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**Predicting Cardiac Arrest in the Pediatric ICU**

**Study Purpose and Rationale**

Patients in the pediatric intensive care unit (PICU) have relatively high morbidity and mortality compared to patients admitted to general inpatient units and are at higher risk of cardiac arrest.[1] The long-term outcomes of pediatric cardiac arrest, while improving, are still poor, and include neurodevelopmental delay, cardiac injury, extended hospitalizations and time in rehabilitation facilities, and death.[2] The ability to predict and prevent cardiac arrest has the potential to significantly improve outcomes for critically ill children.

Intensive care patients are continuously monitored, both objectively and subjectively. Objective monitoring includes vital signs (heart rate, respiratory rate, temperature, and blood pressure) as well as the overall balance between fluid input and fluid output (e.g., urine). Subjective monitoring includes the Pediatric Early Warning Score (PEWS), which has been previously validated as a predictor of adverse events in hospitalized children.[3] Data collected from objective and subjective monitoring has been used to build predictive models for cardiac arrest; however, no model developed thus far is sufficiently accurate to be clinically useful.[4-6]

Progress in machine learning over the last decade had introduced a battery of methods for analyzing high dimensional and temporal data, demonstrating impressive achievements.[7,8] These methods, including kernelized Support Vector Machines (SVM), Adaptive Boosting (AdaBoost), artificial Neural Networks (NN), and Hidden Markov Models (HMM), are geared towards detecting hidden classes of databased items and non-linear signals in combinations of measurements not specified in advance. Our study will apply these methods to patients in the pediatric ICU in order to develop an algorithm accurate enough to be used in a clinical setting.

**Study Design and Statistical Analysis**

We will perform a retrospective chart review study spanning Pediatric ICU admissions at Morgan Stanley Children's Hospital of New York from January 1, 2011 to January 1, 2017 (6 years). The study cohort will include:

a. All patients experiencing cardiac arrest (defined as need for chest compressions and/or shock delivery) in the PICU during the above period (estimated N = 200), as the primary analysis outcome
b. Age- and sex- matched controls, outnumbering the above cardiac arrest cases 10 to 1 (estimated N=2000)

Patient data will be obtained from the TRAC database, which is a repository of clinical data specific to patients at New York Presbyterian Hospital. Patients who experienced cardiac arrest will be requested by medical record number, obtained from internal records in the pediatric intensive care unit. We will request basic demographic information, including age and sex, for patients who experienced cardiac arrest. Ten controls, age (within 12 months) and sex matched, will be requested per primary analysis patient. Data to be included will include: a) vital signs: heart rate, respiratory rate, blood pressure (systolic, diastolic and mean arterial pressure), measured by invasive (arterial line) and non invasive (cuff) methods, and temperature; b) fluid input (intravenous fluid and medication as well as oral intake, if any) and output (urine and stool output), and PEWS for the 12 hours prior to arrest during their PICU hospitalization. We will also request the outcome of the ICU hospitalization: death at time of arrest, death >24 hours after arrest, or survival to discharge. For control patients, 12 hours of data per patient will be requested, with the specific block of time corresponding to the arrest cases (i.e. if a patient arrests at 12am, we will request the above data from 12pm to 12am for the patient who arrested and all age-matched controls). All samples will be de-identified prior to statistical analysis, per standard protocols.

We will apply prediction tools implemented in the *scikit-learn* software library for classification of the cases (patients who experienced cardiac arrest vs. controls. Specifically, the data will be pre-processed to detect outliers, impute/filter out missing/faulty data points, scale the coordinates by quantile normalization, and reduce dimensionality by multidimensional scaling thereby removing both noise and redundant measurements.
After pre-processing, we will apply multiple classification methods, specifically:

a. SVM with Radial Basis Function (RBF) kernel and polynomial kernel of degree $\leq 3$
b. AdaBoost with the elementary unit being a linear classifier or a decision tree (Random Forest)
c. Recurrent NN, specifically Long Short-Term Memory (LSTM)
d. HMM for continuous measurements (Kalman filters)

All methods will be applied to a training subset of the data, and 5-fold cross-validated against individuals not used for training. We will calculate the sensitivity and specificity of our models against control cases. Additionally, we will use AOC and ROC to see how well our algorithm differentiates between arrest cases and non-arrest (control) cases.

**Study Procedures**

No procedures are being performed as part of this study.

**Study Drugs**

No drugs are being administered as part of this study.

**Study Questionnaire**

No questionnaires are being used.

**Study Subjects**

Subjects are children who were admitted to the pediatric ICU from 1/1/07 to 1/1/17 who experienced cardiac arrest during their PICU admission. Controls are age and sex-matched patients who did not experience cardiac arrest during their PICU admission.

**Recruitment of Subjects**

This is a retrospective chart review, no recruitment will take place.

**Confidentiality of Study Data**

All study data will be de-identified and stored on password-protected files on CUMC computers, in accordance with university policy.

**Potential Conflict of Interest**

There are no conflicts of interest for any study investigator.

**Location of Study**

All data was collected as part of routine clinical care. Patients were admitted to the Pediatric ICU at CHONY

**Potential Risks**

There are no potential risks; this is a retrospective chart review

**Potential Benefits**

There are no potential benefits to study subjects.

**Alternative Therapies**

N/A, this is a retrospective chart review.

**Compensation to Subjects**

No compensation will be offered to subjects.

**Cost to Subjects**

This is a retrospective chart review; there is no cost to subjects.

**Minors as Research Subjects**

This is a retrospective chart review that poses no more than minimal risk to subjects. All subjects enrolled will be minors. The CUMC IRB for Human Subjects is currently reviewing the protocol.

**Radiation and Radioactive Substances**

No radiation or radioactive substances are used in this study.

**References**