Syndrome post-arrêt cardiaque

Alain Cariou
Intensive Care Unit - Cochin Hospital
Paris Descartes University – INSERM U970
COI disclosure

- Lilly France
- Edwards LifeSciences
- Bard
Paul M, 50 yo

- Past medical history
  - Appendectomy
  - Smoker

- Ongoing medication
  - None
April 12, 2015…

- 11:21 First collapse
- 11:23 EMS call
- 11:25 Second collapse
- 11:29 EMS arrival (start CPR, AED use)
AED pattern
Defibrillations, n=6
ROSC

No-flow = 3-4 minutes, low-flow = 24 minutes
After ROSC

- $\text{SpO}_2 = 95\%$, AP 103/55 mmHg, HR= 105 /min
- Glasgow Coma Scale 3
- Spontaneous ventilation, aspiration
- Intubation, mechanical ventilation
- First ECG: unclear but no ST elevation
Paul M.  Shock  Coma  Multiple Organ Failure
The challenge is not only before hospital arrival!

- 40,000 SCA/yrs
- 60% CPR
- 15-20% ROSC...

...and ICU admission

- 5-10% survivors
- 7% no or minor sequel

Long-term

Post-resuscitation:
- Post-cardiac arrest shock
- Brain damages
Vladimir Negovski with Peter Safar in 1962, Moscow
Shock
ICU mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort
Lemiale V, Dumas F, Mongardon N, Giovanetti O, Charpentier J, Chiche JD, Carli P, Mira JP, Nolan J, Cariou A
Intensive Care Med 2013
Paul M, ICU admission
Reversible myocardial dysfunction after CPR
Myocardial Dysfunction After Resuscitation From Cardiac Arrest: An Example of Global Myocardial Stunning

**Design:** 28 domestic swines studied before and after CA

![Graph showing myocardial blood flow and ejection fraction before and after 30 min, 2 hours, 5 hours, and 48 hours.]
Post-CA myocardial dysfunction

Defibrillation

Coronary occlusion

Ischemia-reperfusion

Drug toxicity (epinephrine?)

SIRS
# Percutaneous Circulatory Support

## IABP vs. TandemHeart

<table>
<thead>
<tr>
<th></th>
<th>IABP</th>
<th>TandemHeart</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pump mechanism</td>
<td>Pneumatic</td>
<td>Centrifugal</td>
</tr>
<tr>
<td>Insertion</td>
<td>Retrograde 7–9F balloon catheter into the descending aorta via the femoral artery</td>
<td>21F inflow cannula into the left atrium via the femoral artery</td>
</tr>
<tr>
<td>Difficulty of insertion</td>
<td>+++</td>
<td>+ + (Increased CO by 2.5 L/min)</td>
</tr>
<tr>
<td>Degree of circulatory support (with ideal SVR)</td>
<td>+++</td>
<td>++++ (Increased CO to ( \geq 4.5 ) L/min)</td>
</tr>
<tr>
<td>Implantation time, minutes</td>
<td>11–25</td>
<td>10–15</td>
</tr>
<tr>
<td>Limb ischemia</td>
<td>+++</td>
<td>+ +</td>
</tr>
<tr>
<td>Hemolysis</td>
<td>+++</td>
<td>+++</td>
</tr>
<tr>
<td>Bleeding risk</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>510k Approval by FDA</td>
<td>6</td>
<td>++++</td>
</tr>
<tr>
<td>Evidence of efficacy</td>
<td>Increased CO and coronary and peripheral perfusion; deceased afterload</td>
<td>Increased CO, MAP, ( M_{\text{VO}_2} ), and urine output; decreased lactic acid, creatinine, and PCWP</td>
</tr>
<tr>
<td>Evidence of efficacy</td>
<td>Increased CO and MAP; decreased lactic acid and PCWP</td>
<td>Increased CO, MAP, and oxygenation</td>
</tr>
</tbody>
</table>

SVR indicates systemic vascular resistance; CO, cardiac output; MAP, mean arterial pressure; \( M_{\text{VO}_2} \), mixed venous oxygen saturation; and PCWP, pulmonary capillary wedge pressure.

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Bridges to neurological evaluation
Myocardial dysfunction

Systemic Inflammatory Response

Coronary occlusion

Oxygen toxicity

Post-resuscitation shock
Reversible Myocardial Dysfunction in Survivors of Out-of-Hospital Cardiac Arrest
J Am Coll Cardiol 2002
Successful CPR After Cardiac Arrest as a "Sepsis-Like" Syndrome

Kinetics of cytokines and sTNFRII levels on admission and over a 7-day period in 61 resuscitated survivors (n=18, open diamonds) and nonsurvivors (n=43, black squares) of OHCA.

Adrie et al. Circulation. 2002;106:562
1. Ischemia and reperfusion syndrome
2. Inflammatory response
3. Coagulopathy
4. Circulatory failure
5. Adrenal dysfunction
Markers of intestinal injury are associated with endotoxemia in successfully resuscitated patients
Grimaldi D et al. Resuscitation 2013

Gut injury is common after cardiac arrest

Endotoxemia is frequent after OHCA and is correlated with biomarkers of gut injury
High level of endotoxemia following out-of-hospital cardiac arrest is associated with severity and duration of post cardiac arrest shock

Vasopressor free days according to endotoxemia level

Etx level according to the presence of post-CA shock
The splanchnic hypothesis...

Gut injury

- ↑ urinary IFABP
- ↓ plasmatic Citrulline

⇒ LPS

⇒ Shock

Inflammatory gene expression
High-Volume Hemofiltration after Out-of-Hospital Cardiac Arrest. A randomized study.
J Am Coll Cardiol 2005

Six-month survival:
- Controls 21%
- HF alone 42% \( p=0.28 \)
- HF + HT 32%

Death by intractable shock (IS):
- Controls 42%
- HF alone 10% \( p=0.009 \)
- HF + HT 14%

Relative risk of death by IS:
- HF alone 0.21 (95% CI 0.5-0.85)
- HF + HT 0.29 (95% CI 0.09-0.91)

Multivariate analysis:
- HF and six-month death: OR 0.21 (95% CI 0.5-0.85)
- HF and death by IS: OR 0.29 (95% CI 0.09-0.91)
Hemodynamic Efficiency of an Hemodialysis Treatment With High Permeability in Post-resuscitation Shock (Hyperdia)

This study is currently recruiting participants. (see Contacts and Locations)

Verified April 2015 by Assistance Publique - Hôpitaux de Paris

Sponsor:
Assistance Publique - Hôpitaux de Paris

Collaborator:
Gambro Industries, MEYZEU, France

Information provided by (Responsible Party):
Assistance Publique - Hôpitaux de Paris

ClinicalTrials.gov Identifier:
NCT00780289

First received: October 24, 2008
Last updated: April 20, 2015
Last verified: April 2015

Purpose

Rationale: Despite spontaneous cardiac activity recovery, a shock occurs in more than half of patients after resuscitation for cardiac arrest. This acute circulatory insufficiency presents similar characteristics with septic shock and is responsible of most early deaths. Most frequently, usual treatments are unable to control this shock and to avoid the appearance of multiple organ failure.

Aim of the study: In addition to conventional therapeutics, an early plasma epuration of inflammatory mediators (HDHP) could be able to improve hemodynamic parameters and to reduce the shock duration. This improvement could have an impact on multiple organ dysfunctions and also on early mortality.
Should we care about oxygen after cardiac arrest?
In particular, a 25 mmHg increase in PaO2 was associated with 6% increase in relative risk of death (odds ratio [OR] 1.06 [1.05-1.07]).
## Experimental studies on effects of avoiding hyperoxia after cardiac arrest

<table>
<thead>
<tr>
<th>Author, year</th>
<th>N. of subjects (species)</th>
<th>FiO₂ prior to cardiac arrest</th>
<th>FiO₂ after ROSC in the low FiO₂ group</th>
<th>FiO₂ after ROSC in control group</th>
<th>Titration</th>
<th>Main findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Balan 2006 29</td>
<td>17 (beagle)</td>
<td>21%</td>
<td>100% titrated to 21-30% in 12 min (target: 95-96% SpO₂)</td>
<td>100% for 1 h</td>
<td>Yes</td>
<td>Oximetry-guided reoxygenation was associated to a significantly lower NDS and less histopathological changes</td>
</tr>
<tr>
<td>Brucken 2010 28</td>
<td>15 (pig)</td>
<td>21%</td>
<td>100% in the first 10 min followed by 30%</td>
<td>100% for 1 h</td>
<td>No</td>
<td>Normoxic animals had a lower NDS and significantly less histopathological changes</td>
</tr>
<tr>
<td>Lipinski 1999 24</td>
<td>22 (rat)</td>
<td>Not reported (1)</td>
<td>21%</td>
<td>100% for 1 h</td>
<td>Yes</td>
<td>NDS and histopathological changes did not significantly differ between the two groups</td>
</tr>
<tr>
<td>Liu 1998 20</td>
<td>20 (beagle)</td>
<td>21%</td>
<td>21%-30%</td>
<td>100% for 1 h</td>
<td>Yes</td>
<td>Normoxic animals had a lower NDS and significantly less histopathological changes</td>
</tr>
<tr>
<td>Marsala 1992 26</td>
<td>10 (mongrel)</td>
<td>21%</td>
<td>21%</td>
<td>100% for 1 h</td>
<td>No</td>
<td>Normoxic animals had significantly less histopathological changes</td>
</tr>
<tr>
<td>Richards 2006 22</td>
<td>16 (beagle)</td>
<td>21%</td>
<td>21-30% for 2 h</td>
<td>100% for 1 h and titration for 1 h</td>
<td>Yes (2)</td>
<td>Normoxic animals had less metabolic changes in the brain</td>
</tr>
<tr>
<td>Richards 2007 21</td>
<td>13 (beagle)</td>
<td>21%</td>
<td>21-30% for 2 h</td>
<td>100% for 1 h and titration for 1 h</td>
<td>Yes (2)</td>
<td>Normoxic animals had less metabolic changes in the brain</td>
</tr>
<tr>
<td>Vereczki 2006 23</td>
<td>12 (beagle)</td>
<td>21%</td>
<td>21% for 1 h</td>
<td>100% for 1 h</td>
<td>Yes (3)</td>
<td>Normoxic animals had less histopathological and metabolic changes in the brain</td>
</tr>
<tr>
<td>Zwemer 1995 25</td>
<td>19 (mongrel)</td>
<td>21%</td>
<td>21% for 15 min</td>
<td>8.5% or 12% for 15 min</td>
<td>No</td>
<td>Normoxic animals had a higher NDS than hypoxic group</td>
</tr>
</tbody>
</table>

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_Sandroni C. Minerva Anesth 2014_
Comparison of 30 and the 100% inspired oxygen concentrations during early post-resuscitation period: a randomised controlled pilot study

Kuisma M et al. Resuscitation 2006

"Except in the (very) small subgroup of patients who were not treated with hypothermia, neither blood levels of neuron-specific enolase (NSE) and S-100 protein nor survival to discharge differed significantly between the two group"
ICU management

- Temperature control: constant temperature 32°C – 36°C for ≥ 24h; prevent fever for at least 72 h
- **Maintain normoxia and normocapnia; protective ventilation**
- Optimise haemodynamics (MAP, lactate, ScvO₂, CO/Cl, urine output)
- Echocardiography
- Maintain normoglycaemia
- Diagnose/treat seizures (EEG, sedation, anticonvulsants)
- Delay prognostication for at least 72 h
Myocardial dysfunction

Systemic Inflammatory Response

Coronary occlusion

Oxygen toxicity

Post-resuscitation shock
Paul M, post ROSC

Should we perform a coronary angiogram?

If yes, when?

If there’s a culprit lesion, should we do a PCI?
Benefit of an early and systematic imaging procedure after cardiac arrest: insights from the PROCAT (Parisian Region Out of Hospital Cardiac Arrest) registry.

J CHELLY, N MONGARDON, F DUMAS, O VARENNE, C SPAULDING, O VIGNAUX, P CARLI, J CHARPENTIER, F PENE, JD CHICHE, JP MIRA, A CARIOU

Resuscitation 2009
Is emergent PCI associated with a clinical benefit in post-cardiac arrest patients without ST segment elevation pattern? Insights from the Parisian registry (PROCAT II)
Immediate percutaneous coronary intervention is associated with improved short and long-term outcome after out-of-hospital cardiac arrest


Circulation Cardiovasc Interv 2015
Targeted Temperature Management for Comatose Survivors of Cardiac Arrest

Michael Holzer, M.D.
ICU management

- Temperature control: constant temperature 32°C – 36°C for ≥ 24h; prevent fever for at least 72 h
- Maintain normoxia and normocapnia; protective ventilation
- Optimise haemodynamics (MAP, lactate, ScvO₂, CO/Cl, urine output)
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ICU mortality after cardiac arrest: the relative contribution of shock and brain injury in a large cohort

Lemiale V, Dumas F, Mongardon N, Giovanetti O, Charpentier J, Chiche JD, Carli P, Mira JP, Nolan J, Cariou A

Intensive Care Med 2013

Need for neuroprotective treatments...
Early high-dose erythropoietin therapy after out-of-hospital cardiac arrest: a multicentre, randomized controlled trial (EPO-ACR 02)

EPO-ACR 02 Scientific committee:
- Alain Cariou (PI)
- Pierre Carli
- Christian Spaulding
- Olivier Hermine

EPO-ACR 02 Executive committee:
- Nicolas Deye
- Maryline Delattre
- Benoit Vivien

Statisticians:
- Myriam Ben Boutieb
- Joël Coste

Pharmacist:
- Florence Barat

Funding:
- French Ministry of Health

EPO-ACR 02 Investigators:
- P. Asfar (Angers)
- A. Bourg (Limoges)
- C. Buléon (Caen)
- JD. Chiche (Paris)
- A. Combes (Paris)
- A. Cravoisy (Nancy)
- C. Daubin (Caen)
- PF. Dequin (Tours)
- P. Ecollan (Paris)
- J. Frey (Nancy)
- L. Huet (Créteil)
- A. Khimoun (Nancy)
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- JS. Marx (Paris)
- A. Mathonnet (Orléans)
- JP. Mira (Paris)
- S. Narcisse (Orléans)
- D. Payen (Paris)
- F. Pène (Paris)
- N. Pichon (Limoges)
- K. Razazi (Créteil)
- O. Richard (Versailles)
- E. Wiel (Lille)
EPO-ACR 02: primary endpoint

CPC level at day 60 (%)

OR 1.01
95% CI
0.68-1.48

32.4 32.1
EPO-ACR 02: primary endpoint

CPC level at day 60 (%)

P=0.90

OR 1.01
95%CI
0.68-1.48

* 1 unknown
Neuroprotection after cardiac arrest: what’s new?

- Calcium channel antagonists
- NMDA receptor antagonists
- Dexamabinol
- Lubeluzole (Nitrous oxide modulator)
- CDP-choline
- Tirilizad (free radical scavenger)
- Anti-ICAM-1 antibody
- GM-1 ganglioside
- Clomethiazole
- Fosphenytoin
- Piracetam

Erythropoietin
Selenium
Ciclosporine
Trends in Short- and Long-Term Survival Among OHCA Patients Alive at Hospital Arrival
Wong MKY et al. Circulation 2014
Suite à un arrêt cardiaque le 1er juillet, notre père a été hospitalisé dans votre service. Nous voulons vous remercier pour votre efficacité, non seulement technique, mais aussi votre aptitude à expliquer, à répondre aux questions de manière compréhensible et votre disponibilité.

Néanmoins, toute votre équipe soignante — pour son investissement et pour le soutien moral, en particulier l'intervenant de la kiné qui était à l'habitude aussi que de ma vie — ainsi que les soins médicaux et les soins de confort qu'apportent à notre père.

Salutations distinguées,

Julia
et ses frères et sœurs.

27.01.2015
Quality of Life and Functional Outcomes 12 Months After OHCA

Smith K et al. Circulation 2014

EuroQoL-5D scores at 12 months postarrest. n=687.

Standardized mean difference of SF-12 scores at 12 months for survivors vs Australian population norms. n=509