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Clinical paper

Hydrocortisone and arginine vasopressin in post-resuscitation shock: the HYVAPRESS trial



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Abstract

Background: Acute circulatory failure after successful resuscitation of cardiac arrest remains challenging and multifactorial. As the main driver of early mortality after restoration of spontaneous circulation, its therapeutic management essentially relies on fluids administration and vasopressive support using noradrenaline. Data also support the potential impact of a hormonal defect in this setting. Steroids substitution as well as arginin-vasopressin treatment should be evaluated in these patients.

Methods: The HYVAPRESS trial is a 2x2 factorial randomized placebo-controlled multicentric trial evaluating the effect of both hydrocortisone and arginin-vasopressin in successfully resuscitated (in-hospital and out-of-hospital) cardiac arrest patients suffering an acute circulatory failure in the first 24 h after restoration of spontaneous circulation. The main outcome will be the favourable neurological outcome assessed by the Glasgow Outcome Scale (GOS). 380 patients will be included, i.e. 95 patients in each arm, allowing the detection of a 15% difference in mortality using a power of 80% and an alpha-risk of 5%.

Discussion: Assessing therapeutics in the hemodynamic failure in post –cardiac arrest patients is challenging as the mortality is very high. Besides the vasopressive support, few investigation have been led so far to improve the management of these patients. While hydrocortisone and arginin-vasopressive have been evaluated in septic shock patients, data are lacking in this very specific subgroup of patients suffering from a very high mortality. Enrollement is ongoing.

Trial registration: Clinical Trials NCT04591990, registered on 2020, October 19th.

Keywords: Cardiac arrest, Post-resuscitation shock, Arginin-vasopressin, Hydrocortisone

Introduction

Despite advancements in prehospital management and standardization of advanced life support through wide diffusion of international guidelines, the overall prognosis of patients who suffered cardiac arrest (CA) remains poor. About 20 up to 30% of patients admitted to the hospital after a successful resuscitation of out-of-hospital CA are discharged alive and free from significant neurological impairment^{1,2}. For in-hospital CA, the survival rate reaches approximately 25%, although patients who experience CA in non-monitored units such as medical and surgical wards have the worst outcomes, with

survival rates below 5%.³ This high early mortality rate is attributed to the concept of post-resuscitation syndrome, typically divided into two consecutive phases: an initial reperfusion injury leading to multiple organ failure and subsequent poor neurological outcomes resulting from anoxic brain injury.⁴

The pathogenesis of this post-resuscitation syndrome is completely elucidated and related to multiple and intricate factors.⁵ Its complexity led to the description of the similarities with sepsis, as a “sepsis-like syndrome”.⁶ This syndrome is characterized by a series of events that vary in intensity but are generally proportional to the duration of the no-flow and low-flow periods, as well as the challenges encountered during the resuscitation process.⁷

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admitted to the ICU, 3) diagnosed with post-resuscitation shock defined as arterial hypotension (systolic arterial blood pressure [ABP] < 90 mmHg or mean ABP < 65 mmHg) unresponsive to adequate fluid loading, which occurred within the first 24 h after ROSC and requiring norepinephrine/epinephrine continuous infusion at a dose greater or equal to 0.2 µg/kg/min (equivalent tartrate) for at least 3 h and 4) Randomization must occur within a maximum of nine hours after the initiation of vasopressor therapy.

These time intervals considered for inclusion may be summarized using the Fig. 1.

Participants will be excluded if they have any of the following conditions: a traumatic or neurological cause of cardiac arrest, shock due to uncontrolled hemorrhage, pre-existing adrenal insufficiency, ongoing steroid treatment, mechanical circulatory support, recent gastrointestinal bleeding, pregnancy or breastfeeding, hypersensitivity to AVP or HSHC or their excipients, legal protection status (inability to consent, guardianship, incarceration), or current participation in another interventional study.

Interventions

Intervention description

AVP is prepared as a 40 IU/ampoule solution and diluted in 0.9% sodium chloride to a final concentration of 0.8 IU/mL. The initial AVP infusion rate is 0.6 IU/hour (0.75 mL/hour) and can be increased to a maximum of 1.8 IU/hour (2.25 mL/hour) to maintain a targeted mean arterial blood pressure of 65 mmHg. Once the intervention medication (either AVP or placebo) will be increased up to the maximal rate, the adjustment of norepinephrine infusion rate will be resumed to target the 65 mmHg mean arterial blood pressure, if

not already. The goal of the HYVAPRESS trial is to maximize the AVP dosage and to spare norepinephrine. When the 65 mmHg mean arterial blood pressure target is achieved, norepinephrine is decreased first while AVP dosage is maintained. Norepinephrine may be then weaned if mean arterial blood pressure is still greater or equal to 65 mmHg. Once norepinephrine is weaned, AVP may be tapered and eventually weaned as well. AVP administration is capped at three days.

If vasopressor support is still needed after day-3, norepinephrine will be resumed.

The management of vasopressive drugs can be summarized in the Fig. 2.

Placebo of AVP will be vials of sodium chloride (NaCl 0.9%) for injection 2 mL, provided by the sponsor.

HSHC will be provided by SERB Pharmaceuticals using vials with lyophilisate (100 mg hydrocortisone). HSHC will be administered as a 50 mg intravenous bolus every 6 h after a initial dose of 100 mg for max 7 days. It will be stopped without tapering.

Placebo of HSHC will be powder for solution for injection provided by SERB Pharmaceuticals.

Criteria for discontinuing or modifying allocated interventions for a given trial participant

No crossover between intervention groups is planned.

Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence

To ensure adherence, healthcare professionals will complete a monitoring form to document all study drug administrations, which will be

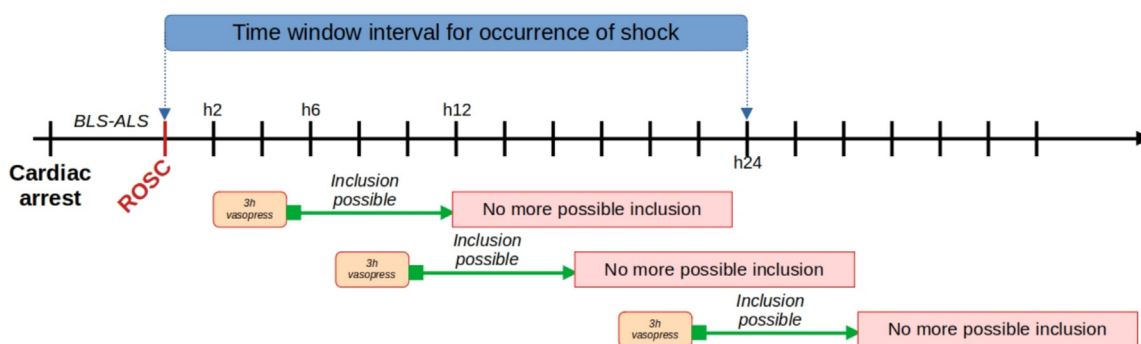


Fig. 1 - HYVAPRESS time intervals for catecholamines infusion and inclusion.

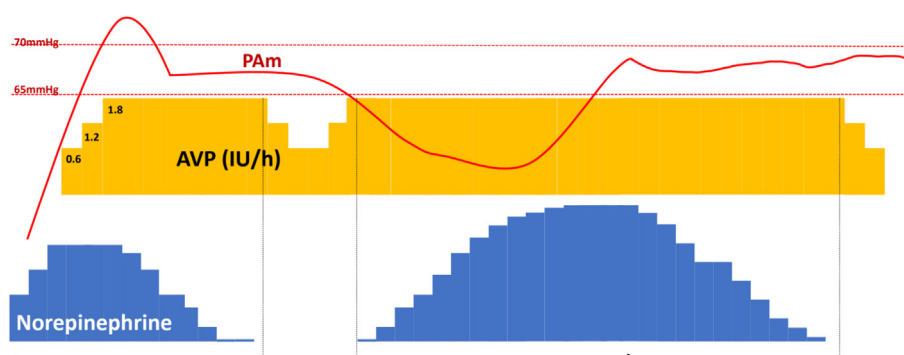


Fig. 2 - Adjustment for AVP and norepinephrine doses during the HYVAPRESS trial.

stored in each patient's chart. Detachable stickers from each drug box will be recorded in a patient/nurse booklet, and key information about the trial will be displayed in ICU rooms to remind staff.

Relevant concomitant care and interventions that are permitted or prohibited during the trial

Post-resuscitation care will be provided following the most recent and current guidelines including a search for the cause of CA, especially coronary artery occlusion and targeted temperature management.¹⁸

Regards to the hemodynamic failure, norepinephrine tartrate 8 mg/4mL will be used in all patients included in the HYVAPRESS study. To make the doses of norepinephrine comparable across involved centres, the dilution as well as the infusion rate and the weight of the patient will be collected.¹⁹ The final results will be expressed as norepinephrine-base.²⁰ In case of myocardial dysfunction, inotropic support will be used at the physician in charge discretion.

Neuroprognostication will be performed on all patients still comatose in the ICU 96 h after randomization. The prognostication process will be based on the European Resuscitation Council and European Society for Intensive Care Medicine guidelines.²¹ All patients will be actively treated for 96 h after CA except in two cases: 1) patients in whom further treatment is considered unethical due to irreversible organ failure, disseminated malignancy or other reasons and 2) patients in whom brain death is established.

Outcomes

Primary, secondary and other outcomes

The primary outcome is a favorable neurological status at 30 days, defined as a score of 4 or 5 on the Glasgow Outcome Scale (GOS).²² This will be assessed via in-hospital visits or phone calls to patients, relatives, or general practitioners. The GOS has been widely used in the evaluation of the post-anoxic damage and is a reliable tool in in-person and phone interviews.^{23–25}

The secondary outcomes will include: day-30 all-cause mortality, cause of death according to the classification provided by Witten and colleagues²⁶ (day-30 mortality attributed to irreversible hemodynamic failure, neurological withdrawal of care based on expectations of a poor neurological recovery, comorbid withdrawal of care based on the expectation of a poor quality of life, related to a preexisting or newly discovered terminal illness or other serious medical condition, brain death, recurrent cardiac arrest), neurological recovery at day-30, using the GOS-extended score, brain damage, using the neuron-specific enolase blood level at h48 and h72, number of days between inclusion and day-30 without 1) catecholamines, 2) norepinephrine, 3) AVP, 4) inotropic support, 5) mechanical ventilation, 6) renal replacement therapy, atrial fibrillation new onset between inclusion and day-30, left ventricular systolic function assessed at day-1, 2, 3 and 7, acute kidney injury at day-7 and day-30 according to the KDIGO (Kidney Disease – Improving Global Outcome) classification,²⁷ safety related to AVP use: acute coronary syndrome, mesenteric ischemia and digital ischemia, safety related to HSHC use: gastrointestinal bleeding and hyperglycemias, ICU and hospital length of stay.

To categorize patients with multiple potential causes of death, an attempt should be made to identify the primary cause of death of reason for withdrawal of care. The classification of cause of death will be performed by a blinded adjudication committee, according to the classification described above.

Participant timeline

The participant timeline is provided in the [Table 1](#).

Hemodynamic data will be recorded every 2 h for the first 3 days. Urine output will be recorded every 6 h. All the other variables will be daily collected.

From day-3 to day-7, hemodynamic data will be recorded every 12 h.

Daily blood sample includes troponine, sodium, potassium and creatinine blood levels.

Recruitment

The HYVAPRESS study will be supported by two active research networks, highly trained in supporting multicentre trials: the INI-CRCT as well as the AfterRosc networks.

The Investigator Network Initiative Cardiovascular and Renal Clinical Trialists (INI-CRCT) is an international organization of academic cardiovascular and renal clinical trialists dedicated to improving outcomes among patients with chronic renal or cardiac disease (<https://www.inicrct.org/en/home>). This international consortium has large experience in clinical trials and have long been recruiting in trials. Several INI-CRCT members are involved in the present application. Logistic assistance will be provided by the INI-CRCT network (with e-learning software, elaboration of communication tools (flyers, newsletters... organization of investigator meetings) aiming at optimizing the proactive recruitment strategies and ensure optimal compliance to the protocol. A flyer summarizing the protocol (goals, design, potential risks and benefits for the patient) will be handed to the hospital staffs (praticians, nurse).

The After-ROSC network (<https://afterrosc.org>) gathers a large number of critical care physicians specialized in post CA care in France and Belgium. Support from the After-ROSC network ensures participation of very active teams since most of participants are involved in post resuscitation clinical research. Most of the After-ROSC network members are involved in the current project.

Methods: Assignment of interventions

Allocation concealment mechanism

Patients will be randomized centrally using stratified blocked randomization into four groups at the baseline visit. The randomization will be centralized and performed with an internet-centralized service running 24/24 using the Cleanweb software, also used for the electronic case report form (eCRF). Randomization will be performed in a 1:1:1:1 ratio using an eCRF by the principal investigator or a physician representing the investigator. The patient will be randomized after informed consent as soon as possible once he will meet the inclusion criteria. Randomization will be stratified on centres at the time of inclusion.

Blinding

All investigators, nurses, and healthcare providers involved in patient care will be blinded to treatment allocation. To achieve blinding, HSHC and placebo vials will be prepared identically by SERB Pharmaceuticals, while AVP vials will be masked using a thermoformed sheath as illustrated in [Fig. 3](#). Unblinding will only be permissible in emergency cases where the patient's clinical condition necessitates knowledge of the treatment received or in response to a suspected unexpected serious adverse event.

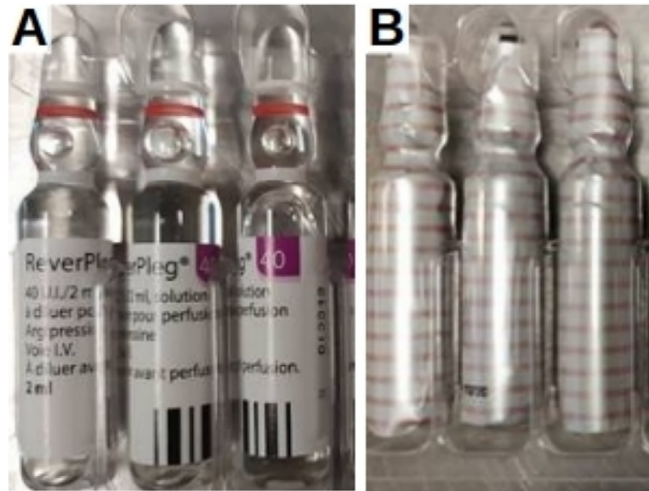


Fig. 3 – Blinding using thermoformed sheath.

Statistical methods

The HYVAPRESS study is an intention-to-treat designed study. No interim analysis is planned. Statistical analyses will be performed at the end of the follow-up of all randomized patients. Data will be analyzed using the R language (v3.0 R Foundation for Statistical Computing, Vienna Austria. <https://www.R-project.org/>).

Baseline characteristics of patients will be described according to the nature of the variable. Continuous variables will be expressed as means \pm standard deviations and median [interquartile range] as appropriate for the whole population and for each of the four arms separately. Categorical variables will be expressed as number and percentage, for the whole population and for each of the four arms separately.

Primary and secondary outcomes

The study was designed for efficiency and assumed no interaction between the interventional drugs. Thus, the main effects of each drug will be analysed separately. The primary endpoint will be evaluated using a logistic regression with main terms corresponding to AVP and hydrocortisone, allowing to assess the overall effect of each drug. However, the interaction between the two drugs will be explored as a sensitivity analysis. All secondary outcomes expressed as proportions will be evaluated similarly to the primary outcome, as well as the GOS-extended score at day-30. Time to death (overall mortality, specific cause of mortality and other cause of mortality) will be analysed using a Cox regression model to estimate hazard ratios between the groups. The distribution of the other secondary and quantitative outcomes will be compared between patients randomised to AVP and those randomised to hydrocortisone using a Student test or a Wilcoxon test. A per-protocol analysis will be performed as well to evaluate the effect of treatments on patients with no protocol deviation.

The following sub-group analyses will be performed on the primary outcome: 1/ patients with acute kidney injury at admission, according to the severity assessed by the KDIGO classification, 2/ patients with myocardial dysfunction, 3/ Patients classified according to the CAHP (Cardiac Arrest Hospital Prognosis) score²⁸ divided in 3 categories: <150, 150–200 and > 200.

Sample size calculation

The study assumes a 30% rate of favorable neurological outcomes (GOS 4 or 5) at day 30. Given the 2x2 factorial design and a two-

sided test, 95 patients are needed in each group (for a total of 380 participants) to detect an absolute difference of 15 percentage points in the primary outcome with a significance level of 0.05 and a power of 85%, accounting for an estimated 3% loss to follow-up. No interactions between the interventions are anticipated.

Participants lost to follow-up, deceased, or withdrawn from the study will be censored at their last recorded date. Missing data will be imputed using the Last Observation Carried Forward (LOCF) method, with multiple imputations performed if necessary. In cases where participants are lost to follow-up at day 30, the National Registry of Identification of Physical Persons (RNIPP) will be consulted to determine vital status.

All statistical analyses will be performed with a two-tailed significance level of 5%. Results will be presented with 95% confidence intervals.

Discussion

The HYVAPRESS trial will be the first randomized controlled study to evaluate the combined effects of arginine-vasopressin and hydrocortisone in managing acute circulatory failure during the early stages of post-resuscitation shock. This approach addresses a potentially critical hormonal deficiency that may exacerbate the already complex and multifactorial hemodynamic failure seen in these patients.

There is a lack of evidence that could support the daily use of AVP in successfully resuscitated cardiac arrest patients. In the international guidelines, no reference is made on the possibility to use AVP in this setting. Most recent guidelines discussed the potential interest of hormonal supplementation but mostly highlight the lack of evidence to support a systematic use of steroids in hemodynamic failure related to post-resuscitation shock.²⁹ Moreover, the interaction between AVP and steroids remains a matter of debate. In hemodynamic unstable patients successfully resuscitated from cardiac arrest, no available data might help to resolve the debate. While there is evidence for depletion in both hormones in these patients, no data can support or refute the presence or the absence of a clinically relevant interaction between these two treatments. Finally, the potential beneficial effect of AVP on the kidney function during vasoplegia will be of interest. Besides the direct impact of AVP on hemodynamic condition, it has been reported

that AVP may prevent organ dysfunction, especially acute kidney injury.^{30,31} Taken together, we believe that the combination of AVP and steroids, as an active substitutive opotherapy, could counteract deleterious effects of post-resuscitation events, mostly related to hemodynamic failure and spare adverse effects of norepinephrine on splanchnic and renal perfusions.

To date, limited trials have focused on acute circulatory failure in patients successfully resuscitated from cardiac arrest. This scarcity may be attributed to two key factors: first, a perception that a portion of these patients are moribund and therefore unsuitable for inclusion in randomized controlled trials; second, a belief that targeting specific drugs in such a complex clinical scenario might be futile. Despite these challenges, we believe that the early inclusion of patients with post-resuscitation shock in clinical trials is crucial. It is the only way to address the mortality driven by organ failure and thus accurately assess the extent of anoxic brain damage. Additionally, the factorial design of the HYVAPRESS trial is expected to mitigate numerous biases that may arise in this context.

At the time of protocol design and writing, we made the choice of the GOS as the main endpoint of the HYVAPRESS trial. In the meantime, the ILCOR COSCA highlighted the importance of the modified Rankin scale as an outcome in cardiac arrest patients.³² The GOS and the modified Rankin scale strongly correlate and Gaasta and colleagues reported the possibility of interconnection between both scores in brain-injured patients.³³ Moreover, we planned to collect as a secondary outcome the GOS-extended, which is considered by the ILCOR COSCA to provide improved granularity.

Ethics and dissemination

Research ethics approval

The HYVAPRESS study has been granted authorization from the Research Ethics Committee as well as from the French Health Products Safety Agency (risk "C": drugs already authorized in other medical conditions).

Consent or assent

As the patient eligible for the study will be unable to provide consent within the time window allowed by the protocol, his or her authorized persons (members' family, trusted person) may be approached in person. The local medical team could also enrol eligible patients and obtain consent subsequently.

Furthermore, this study is conducted in emergency situations (Article 35 of the European regulation N°536/2014) and involving individuals potentially unable to give consent. If the patient's legally authorized close relative is not present at the time of inclusion criteria fulfillment, the patient will be included in emergency situation (article 35 of the European regulation N°536/2014). The patient or, where applicable, the members of the family or the of trust shall be informed as soon as possible and their consent shall be sought from them for the possible continuation of such research. They may also object to the use of personal data in the context of this research.

The use of an emergency inclusion in last resort will be justified by the following arguments: –The potential lack of next ok kin available in the time window of inclusion –The urgent need to include patients 24/24 7/7.

If the person is physically unable to give his or her written consent, consent may be witnessed, in descending order of priority, from a trustworthy person, a family member or a close relative. These persons must be fully independent of the investigator and of the sponsor.

The clinical research team, after checking the inclusion criteria will acquire consent of the next-of-kin, and afterwards of the patient if he is able to give it.

The HYVAPRESS trial has already been approved by a national REB (CPP SUD-EST IV, initial approval on 2021/01/13, last updated approval 2024/04/04) and authorized by the ANSM (Autorité Nationale de Sécurité du Médicament) on 2021/01/08.

Access to data

Data will be accessible on reasonable request.

Ancillary care and care after the trial

Standard care will be provided after completion of the trial.

Dissemination policy

The results will be submitted for publication in a peer-review journal. They may also be presented in international meetings.

Ethics approval and consent to participate
Consent for publication
Availability of data and materials
Competing interests
Funding
Authors' contributions
Acknowledgements
Authors' information (optional).

Declaration of interests

The coordinator-investigator (GG) received consulting fees from BD/BARD in 2021 and 2022. No involvement of BD/BARD in any kind is ongoing in the HYVAPRESS trial.

CRedit authorship contribution statement

Guillaume Geri: Supervision, Resources, Methodology, Investigation, Conceptualization. **Jean-Baptiste Lascarrou:** Methodology, Investigation, Conceptualization. **Bruno Levy:** Investigation. **Pierre Asfar:** Investigation. **Grégoire Muller:** Investigation. **Stéphane Legriel:** Investigation. **Sylvie Ricôme:** Investigation. **Martin Cour:** Investigation. **Kada Klouche:** Investigation. **Bertrand Sauneuf:** Investigation. **Jean Pierre Quenot:** Investigation. **Wulfran Bougouin:** Investigation, Conceptualization. **Alain Cariou:** Writing – original draft, Resources, Methodology, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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REFERENCES

- Bougouin W, Lamhaut L, Marijon E, et al. Characteristics and prognosis of sudden cardiac death in Greater Paris. *Intensive Care Med* 2014;40(6):846–54.
- Binois Y, Renaudier M, Dumas F, et al. Factors associated with circulatory death after out-of-hospital cardiac arrest: A population-based cluster analysis. *Ann Intensive Care* 2023;13(1):49.
- Chan PS. A validated prediction tool for initial survivors of in-hospital cardiac arrest. *Arch Intern Med* 2012;172(12):947–57.
- Lemiale V, Dumas F, Mongardon N, et al. Intensive care unit mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort. *Intensive Care Med* 2013;39(11):1972–80.
- Mongardon N, Dumas F, Ricome S, et al. Postcardiac arrest syndrome: from immediate resuscitation to long-term outcome. *Ann Intensive Care* 2011;1(1):45.
- Adrie C, Adib-Conquy M, Laurent I, et al. Successful cardiopulmonary resuscitation after cardiac arrest as a “sepsis-like” syndrome. *Circulation* 2002;106(5):562–8.
- Chang WT, Ma MHM, Chien KL, et al. Postresuscitation myocardial dysfunction: correlated factors and prognostic implications. *Intensive Care Med* 2007;33(1):88–95.
- Roberts BW, Kilgannon JH, Chansky ME, Mittal N, Wooden J, Trzeciak S. Association between postresuscitation partial pressure of arterial carbon dioxide and neurological outcome in patients with post-cardiac arrest syndrome. *Circulation* 2013;127(21):2107–13.
- Trzeciak S, Jones AE, Kilgannon JH, et al. Significance of arterial hypotension after resuscitation from cardiac arrest*. *Crit Care Med* 2009;37(11):2895–903.
- Grimaldi D, Guivarch E, Neveux N, et al. Markers of intestinal injury are associated with endotoxemia in successfully resuscitated patients. *Resuscitation* 2013;84(1):60–5.
- Little RA, Frayn KN, Randall PE, et al. Plasma catecholamines in patients with acute myocardial infarction and in cardiac arrest. *Q J Med* 1985;54(214):133–40.
- Lindner KH, Haak T, Keller A, Bothner U, Lurie KG. Release of endogenous vasopressors during and after cardiopulmonary resuscitation. *Heart* 1996;75(2):145–50.
- Russell JA, Walley KR, Gordon AC, et al. Interaction of vasopressin infusion, corticosteroid treatment, and mortality of septic shock. *Crit Care Med* 2009;37(3):811–8.
- Russell JA, Walley KR, Singer J, et al. Vasopressin versus norepinephrine infusion in patients with septic shock. *N Engl J Med* 2008 Feb;358(9):877–87.
- Mayr V, Luckner G, Jochberger S, et al. Arginine vasopressin in advanced cardiovascular failure during the post-resuscitation phase after cardiac arrest. *Resuscitation* 2007;72(1):35–44.
- Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest. *JAMA* 2013;310(3):270.
- Donnino MW, Andersen LW, Berg KM, et al. Corticosteroid therapy in refractory shock following cardiac arrest: a randomized, double-blind, placebo-controlled, trial. *Crit Care* 2016;1–8.
- Nolan JP, Berg RA, Andersen LW, et al. Cardiac Arrest and Cardiopulmonary Resuscitation Outcome Reports: Update of the Utstein Resuscitation Registry Template for In-Hospital Cardiac Arrest: A Consensus Report From a Task Force of the International Liaison Committee on Resuscitation (American Heart Association, European Resuscitation Council, Australian and New Zealand Council on Resuscitation, Heart and Stroke Foundation of Canada, InterAmerican Heart Foundation, Resuscitation Council of Southern Africa, Resuscitation Council of Asia). *Resuscitation* 2019;144:166–77.
- Leone M, Goyer I, Levy B, Dünser MW, Asfar P, Jentzer JC. Dose of norepinephrine: The devil is in the details. *Intensive Care Med* 2022;48(5):638–40.
- Kotani Y, Belletti A, D’Andria Ursileo J, Salvati S, Landoni G. Norepinephrine dose should be reported as base equivalence in clinical research manuscripts. *J Cardiothorac Vasc Anesth*. 2023;37(9):1523–4.
- Nolan JP, Soar J, Cariou A, et al. European Resuscitation Council and European Society of Intensive Care Medicine 2015 guidelines for post-resuscitation care. *Intensive Care Med* 2015;41(12):2039–56.
- Jennett B, Bond M. Assessment of outcome after severe brain damage. *Lancet* 1975;1(7905):480–4.
- Rana OR, Saygili E, Schiefer J, Marx N, Schauer P. Biochemical markers and somatosensory evoked potentials in patients after cardiac arrest: The role of neurological outcome scores. *J Neurol Sci*. 2011;305(1–2):80–4.
- Pettigrew LEL, Wilson JTL, Teasdale GM. Reliability of ratings on the glasgow outcome scales from in-person and telephone structured interviews. *J Head Trauma Rehabil* 2003;18(3):252–8.
- Wilson JT, Pettigrew LE, Teasdale GM. Structured interviews for the glasgow outcome scale and the extended glasgow outcome scale: Guidelines for their use. *J Neurotrauma*. 1998;15(8):573–85.
- Witten L, Gardner R, Holmberg MJ, et al. Reasons for death in patients successfully resuscitated from out-of-hospital and in-hospital cardiac arrest. *Resuscitation* 2019;136:93–9.
- KDIGO AKI Guideline Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney International Supplements*. 2012;2(1):1–138.
- Maupain C, Bougouin W, Lamhaut L, et al. The CAHP (cardiac arrest hospital prognosis) score: A tool for risk stratification after out-of-hospital cardiac arrest. *Eur Heart J* 2016;37(42):3222–8.
- Nolan JP, Sandroni C, Böttiger BW, et al. European resuscitation council and european society of intensive care medicine guidelines 2021: Post-resuscitation care. *Resuscitation* 2021;161:220–69.
- Gordon AC, Russell JA, Walley KR, et al. The effects of vasopressin on acute kidney injury in septic shock. *Intensive Care Med* 2010;36(1):83–91.
- Gordon AC, Mason AJ, Thirunavukkarasu N, et al. Effect of early vasopressin vs norepinephrine on kidney failure in patients with

- septic shock: the VANISH randomized clinical trial. *JAMA* 2016;316(5):509–18.
32. Haywood K, Whitehead L, Nadkarni VM, et al. COSCA (core outcome set for cardiac arrest) in adults: An advisory statement from the international liaison committee on resuscitation Available from. *Circulation* [Internet] 2018;137(22):e783–801. Available from: <https://www.ahajournals.org/doi/abs/10.1161/CIR.000000000000562>.
33. Gaastra B, Ren D, Alexander S, et al. Evidence-based interconversion of the glasgow outcome and modified rankin scales: Pitfalls and best practices. *J Stroke Cerebrovasc Dis* 2022;31(12) 106845.