State of the art lecture:
21st Century Post resuscitation management

ACCA Masterclass 2017

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Intensive Care Unit - Cochin Hospital (APHP)
Paris Descartes University – INSERM U970 - France
COI disclosure

• **Bard** (fees for conferences)
The challenge is not only before hospital arrival!

Pre-hospital period:
- 40,000 SCA/yrs
- 60% CPR
- 15-20% ROSC...

...and ICU admission:
- 5-10% survivors
- 7% no or minor sequelae

Post-resuscitation:
- Post-cardiac arrest shock
- Brain damages

Long-term?
Trends in Short- and Long-Term Survival Among OHCA Patients Alive at Hospital Arrival
Wong MKY et al. Circulation 2014
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, hiche JD, Carli P, Mira JP, Nolan J, Cariou A.
Intensive Care Med 2013

![Graph showing delays between ICU admission and death (days)]
Coronary occlusion
Myocardial dysfunction
Systemic Inflammatory Response
Post-resuscitation shock
Post-CA myocardial dysfunction

- Coronary occlusion
- Ischemia-reperfusion
- Defibrillation
- Drug toxicity (epinephrine?)
- SIRS
Post-cardiac arrest shock
Bougouin W & Cariou A. Curr Opinion Crit Care  2013

- Diagnostic of PRMD
- Screening for ischemic cause
- Preload assessment
- Persistent hypoperfusion
- Refractory cardiogenic shock
- Persistent hypoperfusion despite conventional therapies
- Neurological prognosis assumed favorable?
- Fluid loading
- Inotropic + vasopressors
  - Dobutamine / Norepinephrine
- LV percutaneous mechanical assistance
  - IABP, minLV devices
- Mechanical heart assistance
  - ECLS

Hemodynamic optimization

Echocardiography
Coronary angiography
PCI

https://www.escardio.org/ACCA
Venoarterial extracorporeal membrane oxygenation for refractory cardiogenic shock post-cardiac arrest

Marc Pineton de Chambrun1,2, Nicolas Bréchet1,2, Guillaume Lebreton3, Matthieu Schmidt1,2, Guillaume Hekimian1,2, Pierre Demondion1, Jean-Louis Trouillet1,2, Pascal Leprince3, Jean Chastre1,2, Alain Combes1,2 and Charles-Edouard Luyt1,2


954 Venoarterial-extracorporeal membrane oxygenation–treated patients

94 Patients in cardiogenic shock post-cardiac arrest resuscitation

61 Patients not weaned-off venoarterial-extracorporeal membrane oxygenation

55 Deaths
39 Multiorgan failures
7 Anoxic encephalopathies
9 Brain deaths

6 28-day Survivors
(4 with left ventricle assist devices; 2 heart transplantsations)

3 Deaths after day 28

3 1-year Survivors

33 Patients successfully weaned-off venoarterial-extracorporeal membrane oxygenation

9 Deaths
2 Multiorgan failures
2 Anoxic encephalopathies
2 Brain deaths
3 Recurrent cardiac arrests

24 28-day Survivors

2 Deaths after day 28

22 1-year Survivors

860 Patients without prior cardiac arrest or refractory cardiac arrest

27%
Coronary occlusion

Myocardial dysfunction

Systemic Inflammatory Response

Post-resuscitation shock
Mild therapeutic hypothermia in patients after out-of-hospital cardiac arrest due to acute ST-segment elevation myocardial infarction undergoing immediate percutaneous coronary intervention

Sebastian Wolff, MD; Christian Pierau; Peter W. Radke, MD; Heribert Schunkert, MD; Volkhard Kurowski, MD

Acute Ischemic Heart Disease

Acute coronary angiographic findings in survivors of out-of-hospital cardiac arrest

Zacharias Alexandros Argyfantis, MD, a,1 Gabriel Baron, MSc,1 Pierre Aubry, MD, a Dominique Hemberter, MD, a Laurent J. Feldman, MD, PhD, a Jean-Michel Juliard, MD, a Agnès Ricard-Hibon, MD, a Alexis Baroud, MD, a Dennis V. Kokkinos, MD, b and Philippe Gabriel Seg, MD a Paris and Clichy, France and Athens, Greece

Six-Month Outcome of Emergency Percutaneous Coronary Intervention in Resuscitated Patients After Cardiac Arrest Complicating ST-Elevation Myocardial Infarction

Philippe Garot, MD; Thierry Lefèvre, MD; Hélène Eltchaninoff, MD, PhD; Marie-Claude Morice, MD; Fabienne Tamion, MD; Bernard Aubry, MD; Pierre-François Lesault, MD; Jean-Yves Le Tarnec, MD; Claude Pouges, MD; Alain Margenet, MD; Mehran Monchi, MD; Ivan Laurent, MD; Pierre Dumas, MD; Jérôme Garot, MD, PhD; Yves Louvard, MD

Clinical paper

Post-resuscitation electrocardiograms, acute coronary findings and in-hospital prognosis of survivors of out-of-hospital cardiac arrest

Julio Garcia-Tejada a,*, Alfonso Jurado-Román a, Jesús Rodríguez b, Maite Velázquez a, Felipe Hernández a, Agustín Albarrán a, Roberto Martín-Asenjo b, Carolina Granda-Nistal a, Raúl Coma b, Juan Tascón a

Resuscitation 85 (2014) 1245–1250

CrossMark
Should We Perform an Immediate Coronary Angiogram in All Survivors of OHCA With No Obvious Extra-Cardiac Cause? Insights from the PROCAT registry

No obvious extra-cardiac cause
Immediate coronary angiogram
N=435

- ST-segment elevation
  N=134

  - At least one significant lesion
    N=128 (96%)

    - PCI attempted
      N=110 (82%)

      - PCI successful
        N=99 (74%)

- Other ECG pattern
  N=301

Dumas F, Cariou A, Spaulding C. Circulation Cardiovasc Interv 2010
Multivariate analysis of early predictors of survival in OHCA pts without obvious extra-cardiac etiology

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>[95% Conf.Interval]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BLS to ROSC &gt; 15 minutes</td>
<td>0.28</td>
<td>(0.19-0.55)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Collapse to BLS &gt; 5 minutes</td>
<td>0.32</td>
<td>(0.17-0.49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diabete mellitus</td>
<td>0.42</td>
<td>(0.20-0.84)</td>
<td>0.015</td>
</tr>
<tr>
<td>Age &gt; 59 yrs</td>
<td>0.45</td>
<td>(0.27-0.75)</td>
<td>0.002</td>
</tr>
<tr>
<td>Blood lactate</td>
<td>0.55</td>
<td>(0.44-0.70)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ST segment elevation</td>
<td>1.09</td>
<td>(0.60-1.98)</td>
<td>0.778</td>
</tr>
<tr>
<td>Initial Arrest Rhythm: VT/VF</td>
<td>1.82</td>
<td>(1.04-3.19)</td>
<td>0.035</td>
</tr>
<tr>
<td>Successful PCI</td>
<td>2.06</td>
<td>(1.16-3.66)</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Dumas F, Cariou A, Spaulding C. Circulation Cardiovasc Interv 2010
European Resuscitation Council Guidelines for Resuscitation 2015
Section 8. Initial management of acute coronary syndromes

Nikolaos I. Nikolaou\textsuperscript{a,\dagger}, Hans-Richard Arntz\textsuperscript{b}, Abdelouahab Bellou\textsuperscript{c}, Farzin Beygui\textsuperscript{d}, Leo L. Bossaert\textsuperscript{e}, Alain Cariou\textsuperscript{f}, Initial management of acute coronary syndromes section Collaborator\textsuperscript{1}

1. Based on the available data, emergent cardiac catheterisation lab evaluation (and immediate PCI if required) should be performed in selected adult patients with ROSC after OHCA of suspected cardiac origin with ST segment elevation on ECG.
Paul A, 67y

- Hypertension, smoking
- Resuscitated 1 hour ago from an OHCA:
  - No flow: 4 minutes
  - Low flow: 12 minutes
    - VF (3 DC shocks)
    - 2 mg epinephrine
- ECG post ROSC:

![ECG Image](image-url)
Should We Perform an Immediate Coronary Angiogram in All Survivors of OHCA With No Obvious Extra-Cardiac Cause? Insights from the PROCAT registry

No obvious extra-cardiac cause
Immediate coronary angiogram
N=435

ST-segment elevation
N=134

- At least one significant lesion
  N=128 (96%)
  PCI attempted
  N=110 (82%)
  PCI successful
  N=99 (74%)

- Other ECG pattern
  N=301

- At least one significant lesion
  N=176 (58%)
  PCI attempted
  N=92 (31%)
  PCI successful
  N=78 (26%)

Dumas F, Cariou A, Spaulding C. Circulation Cardiovasc Interv 2010
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)

Is delayed PCI equivalent to immediate PCI after CA?

- **Postresuscitation ECG**
  - **STEMI**
    - Absence of significant comorbidities and unfavorable cardiac arrest setting
    - **STEMI** fast track
  - **No STEMI**
    - **ER stop for fast diagnostic work up**
      - Additional history
      - Echocardiography
      - CT scan head/torax
      - Laboratory values
    - **Cardiac intensive care unit**

Immediate coronary angiography
Is early PCI associated with a clinical benefit in post-cardiac arrest patients without STEMI pattern? Insights from the Parisian registry (PROCAT II)

Multivariate analysis of predictors for good outcome in OHCA pts without obvious extra-cardiac etiology

<table>
<thead>
<tr>
<th>Predictor</th>
<th>Odds Ratio</th>
<th>[95% Conf. interval]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>0.97</td>
<td>[0.95-0.99]</td>
<td>0.002</td>
</tr>
<tr>
<td>Male gender</td>
<td>1.20</td>
<td>[0.69-2.09]</td>
<td>0.53</td>
</tr>
<tr>
<td>Diabetes</td>
<td>1.64</td>
<td>[0.89-3.0]</td>
<td>0.11</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.04</td>
<td>[0.63-1.72]</td>
<td>0.87</td>
</tr>
<tr>
<td>Smoking</td>
<td>1.18</td>
<td>[0.73-1.91]</td>
<td>0.50</td>
</tr>
<tr>
<td>Public location</td>
<td>1.25</td>
<td>[0.77-2.04]</td>
<td>0.37</td>
</tr>
<tr>
<td>Witnessed CA</td>
<td>3.21</td>
<td>[0.81-12.65]</td>
<td>0.10</td>
</tr>
<tr>
<td>Bystander CPR</td>
<td>1.37</td>
<td>[0.85-2.20]</td>
<td>0.19</td>
</tr>
<tr>
<td>Initial shockable rhythm</td>
<td>3.38</td>
<td>[1.94-5.87]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Resuscitation length &lt; 20 min</td>
<td>3.13</td>
<td>[1.93-5.07]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Epinephrine &lt; 2 mg during CPR</td>
<td>0.27</td>
<td>[0.16-0.46]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Targeted Temperature Management</td>
<td>0.93</td>
<td>[0.41-2.07]</td>
<td>0.85</td>
</tr>
<tr>
<td>Post cardiac arrest shock</td>
<td>0.57</td>
<td>[0.36-0.92]</td>
<td>0.02</td>
</tr>
<tr>
<td>PCI</td>
<td><strong>1.86</strong></td>
<td><strong>[1.13-3.08]</strong></td>
<td><strong>0.016</strong></td>
</tr>
</tbody>
</table>
Survival in patients without acute ST-elevation after CA and association to early coronary angiography - a post hoc analysis from the TTM trial
Direct or Subacute Coronary Angiography for Out-of-hospital Cardiac Arrest (DISCO)

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

Verified January 2015 by Uppsala University

**Sponsor:**
Uppsala University

**Collaborators:**
Stockholm South General Hospital
Stockholm University Hospital

**Information provided by (Responsible Party):**
Uppsala University

ClinicalTrials.gov identifier: NCT02309151
First received: November 17, 2014
Last updated: January 7, 2015
Last verified: January 2015

**Purpose**
The overall aim of this prospective, randomized pilot study is to investigate whether acute coronary angiography (within 120 minutes) with a predefined strategy for revascularization, is safe to implement in patients with out of hospital cardiac arrest. The primary question at issue is whether early angiography (within 120 minutes) with a predefined strategy for revascularization with percutaneous coronary intervention (PCI) is safe to carry out in this group of patients. The patients randomized to acute coronary angiography will be compared with a control group who will be treated according to standard practice with coronary angiography with possible subsequent intervention according to the current routine, which usually does not occur within the first three days after cardiac arrest.

**Criteria**

**Inclusion Criteria:**
- Witnessed out of hospital cardiac arrest
- Regained circulation (ROSC)
- Coronary angiography is expected to be completed within 120 minutes from first medical contact. This medical contact is included by ambulance or at the latest at the emergency room

**Exclusion Criteria:**
- Patient age <18 years
- Obvious extracardiac genesis of cardiac arrest such as trauma, hemorrhagic shock, and/or asphyxia (e.g., drowning, suffocation, hanging, exposure to fire smoke)
- Terminally ill patients with a life expectancy of less than 1 year
- Patients with ST-elevation on the first ECG will not be randomized in the study but observed and followed in the study.
- Known pregnancy
Based on the available data, emergent cardiac catheterisation lab evaluation (and immediate PCI if required) **should be performed** in selected adult patients with ROSC after OHCA of suspected cardiac origin with ST segment elevation on ECG.

In other patients, it is **reasonable to discuss** an emergent cardiac catheterisation lab evaluation after ROSC in patients with the highest risk of coronary cause of CA.
Post-resuscitation disease after cardiac arrest: a sepsis-like syndrome?
Adrie C, Laurent I, Monchi M, Cariou A, Dhainaut JF, Spaulding C.
Current Opinion in Crit Care 2004

1. Ischemia and reperfusion syndrome
2. Inflammatory response
3. Coagulopathy
4. Circulatory failure
5. Adrenal dysfunction
Endotoxemia is correlated with gut injury after cardiac arrest and contributes to post-resuscitation shock

Grimaldi D et al. Resuscitation 2012
Brain damage
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...
Intensive care medicine research agenda on cardiac arrest

Jerry P. Nolan¹,², Robert A. Berg³,⁴, Stephen Bernard⁵, Bentley J. Bobrow⁶, Clifton W. Callaway⁷, Tobias Cronberg⁸, Rudolph W. Koster⁹, Peter J. Kudenchuk¹⁰, Graham Nichol¹¹, Gavin D. Perkins¹², Tom D. Rea¹³, Claudio Sandroni¹⁴, Jasmeet Soar¹⁵, Kjetil Sunde¹⁶,¹⁷, and Alain Cariou¹⁸

Neuroprotective drugs after cardiac arrest

- **Epo**
  - Positive experimental results
  - Encouraging preliminary clinical results
  - Negative phase III RCT
  - Cariou A et al. JACC 2016

- **Exenatide**
  - Positive experimental results
  - Encouraging preliminary clinical results
  - Negative phase II/III RCT

- **Ciclosporin**
  - Positive experimental results
  - Encouraging preliminary clinical results
  - Negative phase III RCT
  - Argaud L et al. JAMA Cardiology 2016

- **Xenon**
  - Positive experimental results
  - Positive phase 2 results
  - On the way
  - Phase III required

Fig. 4 Neuroprotective drugs recently investigated for the treatment of post-cardiac arrest syndrome.
The Big Chill

Lowering the body’s temperature improves the chances of surviving a cardiac arrest and other types of trauma; but as cold therapy expands, researchers are struggling to understand why and for whom it works.
Targeted temperature management after cardiac arrest

WHAT LEVEL?

33°C: the dogma
Targeted temperature management after cardiac arrest

WHAT LEVEL?

33° C: the dogma

36° C: the future?
Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

Nielsen N. NEJM 2013
Targeted Temperature Management at 33°C versus 36°C after Cardiac Arrest

Nielsen N. NEJM 2013

<table>
<thead>
<tr>
<th>Variable</th>
<th>33°C Group</th>
<th>36°C Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPC at follow-up†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total no. of patients</td>
<td>469</td>
<td>464</td>
</tr>
<tr>
<td>Category — no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>195 (42)</td>
<td>183 (39)</td>
</tr>
<tr>
<td>2</td>
<td>23 (5)</td>
<td>39 (8)</td>
</tr>
<tr>
<td>3</td>
<td>17 (4)</td>
<td>20 (4)</td>
</tr>
<tr>
<td>4</td>
<td>6 (1)</td>
<td>2 (0.5)</td>
</tr>
<tr>
<td>5</td>
<td>228 (49)</td>
<td>220 (47)</td>
</tr>
</tbody>
</table>

P value for trend 0.85
2015 Guidelines: Temperature management after cardiac arrest?

**ILCOR and ERC/ESICM:**
Cooling is recommended +++
Target temperature between 32-36 °C
Predicting neurological outcome
Neuroprognostication after cardiac arrest

- Important:
  - To inform patient’s relatives
  - To avoid futile treatments in patients with no chance of recovery
- High specificity and precision essential
  - Lowest possible false positive rate (FPR) with narrow CIs
Total 87 studies
5231 patients

Predictors of poor neurological outcome in adult comatose survivors of cardiac arrest: A systematic review and meta-analysis. Part 2: Patients treated with therapeutic hypothermia

Claudio Sandroni\textsuperscript{a,\textdagger}, Fabio Cavallaro\textsuperscript{a}, Clifton W. Callaway\textsuperscript{b}, Sonia D’Arrigo\textsuperscript{a}, Tommaso Sanna\textsuperscript{c}, Michael A. Kuiper\textsuperscript{d}, Matteo Biancone\textsuperscript{a}, Giacomo Della Marca\textsuperscript{e}, Alessio Farcomeni\textsuperscript{f}, Jerry P. Nolan\textsuperscript{g}

\textsuperscript{a} Department of Anaesthesiology and Intensive Care, Catholic University School of Medicine, Rome, Italy
\textsuperscript{b} Department of Emergency Medicine, University of Pittsburgh, United States
\textsuperscript{c} Department of Cardiovascular Sciences, Catholic University School of Medicine, Rome, Italy
\textsuperscript{d} Department of Intensive Care, Medical Center Leeuwarden, Leeuwarden, The Netherlands
\textsuperscript{e} Department of Neurology, Catholic University School of Medicine, Rome, Italy
\textsuperscript{f} Department of Public Health and Infectious Diseases, Statistics Section, Sapienza University of Rome, Rome
\textsuperscript{g} Department of Anaesthesia and Intensive Care Medicine, Royal United Hospital, Bath, UK
Prognostication

Cardiac arrest

Days 1-2

Controlled temperature

Rewarming

Days 3-5

Exclude confounders, particularly residual sedation

Unconscious patient, M=1-2 at ≥72h after ROSC

One or both of the following:
- No pupillary and corneal reflexes
- Bilaterally absent N20 SSEP wave

Yes

No

Poor outcome very likely (FPR <5%, narrow 95% CIs)

Prognostication

**Cardiac arrest**

Days 1-2

- Exclude confounders, particularly residual sedation
- Unconscious patient, M=1-2 at ≥72h after ROSC
- One or both of the following:
  - No pupillary and corneal reflexes
  - Bilaterally absent N20 SSEP wave

Days 3-5

- Magnetic Resonance Imaging (MRI)
- EEG, NSE
- SSEP

- Two or more of the following:
  - Status myoclonus ≤48h after ROSC
  - High NSE levels
  - Unreactive burst-suppression or status epilepticus on EEG
  - Diffuse anoxic injury on brain CT/MRI

**Prognostication**

- Use multimodal prognostication whenever possible

**Poor outcome likely**

**Poor outcome very likely** (FPR <5%, narrow 95% CIs)

**Indeterminate outcome**

- Observe and re-evaluate

---

2015 ERC-ESICM Guidelines for management of post-cardiac arrest patients

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