented at NAEMSP 2020. This research examined correlation between non-invasive regional cerebral tissue oxygenation (rSO2) and intact neurologically intact survival from sudden cardiac arrest. Swine were treated with conventional CPR in the flat position versus device assisted controlled sequential elevation (DACSE) with an ITD-16 and automated ACD at 100 compression/decompressions per minute. rSO2, along with traditional monitoring parameters were monitored in both groups. Swine with higher rSO2 were found to be more likely to survive neurologically intact in both the conventional CPR group and the DACSE ACD ITD group. rSO2 values correlated highly with ETCO2, which was also predictive of a positive outcome. In addition, the group treated with DACSE ACD ITD had more favorable neurological outcomes with 6/7 neurologically intact at 24 hours and just 1/7 in the conventional group survived neurologically intact.

12. Scheppke K, Pepe P, Antevy P, Lick C, Coyle C, Garay S, et al. (2020). Safety and feasibility of an automated patient positioning system for controlled sequential elevation of the head and thorax during cardiopulmonary resuscitation [Research Poster Presentation]. National Association of EMS Physicians Annual Conference, San Diego, CA.

Poster presented at NAEMSP 2020. This quality improvement project reviewed historical and post intervention data in Palm Beach County Florida where the intervention was a patient positioning device (EleGARD). The vast majority of patients presented with asystole or PEA. The new device was used to provide device-assisted controlled sequential elevation of the head and thorax (DACSE) during ACD CPR with an ITD-16, as part of an expanded cardiac arrest bundle of care. The authors report that use of DACSE was safe and not difficult to use. ETCO2 levels increased post DACSE intervention to normal values in >70% of patients and the ROSC rates in patients presenting with asystole or PEA were 44%.

13. Rojas-Salvador C, Moore J, Salverda B, Lick M, Debaty G, Lurie K. (2020). 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*, EPub ahead of print. doi:10.1016/j.resuscitation.2019.12.011

This porcine study sought to verify the optimal sequence, speed and final height for head and thorax elevation during CPR using a comprehensive bundle of care that includes continuous CPR with ACD+ITD-16.

They assessed an immediate rise (24 seconds) without 'priming' the cardio-cerebral circuit and 2, 4, and 10-minute elevations with a period of priming in the down position. The immediate rise protocol simulates using a transport stretcher to raise the upper body at the waist and the controlled protocols simulate the use of a device for controlled sequential elevation. The primary endpoint was CerPP after 7 minutes of CPR.

The 2-minute rise to a head height of 22cm and heart height of 10 cm after a 2-minute period of priming was found to be the optimal rise time and height. A 2-minute rise time reduces the potential harm of raising the head too quickly, as the arterial pressure can fall, while reaching CerPP that was 50% baseline by 2.5 minutes and 80% by 7 minutes. CorPP was also found to increase over time in the two-minute rise group versus the immediate rise group.

An additional finding of this study was that placement on the automated head and thorax elevation device, which raises the head to 10cm and thorax to 7 cm in the lowest position, immediately reduced ICP by decreasing venous congestion of the brain after receiving CPR in the supine position. The study also documented time to first gasp, a strongly positive neuroprognosticator, occurred 1-2 minutes sooner in the slow rise group versus the quick rise group.

These findings support the immediate placement of an elevation device under a patient receiving CPR, a period of priming the cardio-cerebral circuit with the use of ITD, then a slow progressive 2 min rise to optimize CerPP, CorPP and create an environment that markedly improves survival with good brain function in pigs and could lead to improved neurological outcomes.

II. **Key Topics Related to CPR Advances**

1. Lurie K, Nemergut E, Yannopoulos D, Sweeney M. The Physiology of Cardiopulmonary Resuscitation [Review Article]. *Anesthesia & Analgesia*. 2016;122(3):767-783.

   Comprehensive review of the physiology of resuscitation. Discussed components of S-CPR, identifying common errors and limitations. Introduced improvements to S-CPR with good technique and technology including use of the ITD, ACD, and HUP.

2. Debaty G, Labarere J, Frascone RJ, Wayne M, et al. Long-Term Prognostic Value of Gasping During Out-of-Hospital Cardiac Arrest. *Journal of the American College of Cardiology*, Sep2017. 2017:2017. doi: http://dx.doi.org/10.1016/j.jacc.2017.07.782

   Multicenter, randomized, controlled study. Examined prognostic value of gasping during cardiac arrest. Found that gasping during cardiac arrest, regardless of presenting rhythm, was associated with positive 1-year survival with good neurological outcome.

3. Lurie K, Levy M, Swor R, Moore J. The economic impact of out-of-hospital cardiac arrest. *Journal of Emergency Medical Services*. 2017 (December):10-16.

   Using a formula similar to that for the economic burden of motor vehicle deaths, the cost of OHCA was assessed. Examining both direct and indirect cost to society they show the cost benefit of improving OHCA care.

4. Segal N, Youngquist S, Lurie K. Ideal (i)CPR: Looking beyond the shadows in the cave. *Resuscitation*. 2017;121:81-82. doi: https://doi.org/10.1016/j.resuscitation.2017.10.009.

Commentary emphasizing need for bundled care approach to a multimodal problem. Likens cardiac arrest care to care of any other complex disease. Both require new approaches, advanced technology and pharmocology that individually offer limited gains, but together have an expontential effect on outcomes.

5. Holley J, Moore J, Jacobs M, Rojas-Salvador C, Lick C, Slaverda B, Lick M, Frascone RJ, Youngquist S, Lurie K. (2020). Supraglottic airway devices variably develop negative intrathoracic pressures: A prospective cross-over study of cardiopulmonary resuscitation in human cadavers. *Resuscitation*(2020), 32-38. https://doi.org/https://doi.org/10.1016/j.resuscitation.2019.12.022

This was a human cadaveric study assessing supraglottic airways (SGA) with different CPR methodologies and in different body positions, including flat and HUP. The ability to generate negative intrathoracic pressure was the primary study endpoint. Different SGAs were compared while CPR was performed using conventional/manual, conventional/mechanical (LUCAS 2.0), ACD and HUP ACD with and without ITD-16. The better the airway was sealed during the decompression phase of CPR, the lower the intrathoracic pressure. Multiple prior studies in animals and humans have demonstrated that increased *negative* intrathoracic pressure during the decompression phase of CPR improves blood flow to the heart and brain. In the current study human cadavers received CPR with and without an ITD-16. The study found that when an ITD-16 was used, negative intrathoracic pressures were significantly lower during the decompression phase of CPR, regardless of the method of CPR or the airway adjunct. Using an endotracheal tube as the gold standard, the study found that best airway seal was obtained by iGel, air-Q®sp, and LMA-S. These findings were similar if the body was flat or HUP, confirming it is possible to use a variety of airway adjuncts during both flat and HUP CPR and still maintain an airway seal during CPR.

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III. **Editorials, Commentaries and Special Reports, Including Those Showing No Potential Benefit of Head Up Position CPR**

1. Wesley K, Wesley K. Tilt Angle Significantly Affects CPR [Editorial]. *Journal of Emergency Medical Services*. 2015;40(3).

   EMS commentary on Debaty (2015) research as it applies to EMS. Presents HUP CPR as a simple, novel approach that should be considered for incorporation into EMS protocols.

2. Putzer G, Braun P, Martini J, Niederstatter I. et al. Effects of head-up vs. supine CPR on cerebral oxygenation and cerebral metabolism – a prospective, randomized porcine study. *Resuscitation*. 2018;2018(128):51-55.

   Researchers aimed to study the effect of head elevation in BLS CPR. The study definition of BLS does NOT include the use of an ITD for circulatory support. Study concluded that although HUP CPR decreased ICP and improved CerPP, it did not improve cerebral oxygenation. These findings are similar to work of Ryu et al. (referenced above) showing that HUP CPR is *not* effective unless circulatory enhancers such as the ITD and/or ACD CPR are used currently. Commentaries to this article are listed below.

3. 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; 2018(129):e6-e7. doi.org/10.1016/j.resuscitation.2018.05.023

   Putzer G, Martini J, 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; 2018(129):e8. doi:10.1016/j.resuscitation.2018.06.006.

   Commentaries on 2018 Putzer et al. article in *Resuscitation*. Moore describes what is required for successful HUP CPR and what should and should not be done to get the benefit from this new approach. Moore suggests that lack of ITD therapy in the Putzer study could be a critical compounding factor for the neutral finding of improved CerPP without improved cerebral oxygenation. Putzer rebuts that CerPP should not be the only measure and does concede that a bundled care approach to cardiac arrest is necessary especially in light of emerging technologies.

4. Strobos, NC. Debunking another CPR myth: Lay the patient flat, or head up CPR? [Editorial]. *Resuscitation*. 2018;132:A1-A2. https://doi.org/10.1016/j.resuscitation.2018.07.010

   Editorial addressing study by Moore, et al. in the same issue of *Resuscitation*. Strobos recognized that the traditional approach of "lay the patient flat" may be wrong and credits Moore et al. for "Debunking another CPR myth." She discusses the challenges of translating CPR research to cadavers. Strobos further recognizes that HUP CPR is more than just raising the head during resuscitation. She notes this should not be done cavalierly. It is only beneficial when combined with ACD CPR and ITD in a complete device-assisted head up CPR manner.

5. Shaw G. Is a 'Golden Age' of resuscitation on the horizon [Special Report]. *Emergency Medicine News*. 2018; November:18-19.

   Discusses recent advances that point toward the changing horizon of resuscitation including prognostic indicators, CPR training and techniques such as extracorporeal membrane oxygenation and head up positioning and resuscitation end-point decision making.

6. Park Y, Hong K, Shin S, Kim T, Ro Y, Song K, Ryu H. (2019). Worsened survival in the head-up tilt position cardiopulmonary resuscitation in a porcine cardiac arrest model. *Clnical and Experimental Emergency Medicine, 6*(3), 250-256. https://doi.org/https://doi.org/10.15441/ceem.18.060

   The study examined whether placement of pigs in cardiac arrest in a whole body head up tilt at 30° angle would improve neurologically intact survival rates compared with CPR in the flat position. Both groups were treated with a LUCAS 2.0 device and an impedance threshold device (ITD-10) after 15 minutes of untreated VF. In the whole body head up tilt group, the body was tilted upward rapidly after 15 minutes of VF and then CPR was initiated. None of the head up pigs survived whereas 6/8 in the flat group survived.

   This study, after it was published in abstract form, resulted in Dr. Moore et al. writing a letter to *Resuscitation* entitled "Do's and Don'ts of Head Up CPR" which is previously noted in this bibliography. With the current understanding of the physiology of head up CPR, the findings by Park et al. are predictable and not surprising.

There are several important reasons for their negative study results which should be understood before a head up CPR protocol is considered and implemented.

First, rapid elevation of the head and thorax *without first starting CPR* in the flat position to 'prime the system' and start circulation will lower the arterial pressure and reduce blood flow to the brain immediately. This is why the arterial pressure values reported Park et al. in their report were so low in the whole-body head up tilt group, just 20% of those in the flat position. Rapid elevation of the head and thorax even with CPR ongoing, has been shown to result in poorer outcomes, as was recently reported by Rojas et al. in *Resuscitation*, 2020, also described in this bibliography. A slow controlled elevation timing sequence after 'priming the system' with LUCAS CPR and the ITD-16 optimizes brain blood flow and survival.

Second, prolonged elevation of the head and thorax with a whole body tilt will result in blood pooling in the abdomen and lower extremities over time. This physiology is similar to what happens to alive patients with a whole-body tilt who are prone to syncope: the blood pressure falls as blood pools in the lower extremities.

Third, an ITD-10 was used instead of an ITD-16 by Park et al. The ITD with a 16 cm of H2O resistance prior to opening helps generate greater negative intrathoracic pressures (to -16 cm of H2O versus -10 cm H2O) during the decompression phase of CPR, thereby ultimately providing more blood flow to the brain. This is why the ITD-16 is used in the studies by Moore et al. and Rojas et al.

The 100% mortality after 24-hours with the Park et al. experimental model confirms the necessity to 'prime the pump', elevate the head and thorax slowly, and refrain from the whole body head up tilt position. As such, the findings by Park et al. are completely consistent with the other studies on head up CPR, especially those by Dr. Moore et al. described herein.

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IV. Video Resources/Lectures Related to Progressive Resuscitation Technology

1. AMC Amsterdam Department of Anesthesiology. Innovations in CPR [Vimeo]. Academic Medical Center (AMC) Amsterdam; 2018 [cited 2019 Dec 19]; Dr. Keith Lurie gives a lecture on innovation in CPR. Available from: https://vimeo.com/266253707

   Dr. Keith Lurie presents grand rounds to anesthesia fellows in the Netherlands on the physiology of standard CPR. He discusses innovations, including elevating the head, that, when bundled together with ACD+ITD, have the potential to improve the physiological environment for the resuscitation patient.

2. Society of Critical Care Medicine. A 2020 Vision of CPR: Evolution, Revolution, and Novel Solution 2019 [cited 2019 Dec 19]; Dr. Paul Pepe, plenary speaker, gives a talk at the 48th Critical Care Congress]. Available from: https://www.youtube.com/watch?v=mgixu2iMckM&list=PLsb8sp1zaJWoZAWHK0FIAUPkFE6STk7wx&index=10&t=0s&fbclid=IwAR218HSAnKGrFF6pVCiFi4KWOzRw2tPzxUZn1XEMfVA9tCRpmicUqEzkcrc

   Plenary presentation at Society of Critical Care Medicine 2019 annual conference discusses where CPR has come from, innovations, and new direction for resuscitation. At minute 34:17, there is a discussion of gravity-assisted CPR and the bundle of care needed to deploy this CPR effectively.

3. EMedHome.com. EMedHome's Video with Johanna Moore, MD: Cutting-edge resuscitation: Head-up CPR, eCPR, and more: Emergency Medicine News; [cited 2019 Dec 19]; Dr. Moore explores cutting-edge resuscitation, including head-up CPR, eCPR, and more]. Available from: https://journals.lww.com/em-news/pages/videogallery.aspx?videoId=374&autoPlay=true

   Dr. Johanna Moore presents innovations that are currently in use at Hennepin County Medical Center and the greater Minneapolis area. At minute 5:05, she discusses the findings from her NIH-funded studies for head-up position CPR, where near-normal CerPP was achieved with a bundle of care including use of ACD+ITD+HUP.