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Letters

RESEARCH LETTER

Early Recognition of Clinical Trajectories Using Machine Learning in Hospitalized Heart Failure Patients

Patients hospitalized with acute decompensated heart failure (ADHF) have different clinical trajectories during hospitalization,[1] which impacts length of stay and risk of readmission. Early recognition of in-hospital trajectories, especially those not responding to treatment, in the hospital course may be crucial to achieve successful decongestion and improve outcomes. While resolution of symptoms and signs, weight loss, decrease in natriuretic peptides, hemoconcentration, and other biomarkers have been used to delineate clinical trajectories, we selected hemoconcentration as a surrogate for decongestion and clinical improvement because it is one of the objective variables that has been associated with favorable outcomes in prior studies.[2-4] This study aims to demonstrate that an artificial intelligence (AI) model can predict a patient's in-hospital trajectory delineated by hemoconcentration within 48 hours of admission.

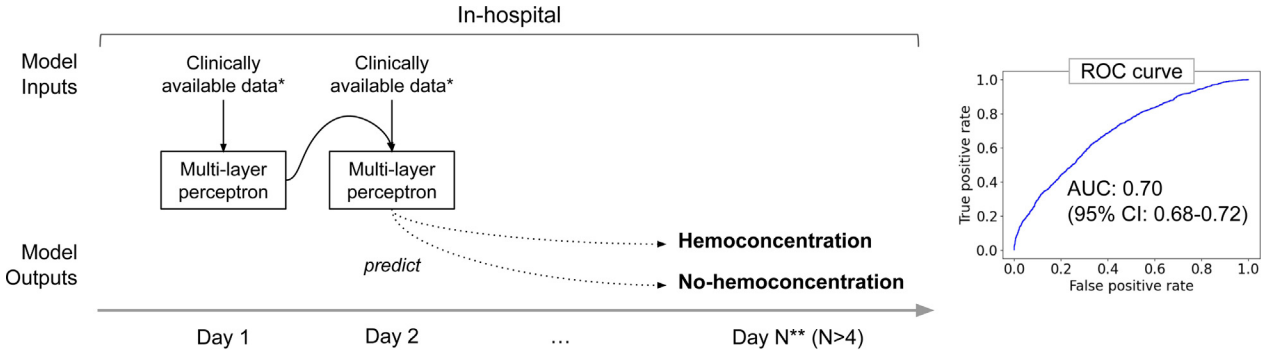
We defined hemoconcentration as an increase in hemoglobin level from admission to discharge during ADHF hospitalization, similar to previous studies.[2] Although other measures such as albumin or hematocrit have also been used to define hemoconcentration, due to the unavailability of repeat albumin levels for most patients, we used hemoglobin.[2-4] The first hemoglobin value collected within the first 48 hours of admission was defined as the "admission hemoglobin"; the last lab collected between day 4 (96 hours) of hospitalization and date of discharge was defined as the "discharge hemoglobin." A patient with an increase in hemoglobin at discharge relative to the admission hemoglobin was considered to have *hemoconcentration* (ie, discharge hemoglobin level > admission hemoglobin level); those with no increase or a decrease were classified as having *no hemoconcentration*. Hemoconcentration achieved by discharge was accepted as a marker of successful decongestion.

This study utilized deidentified clinical data in the MIMIC-IV dataset[5] from patients admitted at Beth Israel Deaconess Medical Center from 2008 to 2019 (inclusive), a major urban care center. The data included demographics, laboratory values, vital signs, body weight, medication administration data, and diagnosis codes obtained from inpatient admission encounters. The clinical data was formulated as a time series. A recurrent neural network (RNN) model to learn features from clinical variables and diuretic regimens available in the first 48 hours of admission was built to predict whether a patient would have hemoconcentration (increased hemoglobin) at discharge. Machine learning algorithms were developed to train the RNN model and by using variables during the first 48 hours of hospitalization to predict whether the patient is on a trajectory to develop successful hemoconcentration, as illustrated in **Figure 1**.

Of the available 190,240 patients' hospitalization records, 4,464 patients (67.2% of the total ADHF patients) and their associated 6,763 ADHF admissions (excluding in-hospital death) had both admission and discharge hemoglobin levels available. In these patients, the median length of stay was 7.0 [IQR: 5.0] days. To evaluate the utility of the AI model to phenotype patients into a *hemoconcentration* group or a *no-hemoconcentration* group, The ADHF admission records were randomly split into *training* (n = 2,204, 1,679 out of the 3,345 admissions had hemoconcentration) and *test* (n = 2,260, 1,744 out of the 3,418 admissions had hemoconcentration) sets. There was no patient overlap between the *training* and *test* sets. The RNN model was pretrained on the data from all patients who were not in the *test* set (*pretraining* set, including patients not admitted for ADHF). Then the RNN model was fine-tuned (trained at a lower learning rate) on the *training* set and evaluated on the *test* set to predict whether a patient would have hemoconcentration.

By the end of day 2, the AI model predicted those who would have hemoconcentration at discharge with an area under the curve of 0.70 (95% CI: 0.68-0.72) (**Figure 1**). We compared the outcomes of the 2 patient groups (predicted *hemoconcentration* vs *no-hemoconcentration* by the AI model) in the *test* set,

FIGURE 1 Illustration of the AI Model Predicting Hemoconcentration Early (at Hour 48 of the Hospitalization)



Panel 1. Recurrent neural network model predicts hemoconcentration based on clinical data available in the first 48 hours of admission.

* In this study, the AI model inputs included body weight, comorbidities, demographics, glomerular filtration rate, laboratory tests, vital signs, and diuretic treatment.
** In this cohort of ADHF hospitalizations that have both admission and discharge hemoglobin levels available, the average length of stay is 8.4 days with a standard deviation of 5.0.

	Overall	AI Predicted Hemo-concentration	AI Predicted No-hemo-concentration	P-Value
n	3,418	1,717 (50.2%)	1,701 (49.8%)	
Mortality, n (%)				
30-day mortality	206 (6.0)	95 (5.5)	111 (6.5)	0.25
6-month mortality	745 (21.8)	343 (20.0)	402 (23.6)	0.01
1-year mortality	1,084 (31.7)	493 (28.7)	591 (34.7)	<0.01

Panel 2A. AI Predicted Trajectory and Mortality.

	Overall	Hemo-concentration	No-hemo-concentration	P-Value
n	6,763	3,423 (50.6%)	3,340 (49.4%)	
Mortality, n (%)				
30-day mortality	405 (6.0)	165 (4.8)	240 (7.2)	<0.01
6-month mortality	1,445 (21.4)	630 (18.4)	815 (24.4)	<0.01
1-year mortality	2,114 (31.3)	944 (27.6)	1,170 (35.0)	<0.01

Panel 2B. Observed Hemoconcentration and Mortality.

Panel 1 illustrates our AI model architecture and its predictive performance in a ROC curve. Panel 2A shows association of AI-predicted hemoconcentration with out-of-hospital mortality. Panel 2B shows association of observed discharge hemoconcentration with out-of-hospital mortality. AI = artificial intelligence; ROC = receiver-operating characteristic.

shown in **Figure 1**. The clinical features included in the AI model that were most predictive of hemoconcentration were admission hemoglobin, presence of malignancy, sodium, age, and presence of renal disease. The AI prediction of *hemoconcentration* during the first 2 days of hospitalization was associated with lower out-of-hospital mortality. Consistent with prior findings, hemoconcentration at discharge was also associated with out-of-hospital mortality.[2-4]

This study demonstrated the potential of utilizing AI to risk stratify and predict clinical trajectories of ADHF patients within the first 2 days of hospitalization to determine those patients who will and will not have hemoconcentration at the time of discharge. Our AI model can predict discharge hemoconcentration early based on admission data; a predicted trajectory and associated out-of-hospital mortality can be defined based on the patient's baseline health status and current treatment regimen.

Machine learning can help unmask trajectories of patients before they become clinically recognized and reveal novel phenotypes that can enable clinicians to predict patient response to treatment and adjust interventions accordingly. The association between AI-predicted trajectory groups and 30-day mortality did not reach statistical significance. Hemoconcentration represents a potentially addressable but surrogate outcome in heart failure. Future studies may include other surrogates and endpoints to delineate clinical trajectories and a randomized controlled study to validate the utility of algorithm-directed care vs usual care, beneficial to differentiate patients who may need rapid escalation of therapies and/or longer hospitalization.

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