## BIBLIOGRAFIA RECOMANADA PEL CCR. SETMANA 1/7/2020

### RCP I COVID-19

1. Eur Heart J. 2020 Jun 20. pii: ehaa508. doi: 10.1093/eurheartj/ehaa508. [Epub ahead of print]

COVID-19 kills at home: the close relationship between the epidemic and the increase of outof-hospital cardiac arrests.

Baldi E(1)(2), Sechi GM(3), Mare C(3), Canevari F(4), Brancaglione A(4), Primi R(5), Klersy C(6), Palo A(7), Contri E(7), Ronchi V(7)(8), Beretta G(9), Reali F(9), Parogni P(10), Facchin F(1), Rizzi U(11), Bussi D(11), Ruggeri S(10), Oltrona Visconti L(5), Savastano S(5); Lombardia CARe researchers.

#### Abstract

AIMS: An increase in out-of-hospital cardiac arrest (OHCA) incidence has been reported in the very early phase of the COVID-19 epidemic, but a clear demonstration of a correlation between the increased incidence of OHCA and COVID-19 is missing so far. We aimed to verify whether there is an association between the OHCA difference compared with 2019 and the COVID-19 epidemic curve. METHODS AND RESULTS: We included all the consecutive OHCAs which occurred in the Provinces of Lodi, Cremona, Pavia, and Mantova in the 2 months following the first documented case of COVID-19 in the Lombardia Region and compared them with those which occurred in the same time frame in 2019. The cumulative incidence of COVID-19 from 21 February to 20 April 2020 in the study territory was 956 COVID-19/100 000 inhabitants and the cumulative incidence of OHCA was 21 cases/100 000 inhabitants, with a 52% increase as compared with 2019 (490 OHCAs in 2020 vs. 321 in 2019). A strong and statistically significant correlation was found between the difference in cumulative incidence of OHCA between 2020 and 2019 per 100 000 inhabitants and the COVID-19 cumulative incidence per 100 000 inhabitants both for the overall territory (p 0.87, P < 0.001) and for each province separately (Lodi: ρ 0.98, P < 0.001; Cremona: ρ 0.98, P < 0.001; Pavia: ρ 0.87, P < 0.001; Mantova: ρ 0.81, P < 0.001). CONCLUSION: The increase in OHCAs in 2020 is significantly correlated to the COVID-19 pandemic and is coupled with a reduction in short-term outcome. Government and local health authorities should seriously consider our results when planning healthcare strategies to face the epidemic, especially considering the expected recurrent outbreaks.

## RCP/COMPRESSIONS TORÀCIQUES MECÀNIQUES

**1.** Resuscitation. 2020 Jun 23;153:111-118. doi: 10.1016/j.resuscitation.2020.05.049. [Epub ahead of print]

Duration and clinical features of cardiac arrest predict early severe cerebral edema. Esdaille CJ(1), Coppler PJ(2), Faro JW(3), Weisner ZM(4), Condle JP(2), Elmer J(2), Callaway CW(5); Pittsburgh Post Cardiac Arrest Service. BACKGROUND: Severe brain edema appears early after cardiopulmonary resuscitation (CPR) in a subset of patients and portends a poor prognosis. We tested whether clinical features of patients or resuscitation during out-of-hospital cardiac arrest (OHCA) are associated with early, severe cerebral edema. METHOD/RESEARCH DESIGN: We reviewed pre-hospital and hospital records for comatose patients surviving to hospital admission after OHCA who had computed tomography (CT) of brain at the time of hospital admission available for inspection. We measured the gray-white ratio (GWR) of X-ray attenuation between the caudate nucleus and posterior limb of the internal capsule, defining severe cerebral edema as GWR < 1.20. We calculated associations between severe cerebral edema and patient or resuscitation variables. RESULTS: Between

2010 and 2019, 1340 subjects were admitted of whom 296 (22%) showed severe cerebral edema on initial CT. Subjects with severe edema had lower survival (5/296, 2% vs. 377/1044, 36%). Severe edema was independently associated with total CPR duration, total dose of epinephrine, younger age, non-shockable arrest rhythms, fewer total number of rescue shocks, rearrest after initial return of pulses, and non-cardiac arrest etiology. Prevalence of severe cerebral edema increased from 2% among subjects with 0-10 min of CPR to 31% among subjects with >40 min of CPR. CONCLUSION: CPR duration along with easily measurable clinical and resuscitation characteristics predict early severe cerebral edema after OHCA. Future interventional trials should consider targeting or preventing cerebral edema after prolonged hypoxic-ischemic brain injury especially in patients with high risk clinical features.

**2.** Resuscitation. 2020 Jun 20. pii: S0300-9572(20)30252-5. doi:10.1016/j.resuscitation.2020.06.016. [Epub ahead of print]

The Impact of Increased Chest Compression Fraction on Survival for Out-of-Hospital Cardiac Arrest Patients with a Non-Shockable Initial Rhythm.

Vaillancourt C(1), Petersen A(2), Meier EN(3), Christenson J(4), Menegazzi JJ(5), Aufderheide TP(6), Nichol G(7), Berg R(8), Callaway CW(5), Idris AH(9), Davis D(10), Fowler R(9), Egan D(11), Andrusiek D(12), Buick JE(13), Bishop TJ(14), Riccardo Colella M(15), Sahni R(16), Stiell IG(17), Cheskes S(18); Resuscitation Outcomes Consortium Investigators.

## Abstract

OBJECTIVE: We evaluated the effect of chest compression fraction (CCF) on survival to hospital discharge and return of spontaneous circulation (ROSC) in out-of-hospital cardiac arrest (OHCA) patients with non-shockable rhythms. METHODS: This is a retrospective analysis (completed in 2016) of a prospective cohort study which included OHCA patients from ten U.S. and Canadian sites (Resuscitation Outcomes Consortium Epistry and PRIMED study (2007-2011)). We included all OHCA victims of presumed cardiac aetiology, not witnessed by emergency medical services (EMS), without automated external defibrillator shock prior to EMS arrival, receiving > 1 minute of

CPR with CPR process measures available, and initial non-shockable rhythm. We measured CCF using the first 5 minutes of electronic CPR records. RESULTS: Demographics of 12,928 adult patients were: mean age 68; male 59.9%; public location 8.5%; bystander witnessed 35.2%; bystander CPR 39.3%; median interval from 911 to defibrillator turned on 10min:04 sec; initial rhythm asystole 64.8%, PEA 26.0%, other non-shockable 9.2%; compression rate 80-120/min (69.1%); median CCF 74%; ROSC 25.6%; survival to hospital discharge 2.4%. Adjusted odds ratio (OR); 95% confidence intervals (95%CI) of survival for each CCF category were: 0-40% (2.00; 1.16, 3.32); 41-60% (0.83; 0.54, 1.24); 61-80% (1.02; 0.77, 1.35); and 81-100% (reference group). Adjusted (OR; 95%CI) of ROSC for each CCF category were: 0-40% (1.02; 0.79, 1.30); 41-60% (0.83; 0.72, 0.95); 61-80% (0.85; 0.77, 0.94); and 81-100% (reference group). CONCLUSIONS: We observed an incremental benefit from higher CCF on the incidence of ROSC, but not survival, among non-shockable OHCA patients with CCF higher than 40%.

#### **REGISTRES, REVISIONS I EDITORIALS**

1. Lancet Neurol. 2020 Jul;19(7):611-622. doi: 10.1016/S1474-4422(20)30117-4. Brain injury after cardiac arrest: from prognostication of comatose patients to rehabilitation. Cronberg T(1), Greer DM(2), Lilja G(3), Moulaert V(4), Swindell P(5), Rossetti AO(6). Abstract

More patients are surviving cardiac arrest than ever before; however, the burden now lies with estimating neurological prognoses in a large number of patients who were initially comatose, in whom the ultimate outcome is unclear. Neurologists, neurointensivists, and clinical neurophysiologists must accurately balance the concern that overly conservative

prognostication could leave patients in a severely disabled state, with the possibility that inaccurately pessimistic prognostication could lead to the withdrawal of life-sustaining treatment in patients who might otherwise have a good functional outcome. Prognostic tools have improved greatly, including electrophysiological tests, neuroimaging, and chemical biomarkers. Conclusions about the prognosis should be delayed at least 72 h after arrest to allow for the clearance of sedative drugs. Cognitive impairments, emotional problems, and fatigue are common among patients who have survived cardiac arrest, and often go unrecognised despite being related to caregiver burden and a decreased participation in society. Through simple screening, these problems can be identified, and patients can be provided with adequate information and rehabilitation.

2. Neurocrit Care. 2020 Jun 22. doi: 10.1007/s12028-020-01027-w. [Epub ahead of print] **Determining Optimal Mean Arterial Pressure After Cardiac Arrest: A Systematic Review.** Rikhraj KJK(1), Wood MD(2), Hoiland RL(2)(3), Thiara S(4), Griesdale DEG(2)(4)(5), Sekhon MS(4).

### **Abstract**

The use of cerebral autoregulation monitoring to identify patient-specific optimal mean arterial pressure (MAP<sub>OPT</sub>) has emerged as a technique to augment cerebral oxygen delivery in post-cardiac arrest patients. Our systematic review aims to determine (a) the average MAP<sub>OPT</sub> in these patients, (b) the feasibility of identifying MAP<sub>OPT</sub>, (c) the brain tissue oxygenation levels when MAP is within proximity to the MAP<sub>OPT</sub> and (d) the relationship between neurological outcome and MAPOPT-targeted resuscitation strategies. We carried out this review in accordance with the PRISMA guidelines. We included all studies that used cerebral autoregulation to determine MAPOPT in adult patients (> 16 years old) who achieved return of spontaneous circulation (ROSC) following cardiac arrest. All studies had to include our primary outcome of MAPOPT. We excluded studies where the patients had any history of traumatic brain injury, ischemic stroke or intracranial hemorrhage. We identified six studies with 181 patients. There was wide variability in cerebral autoregulation monitoring methods, length of monitoring, calculation and reporting of MAPOPT. Amongst all studies, the median or mean MAPOPT was consistently above 65 mmHg (range 70-114 mmHg). Definitions of feasibility varied among studies and were difficult to summarize. Only one study noted that brain tissue oxygenation increased as patients' MAP approached MAP opt. There was no consistent association between targeting MAPOPT and improved neurological outcome. There is considerable heterogeneity in MAP<sub>OPT</sub> due to differences in monitoring methods of autoregulation. Further research is needed to assess the clinical utility of MAP<sub>OPT</sub>-guided strategies on decreasing secondary injury and improving neurological outcomes after ROSC.

## **ACR INTRAHOSPITALÀRIA**

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## **LESIONS PER RCP**

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## **CAUSA DE L'ACR**

**1.** Int J Cardiol. 2020 Jun 19. pii: S0167-5273(20)33392-1. doi:10.1016/j.ijcard.2020.06.014. [Epub ahead of print]

# Intra-day change in occurrence of out-of-hospital ventricular fibrillation in Japan: The JCS-ReSS study.

Otsuki S(1), Aiba T(2), Tahara Y(3), Nakajima K(3), Kataoka N(3), Kamakura T(3), Wada M(3), Ishibashi K(3), Yamagata K(3), Inoue Y(3), Miyamoto K(3), Nagase S(3), Noda T(3), Izumi C(3), Noguchi T(3), Nishimura K(3), Yonemoto N(4), Nonogi H(5), Nagao K(6), Ikeda T(7), Sato N(8), Hiroyuki T(9), Yasuda S(3), Kusano K(3); Japanese Circulation Society With Resuscitation Science Study (JCS-ReSS) Group.

#### Abstract

BACKGROUND: Real-world evidence of out-of-hospital ventricular fibrillation (VF), especially regarding intra-day change, remains unclear. We aimed to investigate that age- and genderdependent difference of intra-day change of VF occurrence. METHOD: We enrolled 71,692 patients (males: 56,419 [78.7%], females: 15,273 [21.3%]) in whom cardiac VF had been documented from the 2005-2015 All-Japan Utstein Registry data. Subjects were divided into four groups: group-I (<18 years old), group-II (18-39), group-III (40-69), and group-IV (≥70). Among four groups in each of male and female, we compared the intra-day change of VF occurrence, and evaluated the risk factors of the unfavorable neurologic outcomes at 1 month after VF. RESULTS: Regardless of age, the incidence of VF was significantly greater in male than in female subjects. In male subjects, VF in group-I, III and IV occurred higher at daytime, however, group-II had no intra-day difference because group-II had a higher VF events at midnight~ early morning compared with other aged groups (Poisson regression analysis, p = .03). While in female, each group showed similar intra-day pattern of VF occurrence. Logistic regression analysis revealed that some of the clinical parameters such as time periods from call receipt to first shock and the presence of bystander cardiopulmonary resuscitation were important for risk of 30-day neurologically unfavorable outcomes. CONCLUSIONS: The intra-day change of VF occurrence was age-dependently different in males but not in females, suggesting age- and gender-dependent differences in underlying cardiac diseases. These might affect the significant difference in unfavorable neurologic outcome.

### 2. Sci Rep. 2020 Jun 22;10(1):10070. doi: 10.1038/s41598-020-66668-5.

Risk of sudden cardiac arrest and ventricular arrhythmia with sulfonylureas: An experience with conceptual replication in two independent populations.

Dhopeshwarkar N(1), Brensinger CM(1), Bilker WB(1), Soprano SE(1), Flory JH(1)(2), Dawwas GK(1), Gagne JJ(3), Hennessy S(1)(4), Leonard CE(5). Abstract

Sulfonylureas are commonly used to treat type 2 diabetes mellitus. Despite awareness of their effects on cardiac physiology, a knowledge gap exists regarding their effects on cardiovascular events in real-world populations. Prior studies reported sulfonylurea-associated cardiovascular death but not serious arrhythmogenic endpoints like sudden cardiac arrest (SCA) or ventricular arrhythmia (VA). We assessed the comparative real-world risk of SCA/VA among users of second-generation sulfonylureas: glimepiride, glyburide, and glipizide. We conducted two incident user cohort studies using five-state Medicaid claims (1999-2012) and Optum Clinformatics commercial claims (2000-2016). Outcomes were SCA/VA events precipitating hospital presentation. We used Cox proportional hazards models, adjusted for highdimensional propensity scores, to generate adjusted hazard ratios (aHR). We identified 624,406 and 491,940 sulfonylurea users, and 714 and 385 SCA/VA events, in Medicaid and Optum, respectively. Dataset-specific associations with SCA/VA for both glimepiride and glyburide (vs. glipizide) were on opposite sides of and could not exclude the null (glimepiride: aHRMedicaid 1.17, 95% CI 0.96-1.42; aHROptum 0.84, 0.65-1.08; glyburide: aHRMedicaid 0.87, 0.74-1.03; aHROptum 1.11, 0.86-1.42). Database differences in data availability, populations, and documentation completeness may have contributed to the incongruous results. Emphasis should be placed on assessing potential causes of discrepancies between conflicting studies evaluating the same research question.

## **END-TIDAL CO<sub>2</sub>**

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## **ECOGRAFIA EN RESSUSCITACIÓ**

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### **MONITORATGE CEREBRAL**

1. Acute Med Surg. 2020 Jun 17;7(1):e528. doi: 10.1002/ams2.528. eCollection 2020 Jan-Dec. Cerebral oxygenation monitoring during resuscitation by emergency medical technicians: a prospective multicenter observational study.

Hamanaka K(1), Shimoto M(2), Hitosugi M(3), Beppu S(1), Terashima M(1), SasahashiN(1), Nishiyama K(1).

#### **Abstract**

AIM: To assess the feasibility and predictive ability of regional cerebral oxygen saturation monitoring during cardiopulmonary resuscitation by emergency medical technicians. METHODS: This prospective observational study included 33 cardiac arrest patients who received cardiopulmonary resuscitation in a prehospital setting. Patients were connected to a near-infrared spectrometer through two disposable probes immediately after entering the ambulance. The monitor, which showed regional cerebral oxygen saturation readings, was obscured by covering it with a sheet of paper. Regional cerebral oxygen saturation was measured continuously until hospital arrival. Outcome variables included the prehospital return of spontaneous circulation, survival to hospital admission, and survival at 90 days. RESULTS: For patients who survived >90 days after hospital admission (n = 2), the

mean regional cerebral oxygen saturation values upon ambulance and hospital arrival were 24% and 60%, respectively; for patients who did not survive (n = 31), the mean regional cerebral oxygen saturation values were 15% and 17%, respectively. Regional cerebral oxygen saturation values increased to a greater extent between ambulance arrival and hospital arrival in patients who survived >90 days (median, 36%; interquartile range, 32-40%) than in those who did not survive (0; 0-6%; P = 0.07). Additionally, regional cerebral oxygen saturation values were not related to the prehospital return of spontaneous circulation or survival to hospital admission. CONCLUSION: Regional cerebral oxygen saturation could be monitored during resuscitation by emergency medical technicians, and it can be used during physiological monitor-guided cardiopulmonary resuscitation.

#### FREE FULL TEXT

2. Crit Care Med. 2020 Jun 19. doi: 10.1097/CCM.000000000004460. [Epub ahead of print] Prognostic Value of P25/30 Cortical Somatosensory Evoked Potential Amplitude After Cardiac Arrest.

Oh SH(1), Oh JS(2), Jung HH(2), Park J(2), Kim JH(3), Park JH(4), Wee JH(4), Kim SH(5), Choi SP(6), Park KN(1); Cerebral Resuscitation and Outcome Evaluation Within Catholic Network (CROWN) Investigators.

#### Abstract

OBJECTIVES: The aim of this study was to evaluate the prognostic performance of the peak amplitude of P25/30 cortical somatosensory evoked potentials in predicting nonawakening in targeted temperature management-treated cardiac arrest patients. DESIGN: Prospective analysis. SETTING: Four academic tertiary care hospitals. PATIENTS: Eighty-seven cardiac arrest survivors after targeted temperature management. INTERVENTIONS: Analysis of the amplitude of P25/30. MEASUREMENTS AND MAIN RESULTS: In all participants, somatosensory evoked potentials were recorded after rewarming, and bilaterally absent pupillary and corneal reflexes were evaluated at 72 hours after the return of spontaneous circulation. We analyzed the amplitudes of the N20 and P25/30 peaks and the N20-P25/30 complex in cortical somatosensory evoked potentials. Upon hospital discharge, 87 patients were dichotomized into the awakening and nonawakening groups. The lowest amplitudes of N20, P25/30, and N20-P25/30 in the awakening patients were 0.17, 0.45, and 0.73 μV, respectively, and these thresholds showed a sensitivity of 70.5% (95% CI, 54.8-83.2%), 86.4% (95% CI, 72.7-94.8%), and 75.0% (95% CI, 59.7-86.8%), respectively, for nonawakening. The area under the curve of the P25/30 amplitude was significantly higher than that of the N20 amplitude (0.955 [95% CI, 0.912-0.998] vs 0.894 [95% CI, 0.819-0.969]; p = 0.036) and was comparable with that of the N20-P25/30 amplitude (0.931 [95% CI, 0.873-0.989]). Additionally, adding resuscitation variables or an absent brainstem reflex to the P25/30 amplitude showed a trend toward improving prognostic performance compared with the use of other somatosensory evoked potential amplitudes (area under the curve, 0.958; 95% CI, 0.917-0.999 and area under the curve, 0.974; 95% CI, 0.914-0.996, respectively). CONCLUSIONS: Our results provide evidence that the absence of the P25/30 peak and a reduction in the P25/30 amplitude may be considered prognostic indicators in these patients.

#### ORGANITZACIÓ I ENTRENAMENT

**1.** Curr Pharm Teach Learn. 2020 Aug;12(8):975-980. doi: 10.1016/j.cptl.2020.04.002. Epub 2020 May 14.

Advanced cardiac life support certification for student pharmacists improves simulated patient survival.

Bingham AL(1), Kavelak HL(2), Hollands JM(3), Finn LA(4), Delic JJ(5), Schroeder N(6), Cawley MJ(6).

#### Abstract

BACKGROUND AND PURPOSE: Basic life support (BLS) and advanced cardiac life support (ACLS) skills performance, as well as simulated patient survival, were compared for student pharmacist teams with and without at least one member with American Heart Association (AHA) ACLS certification. EDUCATIONAL ACTIVITY AND SETTING: Doctor of pharmacy students in their third professional year completed a high-fidelity mannequin simulation. Within the previous year, 30 of 184 students (16%) completed ACLS certification. Rapid response teams (n = 31) of five to six members were formed through random student assignment. Two AHA instructors recorded and assessed performance using a checklist adapted from the AHA's standardized forms for BLS and ACLS assessment. Teams with and without ACLS certified members were compared for skills performance and simulated patient survival (i.e. correct performance of all BLS and ACLS skills). FINDINGS: Teams with ACLS certified members (n = 21) were superior to teams without certified members (n = 10) for correct performance of all observed BLS and ACLS skills, including pulse assessment and medication selection for cardiovascular support. For teams who had ACLS certified members, simulated patient survival was 86% higher. The study groups did not differ in their ability to calculate a correct vasopressor infusion rate if warranted. SUMMARY: BLS and ACLS skills performance were improved by AHA ACLS certification. Additionally, simulated patient survival was improved for teams with students who had at least one ACLS certified member.

**2.** J Emerg Med. 2020 Jun 18. pii: S0736-4679(20)30383-8. doi:10.1016/j.jemermed.2020.04.045. [Epub ahead of print]

A Population-Based Retrospective Analysis of Post-In-Hospital Cardiac Arrest Survival after Modification of the Chain of Survival.

Liu CT(1), Lai CY(2), Wang JC(3), Chung CH(4), Chien WC(5), Tsai CS(1).

#### **Abstract**

BACKGROUND: In 2010, the American Heart Association recommended that postcardiac arrest care should be included in the chain of survival to reduce permanent neurological damage, improve quality of life, and reduce health care expenses of postcardiac arrest care.

OBJECTIVES: To investigate post-in-hospital cardiac arrest (IHCA) survival prior to and after modification of the chain of survival in 2010, with subgroup analyses per age and concomitant coronary heart disease (CHD). METHODS: We retrospectively searched the National Health Insurance Research Database for the 2007-2015 period to collect case data coded as "427.41" or "427.5" per International Classification of Disease Clinical Modification, Ninth revision codes and analyzed the data with SPSS v22.0. RESULTS: The 1-day survival rate in the 2011-2015 period was 2% higher than that in the 2007-2010 period (odds ratio [OR] 1.02, 95% confidence interval [CI] 1.01-1.04). Moreover, in the 2011-2015 period, the survival-to-discharge rate was increased by 1% in patients under 65 years (OR 1.01, 95% CI 1.00-1.02) and 1% in CHD patients (OR 1.01, 95% CI 1.01-1.02) compared with that in the 2007-2010 period. CONCLUSION: For patients with IHCA, the overall short-term survival improved significantly after modification of the chain of survival. Younger patients and patients with CHD had better long-term survival.

**FREE FULL TEXT** 

**3.** Resuscitation. 2020 Jun 21. pii: S0300-9572(20)30251-3. doi: 10.1016/j.resuscitation.2020.06.015. [Epub ahead of print]

Improving response to out-of-hospital cardiac arrest: The verified responder program pilot. Blackwood J(1), Mancera M(2), Bavery S(3), Carbon C(3), Daya M(4), VanKeulen B(5), Alteneder DN(5), Helm J(6), Robertson J(6), Charbonneau J(7), Nania JM(8), Schaeffer B(9), Lopez M(9), Loncon T(9), Collins B(10), Charter M(10), Jorgenson DB(11), Gao M(11), Price R(12), Rea T(13).

## **Abstract**

BACKGROUND: Survival following out-of-hospital cardiac arrest (OHCA) decreases as the interval from collapse to CPR and defibrillation increases. Innovative approaches are needed to reduce response intervals, especially for private locations. METHODS: We undertook the Verified Responder Program in 5 United States communities during 2018, whereby off-duty EMS professionals volunteered and were equipped with automated external defibrillators (AEDs). Volunteers were alerted using a geospatial smartphone application (PulsePoint) and could respond to nearby private and public suspected OHCA. The study evaluated the frequency of Verified Responder notification, response, scene arrival, and initial care prior to EMS arrival. OHCA surveillance used the CARES registry. RESULTS: Of the 651 OHCA events (475 private, 176 public), Verified Responders were notified in 7.4% (n = 49). Among the 475 in a private location, volunteers were alerted in 8% (n = 38), responded in 2.7% (n = 13), arrived on scene in 2.3% (n = 11), and provided initial care in 1.7% (n = 8). Among the 176 in a public location, volunteers were alerted in 6.3% (n = 11), responded in 2.3% (n = 4), arrived on-scene in 2.3% (n = 4), and provided initial care in 2.3% (n = 4). Over 96% surveyed had positive impression of the program and intended to continue participation. No responder reported any adverse event. CONCLUSIONS: In this initial US-based experience of a smartphone program for suspected OHCA in private and public locations, Verified Responders reported a positive experience, though were only involved in a small fraction of OHCA. Studies should determine how this type of program could be enhanced to involve more OHCA events.

**4.** Scand J Trauma Resusc Emerg Med. 2020 Jun 25;28(1):60. doi: 10.1186/s13049-020-00742-9.

Identifying the relative importance of predictors of survival in out of hospital cardiac arrest: a machine learning study.

Al-Dury N(1)(2), Ravn-Fischer A(3)(4), Hollenberg J(5), Israelsson J(6)(7), Nordberg P(8)(9), Strömsöe A(10), Axelsson C(11), Herlitz J(3)(11), Rawshani A(3).

## Abstract

INTRODUCTION: Studies examining the factors linked to survival after out of hospital cardiac arrest (OHCA) have either aimed to describe the characteristics and outcomes of OHCA in different parts of the world, or focused on certain factors and whether they were associated with survival. Unfortunately, this approach does not measure how strong each factor is in predicting survival after OHCA. AIM: To investigate the relative importance of 16 wellrecognized factors in OHCA at the time point of ambulance arrival, and before any interventions or medications were given, by using a machine learning approach that implies building models directly from the data, and arranging those factors in order of importance in predicting survival. METHODS: Using a data-driven approach with a machine learning algorithm, we studied the relative importance of 16 factors assessed during the pre-hospital phase of OHCA. We examined 45,000 cases of OHCA between 2008 and 2016. RESULTS: Overall, the top five factors to predict survival in order of importance were: initial rhythm, age, early Cardiopulmonary Resuscitation (CPR, time to CPR and CPR before arrival of EMS), time from EMS dispatch until EMS arrival, and place of cardiac arrest. The largest difference in importance was noted between initial rhythm and the remaining predictors. A number of factors, including time of arrest and sex were of little importance. CONCLUSION: Using machine learning, we confirm that the most important predictor of survival in OHCA is initial rhythm, followed by age, time to start of CPR, EMS response time and place of OHCA. Several factors traditionally viewed as important, e.g. sex, were of little importance.

**5.** Sci Rep. 2020 Jun 22;10(1):10032. doi: 10.1038/s41598-020-67193-1. **Traditional versus blended CPR training program: A randomized controlled non-inferiority study.**  Chien CY(1)(2), Fang SY(3), Tsai LH(1), Tsai SL(1)(3), Chen CB(1), Seak CJ(1), Weng YM(1)(4), Lin CC(1)(2), Chien WC(1)(3), Huang CH(1)(4), Lin CY(2), Chaou CH(1), Liu PH(1)(3), Tseng HJ(5), Chen JC(1)(4), Peng SY(6), Cheng TH(6), Hsu KH(1)(7)(8), Ng CJ(9).

#### Abstract

Cardiopulmonary resuscitation (CPR) training and its quality are critical in improving the survival rate of cardiac arrest. This randomized controlled study investigated the efficacy of a newly developed CPR training program for the public in a Taiwanese setting. A total of 832 adults were randomized to either a traditional or blended (18-minute e-learning plus 30minute hands-on) compression-only CPR training program. The primary outcome was compression depth. Secondary outcomes included CPR knowledge test, practical test, quality of CPR performance, and skill retention. The mean compression depth was 5.21 cm and 5.24 cm in the blended and traditional groups, respectively. The mean difference in compression depth between groups was -0.04 (95% confidence interval -0.13 to infinity), demonstrating that the blended CPR training program was non-inferior to the traditional CPR training program in compression depth after initial training. Secondary outcome results were comparable between groups. Although the mean compression depth and rate were guideline-compliant, only half of the compressions were delivered with adequate depth and rate in both groups. CPR knowledge and skill retained similarly in both groups at 6 and 12 months after training. The blended CPR training program was non-inferior to the traditional CPR training program. However, there is still room for improvement in optimizing initial skill performance as well as skill retention.

**6.** Stud Health Technol Inform. 2020 Jun 16;270:1357-1358. doi: 10.3233/SHTI200440. **Prediction of ROSC After Cardiac Arrest Using Machine Learning.** Liu N(1)(2), Ho AFW(2)(3), Pek PP(2)(3), Lu TC(4), Khruekarnchana P(5), Song KJ(6), Tanaka H(7), Naroo GY(8), Gan HN(9), Koh ZX(3), Ma HM(4), Ong M(2)(3).

Out-of-hospital cardiac arrest (OHCA) is an important public health problem, with very low survival rate. In treating OHCA patients, the return of spontaneous circulation (ROSC) represents the success of early resuscitation efforts. In this study, we developed a machine learning model to predict ROSC and compared it with the ROSC after cardiac arrest (RACA) score. Results demonstrated the usefulness of machine learning in deriving predictive models.

## **CURES POSTRESSUSCITACIÓ**

1. Clin Cardiol. 2020 Jun 23. doi: 10.1002/clc.23403. [Epub ahead of print]

Development a clinical prediction model of the neurological outcome for patients with coma and survived 24 hours after cardiopulmonary resuscitation.

Wang H(1), Tang L(2), Zhang L(1), Zhang ZL(1), Pei HH(1). **Abstract** 

Abstract

BACKGROUND: Cardiac arrest is still a global public health problem at present. The neurological outcome is the core indicator of the prognosis of cardiac arrest. However, there is no effective means or tools to predict the neurological outcome of patients with coma and survived 24 hours after successful cardiopulmonary resuscitation (CPR). HYPOTHESIS: Therefore, we expect to construct a prediction model to predict the neurological outcome for patients with coma and survived 24 hours after successful CPR. METHODS: A retrospective cohort study was used to construct a prediction model of the neurological function for patients with coma and survived 24 hours after successful CPR. From January 2007 to December 2015, a total of 262 patients met the inclusion and exclusion criteria. RESULTS: The predictive model was developed using preselected variables by a systematic review of the literature. Finally, we get five sets of models (three sets of construction models and two sets of internal verification

models) which with similar predictive value. The stepwise model, which including seven variables (age, noncardiac etiology, nonshockable rhythm, bystander CPR, total epinephrine dose, APTT, and SOFA score), was the simplest model, so we choose it as our final predictive model. The area under the ROC curve (AUC), specificity, and sensitivity of the stepwise model were respectively 0.82 (0.77, 0.87), 0.72and 0.82. The AUC, specificity, and sensitivity of the bootstrap stepwise (BS stepwise) model were respectively 0.82 (0.77, 0.87), 0.71, and 0.82. CONCLUSION: This new and validated predictive model may provide individualized estimates of neurological function for patients with coma and survived 24 hours after successful CPR using readily obtained clinical risk factors. External validation studies are required further to demonstrate the model's accuracy in diverse patient populations.

#### **FREE FULL TEXT**

**2.** Crit Care Res Pract. 2020 Jun 8;2020:2981079. doi: 10.1155/2020/2981079. eCollection 2020.

# Efficacy of Thiamine in the Treatment of Postcardiac Arrest Patients: A Randomized Controlled Study.

Pradita-Ukrit S(1), Vattanavanit V(1).

#### Abstract

BACKGROUND: Thiamine administration has been shown to improve survival in a postcardiac arrest animal study. We aimed to evaluate the efficacy of thiamine in comatose out-of-hospital cardiac arrest (OHCA) patients following return of spontaneous circulation. METHODS: A randomized, double-blinded, placebo-controlled study was conducted. Thirty-seven OHCA patients were randomly assigned to receive either thiamine 100 mg every 8 hours or a placebo. The primary outcome was 28-day all-cause mortality. RESULTS: Over the course of 2 years, 37 patients were randomized to either receive thiamine (n = 20) or a placebo (n = 17). The primary outcome was not different between the groups: 10/20 (50%) in the thiamine group vs. 8/17 (47.1%) in the placebo group (P = 0.93 by the log-rank test). There were no significant differences in secondary outcomes between the groups (good neurological outcome, lactate level, and S100B level). CONCLUSIONS: In this study, there were no significant differences in survival outcome. Further studies with a larger population are necessary to confirm these results.

#### **FREE FULL TEXT**

### **TARGETED TEMPERATURE MANAGEMENT**

**1.** Resuscitation. 2020 Jun 21. pii: S0300-9572(20)30250-1. doi: 10.1016/j.resuscitation.2020.06.014. [Epub ahead of print]

High heat generation is associated with good neurologic outcome in out-of-hospital cardiac arrest survivors underwent targeted temperature management at 33°C.

Lee DH(1), Lee BK(2), Cho YS(1), Jung YH(1), Lee HY(1), Min JH(3), Park JS(3), Jeung KW(1). **Abstract** 

AIM: To examine the association between heat index (HI) during the induction, maintenance, and rewarming periods of targeted temperature management (TTM) and neurologic outcome in out-of-hospital cardiac arrest (OHCA) survivors. METHODS: Adult (≥18 years) comatose OHCA survivors who underwent TTM at 33°C between 2016 and 2018 were included. We collected data on water temperature (WT) recorded every minute during TTM. We calculated HI during induction as the inverse of the average WT×induction time (hours)×100 and HI of maintenance and rewarming as the inverse of the average WT×100. The primary outcome was a poor neurologic outcome, based on Cerebral Performance Category 3-5 after 6 months. RESULTS: Of the 118 included patients, 78 (66.1%) had poor outcome. Poor outcome group had lower HI during each of three periods than good outcome group. The areas under the curves for poor outcome of HI during the induction, maintenance, and rewarming periods

were 0.819 (95% confidence interval [CI], 0.737-0.883), 0.781 (95% CI, 0.696-0.852), and 0.844 (95% CI, 0.765-0.904), respectively. Induction time (odds ratio [OR], 0.991; 95% CI, 0.983-0.999) and HI during induction (OR, 0.916; 95% CI, 0.854-0.983), maintenance (OR, 0.082; 95% CI, 0.011-0.589), and rewarming (OR, 0.009; 95% CI, 0.000-0.285) were associated with poor outcome. CONCLUSIONS: Heat generation was independently associated with neurologic outcome in OHCA survivors who underwent TTM at 33°C. The performance of HI was higher in the rewarming period than in the induction or maintenance period in association with poor neurologic outcomes.

2. Ther Hypothermia Temp Manag. 2020 Jun 23. doi: 10.1089/ther.2020.0013. [Epub ahead of print]

Impact of Hypothermia on Oxygenation Variables and Metabolism in Survivors of Out-of-Hospital Cardiac Arrest Undergoing Targeted Temperature Management at 33°C Versus 36°C. Grand J(1), Hassager C(1), Bro-Jeppesen J(1), Gustafsson F(1), Møller JE(1), Boesgaard S(1), Nielsen N(2), Kjaergaard J(1).

#### Abstract

Targeted temperature management (TTM) exerts substantial impact on hemodynamic function in out-of-hospital cardiac arrest (OHCA) patients. Whole-body oxygen consumption (VO2) and delivery (DO2) have not previously been investigated in a clinical setting during TTM at different levels of temperature after OHCA. A substudy of 151 patients randomized at a single center in the TTM-trial, where patients were randomly assigned TTM at 33°C (TTM33) or  $36^{\circ}$ C (TTM36) for 24 hours. We calculated VO2 according to the principle of Fick (VO2 = cardiac output\*arteriovenous oxygen content difference). DO2 was calculated as cardiac output\*arterial oxygen content. Cardiac output was measured by pulmonary artery catheter with thermodilution. Arteriovenous oxygen content difference was calculated from arterial and mixed venous oxygen saturation and hemoglobin. Oxygen extraction ratio = VO2/DO2. At 24 hours, the VO2 was  $169 \pm 59$  mL O2 per minute in TTM33 and  $217 \pm 53$  mL O2 per minute in TTM36 (p < 0.0001). During 24 hours of TTM, the overall difference was 53 mL O2 minute (95% confidence interval [CI]: 31-74, pgroup < 0.0001). After rewarming at 36 and 48 hours, there was no difference in VO2 between the groups. DO2 was overall 277 mL O2 per minute (95% CI: 175-379, pgroup < 0.0001) higher in the TTM36-group during TTM. Oxygen extraction ratio during TTM was not significantly different between the two groups (2% [95% CI: -0.1 to 5, pgroup = 0.09]). VO2 during the first 36 hours after OHCA correlated significantly with temperature, and VO2 was 19 mL O2 per minute lower per degree reduction in temperature (95% CI: 15-22), p < 0.0001. TTM at 33°C compared to 36°C after OHCA is associated with significantly lower VO2 and DO2, however, oxygen extraction ratio was not significantly different. For each degree lower body temperature, the VO2 fell by 19 mL O2 per minute.

## ELECTROFISIOLOGIA I DESFIBRIL·LACIÓ

**1.** Resuscitation. 2020 Jun 20. pii: S0300-9572(20)30253-7. doi: 10.1016/j.resuscitation.2020.06.017. [Epub ahead of print]

Remodeling of the 12-lead Electrocardiogram in Immediate Survivors of Sudden Cardiac Arrest.

Held EP(1), Reinier K(2), Uy-Evanado A(1), Nakamura K(1), Chugh HS(1), Jui J(2), Chugh SS(3). Abstract

BACKGROUND: The ECG is a critical diagnostic tool for the management of immediate sudden cardiac arrest (SCA) survivors, but can be altered following the SCA event. A limited number of studies report that electrical remodeling post SCA is due to prolonged myocardial repolarization, but a better understanding of this phenomenon is needed. AIM: To identify specific ECG abnormalities that follow SCA in immediate survivors. METHODS: SCA survivors with a pre-arrest ECG and an ECG obtained within 48 hours post-SCA were prospectively

collected in the Oregon Sudden Unexpected Death Study (Portland metro region) from 2002-2015. Ventricular depolarization and repolarization measurements were compared between pre-arrest and post-arrest ECGs using paired t-tests and assessed for association with survival using unpaired t-tests and Pearson's chi-square tests. RESULTS: A pre-arrest ECG and post-arrest ECG were available for 297 SCA cases (67.8  $\pm$  13.4 years; 65.3% male). From the pre- to post-arrest setting, there was a significant mean increase in QRS (21 ms, p < 0.001) and QTc (35 ms, p < 0.001) in each SCA case, while there was no significant change in the JTc (4 ms, p = 0.361). Post-arrest QRS duration was significantly shorter in cases who survived to hospital discharge compared with those who did not survive (mean QRSD 115  $\pm$  29 ms vs 127  $\pm$  34 ms; p = 0.006). CONCLUSIONS: Contrary to expectations, electrical remodeling of the ECG due to SCA occurs due to prolongation of ventricular depolarization (QRSD), and not repolarization (JTc). Prolonged QRSD may also assist with prognostication and warrants further evaluation.

**2.** Resuscitation. 2020 Jun 16. pii: S0300-9572(20)30244-6. doi: 10.1016/j.resuscitation.2020.06.008. [Epub ahead of print]

Double Sequential Defibrillation for Refractory Ventricular Fibrillation Cardiac Arrest: A Systematic Review.

Deakin CD(1), Morley P(2), Soar J(3), Drennan IR(4).

#### Abstract

INTRODUCTION: Cardiac arrests associated with shockable rhythms such as ventricular fibrillation or pulseless VT (VF/pVT) are associated with improved outcomes from cardiac arrest. The more defibrillation attempts required to terminate VF/pVT, the lower the survival. Double sequential defibrillation (DSD) has been used for refractory VF/pVT cardiac arrest despite limited evidence examining this practice. We performed a systematic review to summarize the evidence related to the use of DSD during cardiac arrest. METHODS: This review was performed according to PRISMA and registered on PROSPERO (ID: CRD42020152575) We searched Embase, Pubmed, and the Cochrane library from inception to 28 February 2020. We included adult patients with VF/pVT in any setting. We excluded case studies, case series with less than five patients, conference abstracts, simulation studies, and protocols for clinical trials. We predefined our outcomes of interest as neurological outcome, survival to hospital discharge, survival to hospital admission, return of spontaneous circulation (ROSC), and termination of VF/pVT. Risk of bias was examined using ROBINS-I or ROB-2 and certainty of studies were reported according to GRADE methodology. RESULTS: Overall, 314 studies were identified during the initial search. One hundred and thirty studies were screened during title and abstract stage and 10 studies underwent full manuscript screening, nine included in the final analysis. Included studies were cohort studies (n=4), case series (n=3), case-control study (n=1) and a prospective pilot clinical trial (n-1). All studies were considered to have serious or critical risk of bias and no meta-analysis was performed. Overall, we did not find any differences in terms of neurological outcome, survival to hospital discharge, survival to hospital admission, ROSC, or termination of VF/pVT between DSD and a standard defibrillation strategy. CONCLUSION: The use of double sequential defibrillation was not associated with improved outcomes from out-of-hospital cardiac arrest, however the current literature has a number of limitations to interpretation. Further high-quality evidence is needed to answer this important question.

## **PEDIATRIA**

**1.** Pediatr Crit Care Med. 2020 Jun 25. doi: 10.1097/PCC.000000000002486. [Epub ahead of print]

Pediatric Cardiopulmonary Resuscitation Tasks and Hands-Off Time: A Descriptive Analysis Using Video Review.

Taeb M(1), Schwartz JM(2), Spaeder MC(3), Levin AB(2).

#### Abstract

OBJECTIVES: To characterize tasks performed during cardiopulmonary resuscitation in association with hands-off time, using video recordings of resuscitation events. DESIGN: Singlecenter, prospective, observational trial. SETTING: Twenty-six bed cardiac ICU in a quaternary care free standing pediatric academic hospital. PATIENTS: Patients admitted to the cardiac ICU with cardiopulmonary resuscitation events lasting greater than 2 minutes captured on video. INTERVENTIONS: None. MEASUREMENTS AND MAIN RESULTS: Videos of 17 cardiopulmonary resuscitation episodes comprising 264.5 minutes of cardiopulmonary resuscitation were reviewed: 11 classic cardiopulmonary resuscitation (87.5 min) and six extracorporeal cardiopulmonary resuscitations (177 min). A total of 209 tasks occurred in 178 discrete time periods including compressor change (36%), rhythm/pulse check (18%), surgical pause (18%), extracorporeal membrane oxygenation preparation/draping (9%), repositioning (7.5%), defibrillation (6%), backboard placement (3%), bagging (<1%), pacing (<1%), intubation (<1%). In 31 time periods, 62 tasks were clustered with 18 (58%) as compressor changes and pulse/rhythm check. In the 178 discrete time periods, 135 occurred with a pause in compressions for greater than or equal to 1 second; 43 tasks occurred without pause. After accounting for repeated measures from individual patients, providers were less likely to perform rhythm or pulse checks (p < 0.0001) or change compressors regularly (p = 0.02) during extracorporeal cardiopulmonary resuscitation as compared to classic cardiopulmonary resuscitation. The frequency of tasks occurring during cardiopulmonary resuscitation interruptions in the classic cardiopulmonary resuscitation group was constant over the resuscitation but variable in extracorporeal cardiopulmonary resuscitation, peaking during activities required for cannulation. CONCLUSIONS: On video review of cardiopulmonary resuscitation, we found that resuscitation guidelines were not strictly followed in either cardiopulmonary resuscitation or extracorporeal cardiopulmonary resuscitation patients, but adherence was worse in extracorporeal cardiopulmonary resuscitation. Clustering of resuscitation tasks occurred 23% of the time during chest compression pauses suggesting attempts at minimizing cardiopulmonary resuscitation interruptions. The frequency of cardiopulmonary resuscitation interruptions task events was relatively constant during classic cardiopulmonary resuscitation but variable in extracorporeal cardiopulmonary resuscitation. Characterization of resuscitation tasks by video review may inform better cardiopulmonary resuscitation orchestration and efficiency.

**2.** Pediatr Emerg Care. 2020 Jun 22. doi: 10.1097/PEC.000000000002171. [Epub ahead of print]

Risk Factors for Peri-intubation Cardiac Arrest in a Pediatric Emergency Department. Pokrajac N(1), Sbiroli E(2), Hollenbach KA(3), Kohn MA(1), Contreras E(4), Murray M(2). Abstract

OBJECTIVES: Cardiac arrest is a significant complication of emergent endotracheal intubation (ETI) within the pediatric population. No studies have evaluated risk factors for peri-intubation cardiac arrest (PICA) in a pediatric emergency department (ED) setting. This study identified risk factors for PICA among patients undergoing emergent ETI in a pediatric ED. METHODS: We performed a nested case-control study within the cohort of children who underwent emergent ETI in our pediatric ED during a 9-year period. Cases were children with PICA within 20 minutes of ETI. Controls (4 per case) were randomly selected children without PICA after ETI. We analyzed potential risk factors based on published data and physiologic plausibility and created a simple risk model using univariate results, model fit statistics, and clinical judgment. RESULTS: In the cohort of patients undergoing ETI, PICA occurred in 21 of 543 subjects (3.9%; 95% confidence interval [CI], 2.2-5.9%), with return of spontaneous circulation in 16 of 21 (76.2%; 95% CI, 52.8-91.8%) and survival to discharge in 12 of 21 (57.1%; 95% CI, 34.0-78.2%). On univariate analysis, cases were more likely to be younger, have delayed capillary refill time,

systolic or diastolic hypotension, hypoxia, greater than one intubation attempt, no sedative or paralytic used, and pulmonary disease compared with controls. Our 4-category risk model for PICA combined preintubation hypoxia (or an unobtainable pulse oximetry value) and younger than 1 year. The area under the receiver operating characteristic curve for this model was 0.87 (95% CI, 0.77-0.97). CONCLUSIONS: Hypoxia (or an unobtainable pulse oximetry value) was the strongest predictor for PICA among children after emergent ETI in our sample. A simple risk model combining pre-ETI hypoxia and younger than 1 year showed excellent discrimination in this sample. Our results require independent validation.

## **ECMO**

1. Med Intensiva. 2020 Jun 18. pii: S0210-5691(20)30066-8. doi:10.1016/j.medin.2020.01.017. [Epub ahead of print]

Role of normothermic perfusion with ECMO in donation after controlled cardiac death in Spain.

Rubio Muñoz JJ(1), Dominguez-Gil González B(2), Miñambres García E(3), Del Río Gallegos F(4), Pérez-Villares JM(5).

#### **Abstract**

Spain has become one of the most active countries in donation after controlled cardiac death, using normothermic abdominal perfusion with ECMO in more than 50% of all donors - a situation contributed to by the creation of mobile teams to support hospitals lacking this technology. The donation process must be respectful of the wishes and values of the patients and their relatives, especially if there is pre mortem manipulation, and the absence of cerebral perfusion should be guaranteed. The liver is the most benefited organ by reducing biliary complications as well as the loss of grafts. In renal transplantation, the technique could contribute to reduce the incidence of delayed graft function. In addition, the procedure is compatible with surgical rapid recovery in hypothermia when there is also lung donation. The future lies in the consolidation of cardiac donation by extending normothermic perfusion to the thoracic cavity.

2. Scand J Trauma Resusc Emerg Med. 2020 Jun 23;28(1):58. doi:10.1186/s13049-020-00753-6. Can we predict patient outcome before extracorporeal membrane oxygenation for refractory cardiac arrest?

Siao FY(1)(2)(3), Chiu CW(1), Chiu CC(1), Chang YJ(4), Chen YC(5), Chen YL(5), Hsieh YK(5), Chou CC(1), Yen HH(6)(7).

#### Abstract

BACKGROUND: Refractory cardiac arrest resistant to conventional cardiopulmonary resuscitation (C-CPR) has a poor outcome. Although previous reports showed that extracorporeal cardiopulmonary resuscitation (E-CPR) can improve the clinical outcome, there are no clinically applicable predictors of patient outcome that can be used prior to the implementation of E-CPR. We aimed to evaluate the use of clinical factors in patients with refractory cardiac arrest undergoing E-CPR to predict patient outcome in our institution. METHODS: This is a single-center retrospective study. We report 112 patients presenting with refractory cardiac arrest resistant to C-CPR between January 2012 and November 2017. All patients received E-CPR for continued life support when a cardiogenic etiology was presumed. Clinical factors associated with patient outcome were analyzed. Significant pre-ECMO clinical factors were extracted to build a patient outcome risk prediction model. RESULTS: The overall survival rate at discharge was 40.2, and 30.4% of patients were discharged with good neurologic function. The six-month survival rate after hospital discharge was 36.6, and 25.9% of patients had good neurologic function 6 months after discharge. We stratified the patients into low-risk (n = 38), medium-risk (n = 47), and high-risk groups (n = 27) according to the TLR

score (low-flow Time, cardiac arrest Location, and initial cardiac arrest Rhythm) that we derived from pre-ECMO clinical parameters. Compared with the medium-risk and high-risk groups, the low-risk group had better survival at discharge (65.8% vs. 42.6% vs. 0%, p < 0.0001) and at 6 months (60.5% vs. 38.3% vs. 0%, p = 0.0001). The low-risk group also had a better neurologic outcome at discharge (50% vs. 31.9% vs. 0%, p = 0.0001) and 6 months after discharge (44.7% vs. 25.5% vs. 0%, p = 0.0003) than the medium-risk and high-risk groups. CONCLUSIONS: Patients with refractory cardiac arrest receiving E-CPR can be stratified by pre-ECMO clinical factors to predict the clinical outcome. Larger-scale studies are required to validate our observations.

### **RECERCA EXPERIMENTAL**

**1.** Arch Dis Child Fetal Neonatal Ed. 2020 Jul;105(4):357-363. doi: 10.1136/archdischild-2018-316610. Epub 2019 May 23.

Asynchronous ventilation at 120 compared with 90 or 100 compressions per minute improves haemodynamic recovery in asphyxiated newborn piglets.

Patel S(1), Cheung PY(1), Lee TF(2), Pasquin MP(1), Lu M(2), O'Reilly M(1), Schmölzer GM(3). **Abstract** 

OBJECTIVE: To determine whether different chest compression (CC) rates during continuous CC with asynchronous ventilations (CCaV) reduce time to return of spontaneous circulation (ROSC) and improved haemodynamic recovery in piglets aged 24-72 hours with asphyxiainduced asystole. METHODS: Thirty piglets (aged 24-72 hours) were anaesthetised, intubated, instrumented and exposed to 30 min normocapnic hypoxia followed by asphyxia. Piglets were randomised into four groups: CCaV with CC rate of 90 (CCaV+90, n=8), 100 (CCaV+100, n=8) or 120 compressions per minute (CCaV+120, n=8), and a sham-operated group (n=6). Cardiac function, carotid blood flow, cerebral and renal oxygenation and respiratory parameters were continuously recorded. Cerebral cortical tissue was harvested and assayed for inflammatory and injury markers. RESULTS: All three intervention groups had a similar number of piglets achieving ROSC (6/8, 5/8 and 5/8 for CCaV+120, CCaV+100 and CCaV+90, respectively) and mean ROSC time (120, 90 and 90 s for CCaV+120, CCaV+100 and CCaV+90, respectively). The haemodynamic recovery (indicated by carotid flow, cerebral and renal perfusion) was similar between CCaV+120 and sham by the end of experiment. In comparison, CCaV+90 and CCaV+100 had significantly reduced haemodynamic recovery compared with sham operated (p≤0.05). Inflammatory (interleukin [IL]-6 and IL-1β) and injury markers (lactate) were significantly higher in the frontoparietal cortex of CCaV+90 and CCaV+100 compared with sham, whereas brain injury markers were similar between CCaV+120 and sham. CONCLUSIONS: Although there was no difference between the groups in achieving ROSC, the haemodynamic recovery of CCaV+120 was significantly improved compared with CCaV+90 and CCaV+100, which were also associated with higher cerebral inflammatory and brain injury markers.

**2.** Cardiovasc Drugs Ther. 2020 Jun 19. doi: 10.1007/s10557-020-07026-5. [Epub ahead of print]

Pralidoxime-Induced Potentiation of the Pressor Effect of Adrenaline and Hastened Successful Resuscitation by Pralidoxime in a Porcine Cardiac Arrest Model.

Lee HY(1), Mamadjonov N(2), Jeung KW(3)(4), Jung YH(1)(5), Lee BK(1)(5), Moon KS(5)(6), Heo T(1)(5), Min YI(1)(5).

#### Abstract

PURPOSE: Pralidoxime potentiated the pressor effect of adrenaline and facilitated restoration of spontaneous circulation (ROSC) after prolonged cardiac arrest. In this study, we hypothesised that pralidoxime would hasten ROSC in a model with a short duration of

untreated ventricular fibrillation (VF). We also hypothesised that potentiation of the pressor effect of adrenaline by pralidoxime would not be accompanied by worsening of the adverse effects of adrenaline. METHODS: After 5 min of VF, 20 pigs randomly received either pralidoxime (40 mg/kg) or saline, in combination with adrenaline, during cardiopulmonary resuscitation (CPR). Coronary perfusion pressure (CPP) during CPR, and ease of resuscitation were compared between the groups. Additionally, haemodynamic data, severity of ventricular arrhythmias, and cerebral microcirculation were measured during the 1-h post-resuscitation period. Cerebral microcirculatory blood flow and brain tissue oxygen tension (PbtO<sub>2</sub>) were measured on parietal cortices exposed through burr holes. RESULTS: All animals achieved ROSC. The pralidoxime group had higher CPP during CPR (P = 0.014) and required a shorter duration of CPR (P = 0.024) and smaller number of adrenaline doses (P = 0.024). During the post-resuscitation period, heart rate increased over time in the control group, and decreased steadily in the pralidoxime group. No inter-group differences were observed in the incidences of ventricular arrhythmias, cerebral microcirculatory blood flow, and PbtO2. CONCLUSION: Pralidoxime improved CPP and hastened ROSC in a model with a short duration of untreated VF. The potentiation of the pressor effect of adrenaline was not accompanied by the worsening of the adverse effects of adrenaline.

**3.** Fetal Pediatr Pathol. 2020 Jun 26:1-10. doi: 10.1080/15513815.2020.1783407. [Epub ahead of print]

The Effect of Mild Hypothermia on Nogo-A and Neurological Function in the Brain after Cardiopulmonary Resuscitation in Rats.

Li JL(1), Cao Y(2), Nie H(2).

## Abstract

Objective: We investigated the dynamic changes of Nogo-A protein in brain and the effects of mild therapeutic hypothermia (MTH) on its expression after cardiopulmonary resuscitation (CPR). Methods: Western-blotting and neurological scoring of 45 rats subjected to cardiac arrest and CPR with and without MTR were performed to investigate the changes in the expression of Nogo-A protein in the hippocampus and cortex over a period of time ranging from 6 h to 72 h after restoration of spontaneous circulation (ROSC). Results: Nogo-A expression levels were increased at 6 h after CPR in the hippocampus and cortex, peaked at 24 h in the cortex, and at 48 h in the hippocampus. The expression of Nogo-A in the MTR group was significantly lower at 12 h (p < 0.05) compared to those with no MTR after ROSC. Conclusions: MTR blunts the expression of Nogo-A protein in the hippocampus and cortex after cardiac arrest and resuscitation, and MTR may provide cerebral protection after ischemia.

**4.** J Int Med Res. 2020 Jun;48(6):300060520931260. doi: 10.1177/0300060520931260. Establishment of a swine model of traumatic cardiac arrest induced by haemorrhage and ventricular fibrillation.

Shen P(1)(2)(3), Xu JF(1)(2)(4), Gao YZ(1)(2), Xia SL(1)(2), Liu SY(1)(2), Zhang M(1)(2). **Abstract** 

OBJECTIVE: To establish and evaluate a swine model of traumatic cardiac arrest (TCA) induced by haemorrhage and ventricular fibrillation. METHODS: Thirteen male pigs were divided into a sham group (n = 5) and TCA group (n = 8). Animals in the sham-operated group underwent intubation and monitoring but not haemorrhage and resuscitation, while animals in the TCA group underwent 40% blood volume haemorrhage over 20 min followed by 5 min of ventricular fibrillation and 5 min of cardiopulmonary resuscitation with fluid resuscitation. RESULTS: Restoration of spontaneous circulation was achieved in seven of eight animals in the TCA group. After resuscitation, the heart rate was significantly increased while the mean arterial pressure and ejection fraction were significantly decreased in the TCA group. The TCA group had significant cardiac and neurological injuries post-resuscitation and had higher serum

creatinine and blood lactic acid levels and lower  $PaO_2$  than the sham group. Animals in the TCA group also exhibited significantly higher apoptotic indices and caspase-3 protein levels in the heart, brain and kidney than the sham group. CONCLUSION: Animals in this swine model of TCA exhibited high rates of successful resuscitation, significant vital organ injury and prolonged survival. The model is suitable for use in further TCA research.

**5.** Shock. 2020 Jun 23. doi: 10.1097/SHK.000000000001596. [Epub ahead of print] Remote Ischemic Postconditioning Inhibits Hippocampal Neuronal Apoptosis and Mitophagy After Cardiopulmonary Resuscitation in Rats.

Xie B(1), Gao X, Huang Y, Zhang Y, Zhu S.

## Abstract

BACKGROUND: Studies have shown that remote ischemic postconditioning can improve brain damage caused by ischemia and hypoxia. However, the specific mechanism underlying this phenomenon is still unclear. The purpose of this study was to investigate the effects of remote ischemic postconditioning on neuronal apoptosis and mitophagy after cardiopulmonary resuscitation (CPR) in rats. METHODS: Male Sprague-Dawley rats were used to establish an asphyxia cardiac arrest model by clamping the tracheal duct. Firstly, the expression levels of P53, Cytochrome c (Cytc), and Parkin in the cytoplasm and mitochondria were observed at 3, 6, 24, and 72 hours after the restoration of spontaneous circulation (ROSC). Then, neurological deficit scores (NDS), hippocampal neuron apoptosis, mitochondrial P53 and Parkin, cytoplasmic Cytc, and neuron ultrastructure were evaluated 24 hours after ROSC. RESULTS: P53 and Parkin can translocate from the cytoplasm to the mitochondria, promoting the translocation of cytoplasmic Cytc to mitochondria after CPR, reaching a peak at 24 hours after the ROSC. The P53 inhibitor Pifithrin-µ reduced apoptosis induced by P53 mitochondrial translocation. Apoptosis was induced after cardiac arrest (CA) and attenuated by remote ischemic postconditioning via inhibiting P53 mitochondrial translocation and the release of Cytc to the cytoplasm. In addition, remote ischemic postconditioning could inhibit Parkinmediated mitophagy. CONCLUSION: Taken together, our results show that remote ischemic postconditioning improves neural function after CPR by inhibiting P53 mitochondrial translocation-induced apoptosis and Parkin-mediated mitophagy.

#### **CASE REPORTS**

1. Neurocrit Care. 2020 Jun 24. doi: 10.1007/s12028-020-00990-8. [Epub ahead of print] Cerebral Infarction Observed on Brain MRI in Unconscious Out-of-Hospital Cardiac Arrest Survivors: A Pilot Study.

Baik M(1), Kim KM(1), Oh CM(2), Song D(1), Heo JH(1), Park YS(3), Wi J(4), Kim YS(5), Kim J(6), Ahn SS(7), Cho KH(8), Cho YJ(1).

#### **Abstract**

BACKGROUND: Cumulative evidence regarding the use of brain magnetic resonance imaging (MRI) for predicting prognosis of unconscious out-of-hospital cardiac arrest (OHCA) survivors treated with targeted temperature management (TTM) is available. Theoretically, these patients are at a high risk of developing cerebral infarction. However, there is a paucity of reports regarding the characteristics of cerebral infarction in this population. Thus, we performed a pilot study to identify the characteristics and risk factors of cerebral infarction and to evaluate whether this infarction is associated with clinical outcomes. METHODS: A single-center, retrospective, registry-based cohort study was conducted at Severance Hospital, a tertiary center. Unconscious OHCA survivors were registered and treated with TTM between September 2011 and December 2015. We included patients who underwent brain MRI in the first week after the return of spontaneous circulation. We excluded patients who underwent any endovascular interventions to focus on "procedure-unrelated" cerebral infarctions. We

assessed hypoxic-ischemic encephalopathy (HIE) and procedure-unrelated cerebral infarction separately on MRI. Patients were categorized into the following groups based on MRI findings: HIE (-)/infarction (-), infarction-only, and HIE (+) groups. Conventional vascular risk factors showing p < 0.05 in univariate analyses were entered into multivariate logistic regression. We also evaluated if the presence of this procedure-unrelated cerebral infarction lesion or HIE was associated with a poor clinical outcome at discharge, defined as a cerebral performance category of 3-5. RESULTS: Among 71 unconscious OHCA survivors who completed TTM, underwent MRI, and who did not undergo endovascular interventions, 14 (19.7%) patients had procedure-unrelated cerebral infarction based on MRI. Advancing age [odds ratio (OR) 1.11] and atrial fibrillation (OR 5.78) were independently associated with the occurrence of procedure-unrelated cerebral infarction (both p < 0.05). There were more patients with poor clinical outcomes at discharge in the HIE (+) group (88.1%) than in the infarction-only (30.0%) or HIE (-)/infarction (-) group (15.8%) (p < 0.001). HIE (+) (OR 38.69, p < 0.001) was independently associated with poor clinical outcomes at discharge, whereas infarction-only was not (p > 0.05), compared to HIE (-)/infarction (-). CONCLUSIONS: In this pilot study, procedure-unrelated cerebral infarction was noted in approximately one-fifth of unconscious OHCA survivors who were treated with TTM and underwent MRI. Older age and atrial fibrillation might be associated with the occurrence of procedure-unrelated cerebral infarction, and cerebral infarction was not considered to be associated with clinical outcomes at discharge. Considering that the strict exclusion criteria in this pilot study resulted in a highly selected sample with a relatively small size, further work is needed to verify our findings.