Author’s response to reviews

Title: Successful resuscitation from prolonged hypothermic cardiac arrest without extracorporeal life support (ECLS) – a case report

Authors:

Melanie Kuhnke (melanie.kuhnke@rega.ch)
Roland Albrecht (roland.albrecht@rega.ch)
Joerg Schefold (joerg.schefold@insel.ch)
Peter Paal (peter.paal@bbsalz.at)

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Author’s response to reviews:

JMCR-D-19-00502R1 - Successful resuscitation from prolonged hypothermic cardiac arrest without extracorporeal life support (ECLS) – a case report

Dear editor and reviewers, thank you very much for your important and highly valuable suggestions. We have implemented them and marked all changes to the text green while our notes are in italics. Based on your suggestions the manuscript has improved substantially and we hope that it now meets the criteria for acceptance in the Journal of Medical Case Reports. Thank you!

Reviewer #1:

1. Do you believe the case report is authentic?
   Yes

2. Do you have any ethical concerns? No
   Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.
   Comments: A statement that the patient gave written, informed consent appears in the manuscript.

3. Does the Introduction explain the relevance of the case to the medical literature?
   Yes
4. Does the article report the following information? Where information is missing, please specify.
   a. The relevant patient information, including: Yes to all
      - De-identified demographic information (age, gender, ethnicity):
      - Main symptoms of the patient
      - Medical, family and psychosocial history
      - Relevant past interventions and their outcomes
   b. The relevant physical examination findings: Yes
   c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month: Yes
   d. Diagnostic assessments, including: Yes to all
      - Diagnostic methods
      - Challenges (e.g., financial, language/cultural)
      - Reasoning and prognostic characteristics (e.g., staging), where applicable
   e. Types and mechanism of intervention: Yes
   f. A summary of the clinical course of all follow-up visits: Yes

   Comments:

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented? Yes
   Comments: I suggest the authors to emphasize that despite ECLS development in the last 20 years in order to rewarm hypothermic CA, when ECLS is not available it doesn't mean that the patient is deceased.
   This is the cornerstone of the discussion in our view. When hypothermic CA occurs the chances of success are actually highest.
   Thank you for this critical suggestion. We added the following sentence in the discussion:
   This case should encourage medical teams in their efforts providing continuous CPR in primary hypothermic patients even when ECLS rewarming is not available in the admitting hospital.
   There are case reports where either non ECLS rewarming in patients with primary hypothermic cardiac arrest was successful and was also survived.
   We added the following references:


6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below.
Yes

7. Is the Abstract representative of the case presented?
Comments: Yes

8. Does the case represent a useful contribution to the medical literature?
Comments: Yes

9. Additional comments for the author(s)?
Dear authors,
Thanks for this very interesting article on the possibility of successful cardiopulmonary resuscitation of hypothermic cardiac arrest despite the lack of extracorporeal life support.
I have some suggestions and the form and the background in order to improve the quality of your manuscript.
I hope my comments will be helpful.
Thank you very much for this supportive statement.

Form:
When a acronym appears only once, you don't need to specify the acronym into parenthesis, for example: GCS, ICU, ERC, AHA Similarly, if you specified the significance earlier, you can use the acronym, for example: ROSC, ECLS, CA I suggest you to harmonize terms of ECLS and ECMO in the text and the figure.
In the conclusion, I would not repeat CPR duration (5:44 hours).
Thank you for this advice.
In the figure and legend to figure we changed ECMO to ECLS: ECLS extracorporeal life support We removed some acronyms or respective specifications in the text:
During the last two decades, ECLS rewarming has become a cornerstone in the treatment of patients with hypothermia induced cardiac arrest

ROSC was achieved two more times with a total of six defibrillations

A Swiss rescue helicopter with night-flying capability was requested to transport the patient directly to an ECLS rewarming centre.

On the second day after admission to the ECLS centre, the patient was awake with Glasgow Coma Scale 15.

He was ventilated for 12 days, extubated on day 15 and discharged from the Intensive Care Unit at day 20.

For patients with a core temperature <30°C with persistent VF, the American Heart Association ACLS algorithm states that it may be reasonable to perform further defibrillations and administer vasopressors (class IIb) (8)
In contrast, the European Resuscitation Guidelines recommend a maximum of three defibrillations and no vasopressors (7).

Extensive cardiopulmonary resuscitation was provided making this case one of the longest CPR cases in literature that resulted in a favorable neurological outcome.

In the following text we removed GCS: Glasgow coma scale and ICU: Intensive Care Unit

We have kept the following abbreviations

Background:
Page 4 line 20: do the authors know the blood pressure value?
After the first 6 defibrillations with intermediate ROSC the patient had a blood pressure of 120/70 mmHg
Page 5 line 1: could you please comment and discuss the reason for serum potassium value despite acidosis, in the genesis and the maintenance of ventricular fibrillation cardiac arrest
Low serum potassium in this case is indeed a special finding. We abstained from discussing this in detail because in this case it is an unresolved issue (see also Buse S, et al. The impact of hypothermia on serum potassium concentration: A systematic review. Resuscitation. 2017 Sep;118:35-42. doi: 10.1016/j.resuscitation.2017.07.003). What can be surely stated is that low serum potassium is a prognostically favorable marker. We added the following and some references:
In accidentally hypothermic patients in cardiac arrest serum potassium is a prognostic marker.

References

Page 5 line 50: please specify what do you mean by "despite a sensation deficit in both feet and hands"?
Thank you for this comment. We changed the text to:
Persisting neuropathy in feet and hands

Page 6 line 18: In my opinion, the core of the discussion is here: despite "ECLS rewarming is encouraged in current resuscitation guidelines", it doesn't mean that rescuers should not attempt CPR because hypothermic CA is associated with highest successful chances.
Correct, we changed the sentence accordingly. "Rewarming from hypothermic cardiac arrest is also possible without ECLS."
Thank you for this suggestion, rewarming from hypothermic cardiac arrest is also possible without ECLS as mentioned and referenced above.

Page 6 lines 45-46: "If a patient remains asystolic after rewarming, death most likely occurred (e.g. caused by asphyxia) before the onset of hypothermic cardiac arrest (3).": I don't understand the utility i-of this sentence because your case report focus on the hypothermic phase, not after rewarming. Is there a link between cardiac rhythm before and after rewarming?
Thank you for this suggestion. Our patient had a primary hypothermic cardiac arrest with good chances of neurologically intact survival. A patient will not be resuscitable if he asphyxiated first and only secondly cooled down. We added a sentence explaining this very important pathophysiology better: A patient will not be resuscitable if he asphyxiated first and only secondly cooled down.

Reviewer #2:

1. Do you believe the case report is authentic? yes
   Yes/No

2. Do you have any ethical concerns? Please consider if local Institutional Review Board approval or ethical approval was obtained (if appropriate) and if the patient (or their parent or guardian in the case of children under 18) gave written, informed consent to publish this case and any accompanying images. A statement to this effect should appear in the manuscript.
   Comments: No

3. Does the Introduction explain the relevance of the case to the medical literature? Yes
   Yes/No

4. Does the article report the following information? Where information is missing, please specify.
   a. The relevant patient information, including:
      - De-identified demographic information (age, gender, ethnicity) Yes
      - Main symptoms of the patient Yes
      - Medical, family and psychosocial history No
      - Relevant past interventions and their outcomes No
   b. The relevant physical examination findings Vital parameters at each situation needs to be mentioned
c. Important dates and times in this case (if appropriate, organized as a timeline via a figure or table); if specific dates could lead to patient identification, consider including time relevant to initial presentation, i.e. initial presentation at T = 0, follow up at T = 1 month. Yes

d. Diagnostic assessments, including:
- Diagnostic methods Yes
- Challenges (e.g., financial, language/cultural) Yes
- Reasoning and prognostic characteristics (e.g., staging), where applicable Yes

e. Types and mechanism of intervention Yes

f. A summary of the clinical course of all follow-up visits No

Comments:

5. Is the interpretation (discussion and conclusion) well balanced and supported by the case presented?
   Comments: Yes

6. Is the anonymity of the patient protected? Please consider any identifying information in images such as facial features or nametags, whether the patient is named etc. If not, please detail below. Yes
   Comments: Yes

7. Is the Abstract representative of the case presented?
   Comments: Yes

8. Does the case represent a useful contribution to the medical literature?
   Comments: Yes

9. Additional comments for the author(s)? There is no need to mention date/month, though time of accident and rescue are very important.
   We removed: In July 2017,
   Why was the patient not intubated initially when he became unconscious with low O2 saturation?
   When the patient became unconscious, he was on the glacier with only BLS skilled mountain rescuers on site. We clarified this with an additional sentence: The patient’s trachea was not intubated at this stage because the mountain rescuers on site were only basic life support certified.
   What was the initial ABG report (pre and post intubation)?
   There was no possibility of ABG analysis on scene before or after intubation.
   The first ABG analysis was performed after 3,5 hrs of CPR after arrival at hospital – see below.
   What was the cause of renal failure? How was it managed?
   The patient developed a severe rhabdomyolysis (CK 190000 U/L). He first had continuous haemofiltration, followed by intermittent dialysis with good recovery of the kidney function.
   Was the patient tracheostomised?
   No, a tracheostomy was not performed
Was any CT or MRI brain scan done before patient discharge?
CT scan of the brain has been done at admission with no signs of fracture, ischemia or bleeding.
No MRI of the brain has been performed.

Were there any cervical spine injuries due to the fall?
No, the patient had no spine injury. The patient had fractured ribs and a sternal fracture - probably due to CPR. When the rescuer joined the patient at the bottom of the crevasse, the patient was conscious and told that he was not aware of any injury except for excoriations.

What is the recommendation regarding management of hypothermic Ca in places where ECLS rewarming is NOT available?
Establish continuous high-quality CPR considering automated chest compressions. Rewarm the patient by non-ECLS means. Establish continuous high-quality CPR considering automated chest compressions. Rewarm the patient by non-ECLS means. We discuss this in more detail now in the manuscript.

Is it reasonable to conclude that in this case hypothermia helped the patient recover fully from CA with just defibrillation and mechanical rewarming?
Oxygen demand decreases $6-7\% / ^{\circ}\text{C}$ cooling. In normothermia CPR states with such a long duration are not survivable without neurological damage. Thus, hypothermia was supportive in the survival of this long low flow state. Chest compressions, ventilation and non-invasive rewarming were essential treatment components.

What were his serum potassium levels at various stages?
First blood analysis was after 3,5 hrs of CPR and showed a potassium of 2,7 mmol/l. Two hrs later serum potassium was 4,5 mmol/l. Just before transportation to the ECLS center it was 5,6 mmol/l.

It must be mentioned that this is a case where both ACLS and ATLS guideline principles should be applied.
Yes, this is correct. Thank you for this comment. We added this sentence:
In this case the principles of both ALS and ATLS-guidelines applied.

Please also take a moment to check our website at https://www.editorialmanager.com/jmcr/lasp/i=2342742&id=T2AJ6HVJ for any additional comments that were saved as attachments. Please note that as Journal of Medical Case Reports has a policy of open peer review, you will be able to see the names of the reviewers.
Thank you, we checked the website and adjusted the following:
We changed Introduction in Background. Case report in Case presentation and changed the order of the “competing interests” in the section “declarations”.
The manuscript should now be conform with all requirements set up by the journal.