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CLINICAL INVESTIGATION: Association of hyperfibrinolysis with poor prognosis in refractory circulatory arrest: implications for extracorporeal cardiopulmonary resuscitation

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EDITORIAL: Hyperfibrinolysis: potential guidance for decision-making to avoid futile extracorporeal cardiopulmonary resuscitation

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Out-of-hospital cardiorespiratory arrest (OHCA) is associated with a poor prognosis.

Resuscitation using extracorporeal membrane oxygenation (eCPR) is a potential treatment, although it is invasive, labour-intensive, and expensive, so we need to identify patients that may benefit from it. Even though it is known that OHCA with an extracardiac cause, non-defibrillation rhythms, and prolonged low or no-flow states are associated to a **worse neurological prognosis**, current clinical trials are not conclusive, and so further research is required to determine which patients can benefit from an eCPR.

In that regard, the authors of the commented editorial and research article suggest the analysis of **fibrinolysis** for that purpose. Thus, a clinical situation of **hyperfibrinolysis** may result from prolonged low or no-flow states and, therefore, bad prognosis. Moreover, this analysis can be performed easily and fast, by the bedside, using **point-of-care such as viscoelastic testing** (TEG® or ROTEM®, mostly).

But what would be the **pathophysiological driver of hyperfibrinolysis in the OHCA**? Low-flow states trigger thrombus formation in the microcirculation, which further aggravates tissue hypoxia. Hyperfibrinolysis would be an evolutionary response to survive, promoting an early lysis of the thrombus to maintain the blood flow and prevent hypoperfusion, even at the cost of increased bleeding. In other clinical situations, such as trauma-induced bleeding, almost 100% mortality has been reported when the image of the viscoelastic test has a diamond shape, which is clearest example of early hyperfibrinolysis.

Is there a **definition of fibrinolysis diagnosed using viscoelastic testing**? Although there is no universally

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accepted definition, hyperfibrinolysis is assumed with a lysis index of > 3% by TEG® or a maximum lysis (ML) ≥15 by ROTEM®. Currently, transfusional algorithms using ROTEM® allow for an early prediction of hyperfibrinolysis with the ROTEM® value of $A5_{EXT}$ (amplitude of EXTEM at 5 minutes) or $A10_{EXT}$ (amplitude of EXTEM at 10 minutes). Also, when diagnosed, the administration of tranexamic acid would be indicated.

How can we **classify the post-CPR neurological prognosis**? Using the Cerebral Performance Category (CPC): CPC 1-2 (good prognosis) and CPC 3-5 (bad prognosis).

CPC 1: Complete recovery or mild disability.

CPC 2: Moderate disability, but independent for daily-life activities.

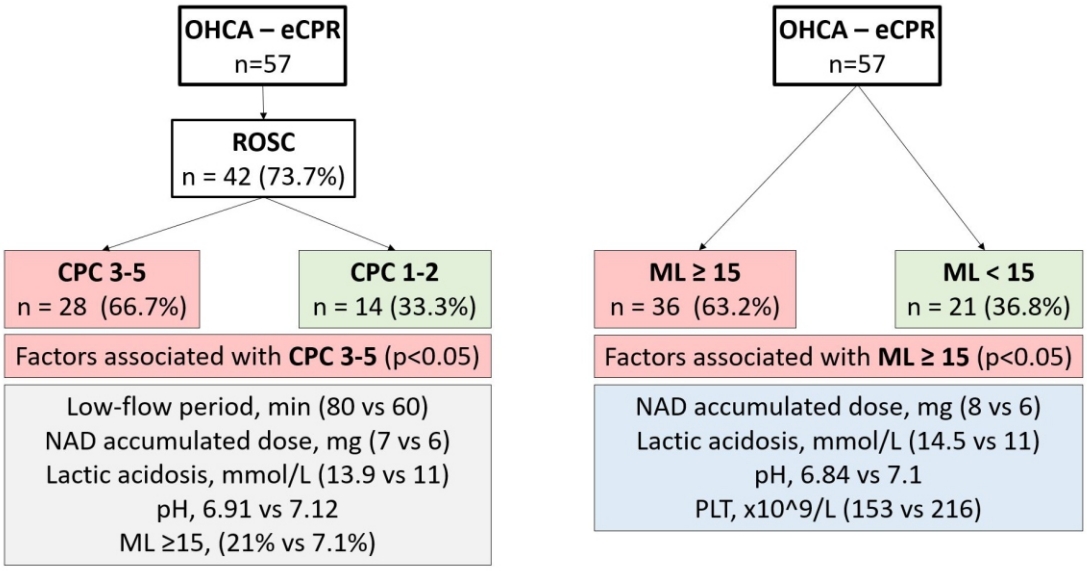
CPC 3: Severe disability. Dependent for daily-life activities.

CPC 4: Persistent vegetative state.

CPC 5: Death.

Magomedov et al. analyzed the lysis state of the clot in 57 patients with OHCA that were treated using eCPR, at the time of hospital admission. They observed that:

A) Factors related to poor neurological prognosis (CPC 3-5) and factors related to hyperfibrinolysis:



OHCA: Out-of-Hospital Cardiorespiratory Arrest; eCPR: Extracorporeal Cardiopulmonary Resuscitation; ROSC: Return of Spontaneous Circulation; CPC: Cerebral Performance Category; NAD: Noradrenaline; PLT: Platelets

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As can be seen, the authors did not find any connection between the existence of hyperfibrinolysis and the low-flow state time (72.5 min in patients with ML ≥15, and 70 min in patients with ML<15). Most likely, this is due to small sample size.

B) Predictors of a poor neurological prognosis (CPC 3-5):

- **Lactic acidosis**, with an AUC of 0.78 (95% CI: 0.63-0.89).
- Transfusional algorithms using ROTEM® are early predictors of hyperfibrinolysis with the $A5_{EXT}$ or $A10_{EXT}$ value. This study show a connection between **$A5_{EXT}$** and **$A10_{EXT}$** with CPC 3-5, with an AUC of 0.76 (95% CI: 0.63-0.89) and 0.79 (95% CI: 0.62-0.9), respectively.
- Given the strong connection between lactic acidosis and ML, they analyzed the connection between **$A5_{EXT}$ / Lactate**, improving the AUC up to 0.89 (95% CI: 0.8-1).

In conclusion, the hypothesis that hyperfibrinolysis may be related to the low or no-flow time in OHCA clearly deserves a multi-centre analysis.

The connection between **$A5_{EXT}$ / Lactate** on admission may be yet another tool, and a fast predictor of an unfavourable neurological outcome (CPC 3-5) in a patient with OHCA for which an eCPR is considered on admission. It may also help optimizing the indication of this invasive, expensive therapy.