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Contents

Development and Validation of a Machine-Learning Algorithm to Predict Rescue ECMO Implantation After Post-Cardiotomy Low Cardiac Output Syndrome

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Introduction:

Post-cardiotomy low cardiac output syndrome (PC-LCOS) is a life-threatening complication. Temporary mechanical circulatory support with veno-arterial extracorporeal membrane oxygenation (VA-ECMO) may be necessary in case of refractory cardiogenic shock, however, its use is still associated with significant mortality [1]. Previous studies have reported improved survival and postoperative outcomes with early implantation directly after cardiopulmonary bypass (CPB) weaning in the operating room compared to delayed implantation in an emergency postoperative setting when organ failure has begun [2].
The objective of our study was to predict, using a machine learning algorithm, the need for rescue VA-ECMO implantation in patients with PC-LCOS who were weaned from CPB. We hypothesized that early identification of patients at risk of deterioration may help clinicians in the management of refractory PC-LCOS to improve their prognosis.

Methods:

We conducted a retrospective cohort study in the cardiac intensive care unit of two university hospitals and included patients with moderate to severe PC-LCOS (defined by a vasoactive inotropic score (VIS [3]) > 10 with clinical or biological markers of impaired organ perfusion or need for mechanical circulatory support after cardiac surgery) from January 2016 to December 2019. Patients with a left ventricular assist device implantation and heart transplants were excluded. The first cohort was used for model development and was split into a training dataset (75%) and internal validation dataset (25%). The second independent cohort was used for external validation of the predictive model. The primary outcome was to predict the need for postoperative rescue VA-ECMO implantation in patients with PC-LCOS who were weaned from CPB. Fifty predictors including baseline demographics, intraoperative variables, and immediate postoperative arterial lactate values were considered. The deep super learner, an ensemble machine learning algorithm, was trained to predict rescue VA-ECMO implantation in ICU [4]. Performance was assessed using receiver operating characteristics area under the curve (ROC AUC). Feature importance was estimated using Shapley values [5]. The study was approved by the local ethics committee.

Results:

Between January 2016 and December 2019, 285 patients were included in the development dataset and 190 patients were included in the external validation dataset.

In the development dataset and the external validation dataset, 46 (16.1%) and 19 (10%) patients required rescue VA-ECMO implantation respectively. Fourteen (73.7%) patients who required rescue VA-ECMO implantation died in the external validation dataset. The deep super learner achieved a 0.863 (CI 95%: 0.793 – 0.928) ROC AUC to predict the primary outcome corresponding to an 89.5% (CI 95%: 73.7% - 100%) sensitivity and a 63.7% (CI 95%: 56.4% - 70.8%) specificity. The five most important features in predicting the primary outcome were immediate postoperative lactate, intraoperative VIS, the absence of angiotensin-converting enzyme treatment, the body mass index, and the EuroSCORE II (Fig. 1-A). Examination of Shapley values also allows exploring the influence of features on individual predictions (Fig. 1-B).

Discussion:

We developed and validated an explainable ensemble machine-learning algorithm to predict the need for rescue VA-ECMO implantation in refractory PC-LCOS patients which showed great performance on the external validation dataset. Variable importance ranking allows the clinician to understand how the algorithm works by limiting the black box effect. Considering the high mortality rate for delayed implanted patients and the improved outcomes reported by previous studies with early implantation, our algorithm may help physicians improve patient outcomes in clinical settings by identifying those with a high risk of requiring rescue VA-ECMO and facilitate early implantation before organ failure occurs.

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Figure 1:

A

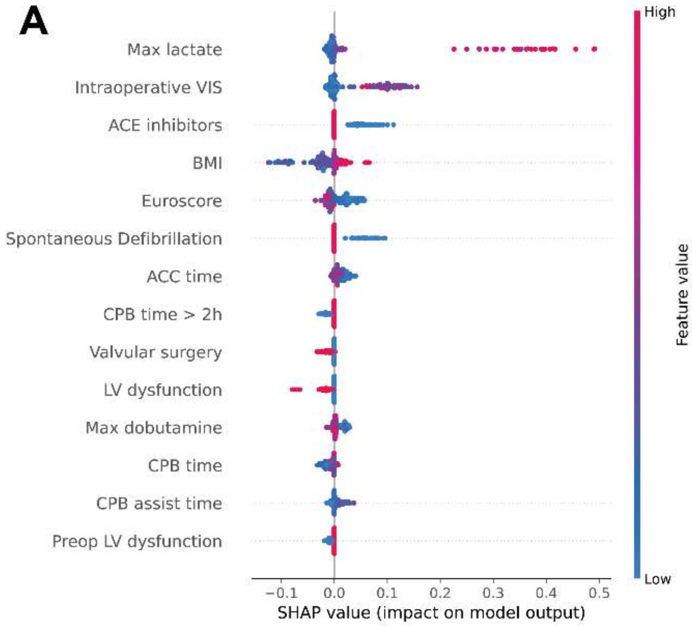

Figure 1A – Variable importance for the external validation dataset based on SHAP values.
The 14 most predictive features are displayed. The SHAP summary dot plot displays feature influence model predictions of positive outcome (rescue VA-ECMO implantation) the most. Features are sorted by their mean absolute SHAP value (reflecting their global importance). For every individual, a dot represents the value for each feature from low (blue) to high (red). ACC: aortic cross clamp, ACE: angiotensin converting enzyme, BMI: body mass index, CPB: cardiopulmonary bypass, LV: left ventricular VIS: vasoactive inotropic score.

B

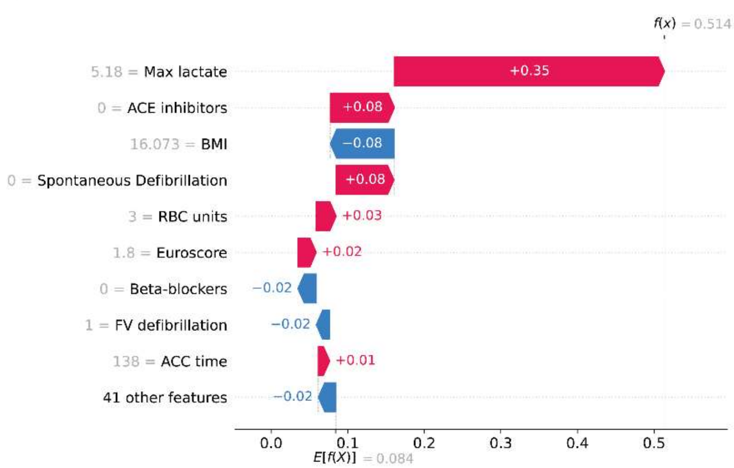

Figure 1B – Impact of the features on the rescue VA-ECMO implantation prediction for a single patient.
The waterfall plot displays the nine features with the highest impact on prediction and the actual features values for this patient is shown on the left. The probability of requiring rescue VA-implantation for this patient was 0.514 according to the Deep Super Learning algorithm. ACC: aortic cross clamp, ACE: angiotensin converting enzyme, BMI: body mass index, FV: ventricular fibrillation.

Patient Prognosis Associated with Breakthrough Temperatures During and After Targeted Temperature Management in Post-cardiac Arrest Patients: A Retrospective Study

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Introduction:

Despite intense research into targeted temperature management (TTM) for post-cardiac arrest patients with return of spontaneous circulation (ROSC) [1-2], there are conflicting findings on whether breakthrough temperatures during and after TTM affect patient outcome. Breakthrough fever after TTM completion was demonstrated by Bro-Jeppesen et al. to be associated with 30-day mortality and poor neurological outcome [3]. Leary et al., however, found no significant survival differences for patients experiencing hyperthermia after TTM completion [4]. Interestingly, Benz-Woerner et al. found patients with quick time to achieving TTM target temperature and longer duration of passive rewarming to have increased mortality [5], suggesting that a lack of thermoregulation in patients post-ROSC may reflect a poor prognosis. The primary objective of this study was to assess the association between breakthrough temperatures (>37.5^{o}C) during TTM and neurological outcome and mortality in the intensive care unit (ICU).

Methods:

In this single-center retrospective cohort study, we identified study subjects using an administrative database. We included all adult post-cardiac arrest patients who attained ROSC and received TTM between January 1st, 2014, and June 30th, 2020. We excluded patients if TTM was intentionally discontinued prior to its completion (i.e. within 24 hours). Patient data were manually extracted by reviewing electronic and paper medical records. The exposure variable was the presence or absence of breakthrough temperatures, defined as any temperature > 37.5 ^{o}C within 48 hours of TTM initiation. The primary endpoints were favorable neurological outcome defined as a cerebral performance category (CPC) score ≤ 2 and ICU death.

We summarized patient demographics, cardiac arrest and TTM characteristics. Single- and multi-variable logistic regressions were performed to assess the association between favorable neurological outcome or ICU death and age, diabetes, coronary artery disease, baseline CPC score, renal replacement therapy, out-of-hospital vs in-hospital arrest, witnessed cardiac arrest, shockable rhythm, ST-elevated myocardial infarction (STEMI) and breakthrough temperature within 48 hours of TTM initiation. We constructed a Kaplan-Meier survival curve of patients with or without breakthrough temperatures and compared the survival differences between two groups using the log-rank test.

Results:

Medical records of 840 study subjects were screened. A total of 591 study subjects were included in the final analysis. The study cohort had a mean (SD) age of 61 (16), 61% were out of hospital cardiac arrests, 75.1% were witnessed, and 39.3% had an initial shockable rhythm.

After adjusting for known confounders, the multi-variable logistic regression model revealed an association between breakthrough temperatures > 37.5 ^{o}C within 48 hours of TTM initiation and favorable neurological outcome (Odds ratio (OR) 1.7 [1.1-2.7, p=0.025]). Younger age, good baseline neurological score, witnessed cardiac arrest, shockable rhythm, STEMI were also associated with favorable neurological outcome. In addition, breakthrough temperatures > 37.5 ^{o}C were associated with lower ICU death (Odds ratio (OR) 0.4 [95% CI: 0.3-0.6 p< 0.0001]) after adjusting for known confounders. The Kaplan-Meier survival analysis (Figure 1) demonstrated a survival benefit with breakthrough temperatures > 37.5 ^{o}C (p < 0.0001).

Discussion:

Any breakthrough temperature > 37.5 ^{o}C during first 48 hours of TTM therapy were associated with favorable neurological outcomes and decreased mortality. In contrast to the general impression of the detrimental effects of breakthrough or rebound hyperthermia, our results suggest that any breakthrough temperature > 37.5 ^{o}C during or after the TTM maintenance phase may be of positive prognostic value. This may be attributed to an intact thermoregulation system, suggesting less neurological injury or a more robust patient physiology. Furthermore, these results also suggest that patients without any breakthrough temperature may require closer attention during post-ROSC care than previously anticipated.

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Figure 1:

Figure 1. Kaplan-Meier survival curve of patients with or without breakthrough temperature (>37.5 °C) during the first 48 hours of their Targeted Temperature Therapy (TTM)