

Artificial intelligence prediction of adverse outcomes in emergency department patients with hyperglycemic crises in real-time

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Abstract

Background

Hyperglycemic crises are associated with high morbidity and mortality. Previous studies proposed methods for predicting adverse outcome in hyperglycemic crises, artificial intelligence (AI) has however never been tried. We implemented an AI prediction model integrated with hospital information system (HIS) to clarify this issue.

Methods

We included 3,715 patients with hyperglycemic crises from emergency departments (ED) between 2009 and 2018. Patients were randomized into a 70%/30% split for AI model training and testing. Twenty-two feature variables from their electronic medical records were collected, and multilayer perceptron (MLP) was used to construct an AI prediction model to predict sepsis or septic shock, intensive care unit (ICU) admission, and all-cause mortality within 1 month. Comparisons of the performance among random forest, logistic regression, support vector machine (SVM), K-nearest neighbor (KNN), Light Gradient Boosting Machine (LightGBM), and MLP algorithms were also done.

Results

Using the MLP model, the areas under the curves (AUCs) were 0.808 for sepsis or septic shock, 0.688 for ICU admission, and 0.770 for all-cause mortality. MLP had the best performance in predicting sepsis or septic shock and all-cause mortality, compared with logistic regression, SVM, KNN, and LightGBM. Furthermore, we integrated the AI prediction model with the HIS to assist physicians for decision making in real-time.

Conclusions

A real-time AI prediction model is a promising method to assist physicians in predicting adverse outcomes in ED patients with hyperglycemic crises. Further studies on the impact on clinical practice and patient outcome are warranted.

1. Background

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) are two types of hyperglycemic crises, the most serious acute complications of diabetes [1]. Precipitating factors include uncontrolled types 1 and 2 diabetes, infection, new-onset diabetes, pancreatitis, acute coronary syndrome, stroke, and medications [2, 3]. In the U.S, emergency department (ED) visit rates for DKA and HHS increased annually. In 2015, they accounted for 3.1 and 2.9 per 10,000 adults with diabetes for DKA and HHS, respectively [1]. Despite advances in treatment, the mortality rate of hyperglycemic crises remains high. A study in Taiwan reported a mortality rate of 10.5% [4]. In addition to short-term mortality, hyperglycemic crises increase the risk for subsequent major adverse cardiovascular events, end-stage renal disease, and long-term mortality [5–7]. Therefore, risk stratification, including sepsis, intensive care unit (ICU) admission, and mortality remain important issues in patients with hyperglycemic crises.

In order to improve the management of hyperglycemic crises, we proposed a predicting the hyperglycemic crisis death (PHD) score in 2013 to help ED physicians stratify the mortality risk and make decisions in patients with hyperglycemic crises [4]. First, we used logistic regression to identify six independent mortality predictors: absent tachycardia (heart rate ≤ 100 /min), hypotension (systolic blood pressure < 90 mmHg), anemia (hemoglobin < 10 g/dL or hematocrit $< 30\%$), severe coma (Glasgow Coma Scale (GCS) ≤ 8), cancer history, and infection [4]. The PHD score was then developed by these predictors, and stratified the patients into three risk groups: (1) low (0%; 95% confidence interval (CI): 0–0.02%): treatment in a general ward or the ED; intermediate (24.5%; 95% CI: 14.8–39.9%): treatment in the ICU or a general ward; and high (59.5%; 95% CI: 42.2–74.8%): treatment in the ICU. The AUC for the rule was 0.925 in the validation set [4]. However, the PHD score is limited by a small derivation sample (235 patients), and no external validation nor real-time feedback to the treating physicians. In addition, the PHD score needs manual calculation, which may not be convenient in a busy ED. In recent years, AI including machine learning (ML) and deep learning (DL) techniques have been found to handle more variables and these are already available in electronic medical records (EMRs) [8]. AI may better predict patient outcome, and become a promising method to assist medical decisions. We searched Google Scholar and PubMed by the keywords of “AI,” “death,” “deep learning,” “diabetic ketoacidosis,”

“emergency department,” “hyperglycemic crises,” “hyperglycemic hyperosmolar state,” “machine learning,” “mortality,” and “outcome,” but did not find AI application in this field. We therefore carried out this study to clarify this issue.

2. Methods

2.1 Study design, setting, and participants

In the Chi Mei Medical Center (CMMC), we established a multi-disciplinary team including emergency physicians, data scientists, information engineers, nurse practitioners, and quality managers for big data and AI implementation. Adults (age ≥ 20 years) with hyperglycemic crises who visited the EDs of three hospitals (CMMC, Chi Mei Liouying Hospital, and Chi Mei Chiali Hospital) between 2009 and 2018 were recruited (Figure 1). The criteria for hyperglycemic crises was defined as the final diagnosis of DKA or HHS in the ED, using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code of 250.1 or 250.2, and ICD-10 of E11.1 or E11.0. Patients who did not have a record of subsequent follow-up were excluded.

2.2 Definition of feature variables

The 22 feature variables retained for analysis were age, sex, body mass index (BMI), vital signs at triage, bedridden, nasogastric tube (NG) feeding, history of hypertension (ICD-9-CM: 401-405 or ICD-10: I10-I16), hyperlipidemia (ICD-9-CM: 272.0–272.5, 277.7 or ICD-10: E78.0-E78.5, E88.81), malignancy (ICD-9-CM: 140–208 or ICD-10: C00-C69), chronic kidney disease (ICD-9-CM: 585 or ICD-10: N18), and laboratory data, including blood urine nitrogen (Bun), serum creatinine, white blood cell count, hemoglobin, glucose, and high sensitive C-reactive protein (hs-CRP), and concomitant infection (ICD-9-CM: 001–139, 320–326, 390–392, 480–488, 540–543, 555–558, 566–567, 599.0, 601, 604, 614–616, 680–686, 730 or ICD-10: A00-B99, G00-G09, I00-I02, J09-J18, K35-K38, K50-K52, K61, K65, N39.0, N41, N45, N70-N77, L00-L08, M86, R65). The feature variables considered were suggested predictors of adverse outcomes in previous studies, and possible risk factors for adverse outcomes in clinical practice [4, 5, 7, 9, 10]. Past history was defined as diagnosis established before the index visit.

2.3 Outcome measurements

We defined three adverse outcomes: (1) sepsis or septic shock <1 month (ICD-9-CM: 038, 790.7 or ICD-10: A40-A41, R65, R7881), (2) ICU admission <1 month, and (3) all-cause mortality <1 month following the index ED visit.

2.4 Ethical statement

This study was approved by the institutional review board of the Chi Mei Medical Center and conducted according to the Helsinki declaration. Informed consent from the patients was waived because this study is retrospective and contains de-identified information, which does not affect the rights and welfare of the patients.

2.5 Data processing, comparison, and application

First, data was extracted from the HIS, transformed, and validated into a data mart for further analysis. Missing and ambiguous data were defined carefully by a group meeting made of emergency physicians, data scientists, information engineers, nurse practitioners, and quality managers. We deleted the data if the feature variable could not be estimated (such as missing “sex”) or if many feature variables were missing. An average value was added if the missing feature variable could be estimated (missing “BMI” for example). Secondly, we divided the data into training (70%) and testing (30%) groups. Multilayer perceptron (MLP), a class of DL, was used to train, and test the data. Next, we deployed the AI prediction model in the AI web service and integrated it in the HIS. After clinical testing and bugs correction, we launched the AI prediction model in the HIS to assist ED physicians for decision making in real-time. An AI button was set up in the HIS and a real-time prediction result was showed after the physician pressed the AI button. We also compared MLP with other ML algorithms, including random forest, logistic regression, support vector machine (SVM), K-nearest neighbors (KNN), and Light Gradient Boosting Machine (LightGBM) for accuracy, precision, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), F1, and area under the curve (AUC).

3. Results

There were 3,715 ED patients with hyperglycemic crises in three hospitals between 2009 and 2018 were recruited into the study (Table 1). The mean age was 62.1 ± 18.1 years, and the percentage of females was 44.6%. The four age subgroups were: 20-34 years (9.4%), 35-49 years (15.3%), 50-64 years (26.0%), and ≥ 65 years (49.3%). The mean BMI was 23.0 ± 4.3 kg/m². There were 57.7% bedridden patients and

7.2% patients using NG feeding. History of hypertension (52.1%), hyperlipidemia (27.9%), malignancy (13.0%), and chronic kidney disease (12.2%) were found. Concomitant infection was found in 43.1%. Within 1 month, 28.5% of patients had sepsis or septic shock, 5.4% required ICU admission, and 10.8% died.

In the testing group, the AUC of the MLP for predicting sepsis or septic shock, ICU admission, and all-cause mortality were 0.808, 0.688, and 0.770, respectively (Table 2). Compared with random forest, logistic regression, SVM, KNN, and LightGBM, the MLP model had a better AUC in predicting sepsis or septic shock and all-cause mortality (Table 3 and Supplementary Figure 1). The feature importance of random forest, logistic regression, and LightGBM were also analyzed (Supplementary Figure 2).

4. Discussion

We implemented a novel AI prediction model using MLP for adverse outcomes in ED patients with hyperglycemic crises. Using a big-data-driven approach, DL algorithm, and integration in HIS, the AI prediction model provides ED physicians with a real-time assistance for decision making. The AUC of the AI prediction model was 0.808 for sepsis or septic shock, 0.688 for ICU admission, and 0.770 for all-cause mortality within 1 month.

Clinical decision rules (CDRs), like the PHD score, are developed to help physicians in critical decision making for the management and disposition of patients [11-13]. The CDRs are psychologically appealing because they are developed to create order out of disorder. Medicine is inherently subjective. However, the CDRs strive to structure and simplify the complexity [11]. Although CDRs have the above strengths, some limitations need to be clarified before implementing them in clinical practice [11, 12]. First, the CDRs should be externally validated in diverse settings before clinical use. The CDRs usually perform well in the derivation sample because they are statistically developed to the specific data set. However, when they are applied in a new sample, they typically perform less well or even fail. Secondly, the CDRs may not be applied to the users' clinical setting or targeted population. Comparison between the original study setting and users' setting is imperative and important [11]. Thirdly, it is not convenient to use the CDRs in the busy ED because they need manual calculation. Although many CDRs have an online version for automatic calculation, they still need keying in the data manually.

AI is a major technologic breakthrough for health care and offers seemingly endless possibilities for the improvement of the health care system. There are currently two major fields of AI: ML and DL [14]. ML, including random forest, logistic regression, SVM, KNN, and LightGBM, is the ability that computer systems automatically improve their functioning or "learn" with continuous data. DL, as the MLP in this study, has a more complex network of nodes between the inputs and outputs for solving complex problems more accurately [14]. MLP is one of the most significant models in artificial neural network and preferred for solving nonlinear problems. MLP has three layers, namely the input, hidden and output layers, and performs like a human brain [15]. Different from other computerized tools, AI does not simply execute tasks according to preprogrammed assumptions [14]. It could "learn," "test," and "generate" autonomously through the analysis of big data [14, 16]. AI provides a new opportunity for improving care in the ED, including image interpretation image, patient outcome prediction, vital signs monitoring, reducing the documentation burden by natural-language-processing, home monitoring systems and prediction tools for infectious outbreaks outside the hospital [16-19].

We implemented the AI prediction model in the HIS, which overcame final barriers between AI research and clinical practice. There are however some barriers at the stage of clinical implementation. First, the hospital's policy for AI implementation. The integration of the technology into the clinical workflow of an ED needs the cooperation and assistance from the information department of the hospital. Therefore, the hospital leader's support for the AI implementation is extremely important, and a key point for success. Secondly, there is a great technological difficulty for incorporating AI in the HIS. A complete overhaul of some or all of the existing information technology systems in the hospital may be needed. Thirdly, rejection by practicing physicians of AI prediction may impede its implementation [14]. Criticisms and questions, including malpractice, accuracy of AI prediction, and fear of being replacing by AI, may significantly affect the willingness of physicians for using AI.

The AUC of all-cause mortality in this study was inferior to that of the PHD score (0.770 vs. 0.925) [4]. As regards death prediction, MLP had a better performance (AUC: 0.770) than the logistic regression (AUC: 0.728), which was the method used in the PHD score [4]. Despite the inferior performance compared with the PHD score, the AI prediction model has the advantages of automatism and potential improvement by inventing new algorithms in the future.

This study has the major strength that implementation of a real-time AI prediction model integrated in the HIS for adverse outcomes in ED patients with hyperglycemic crisis. There are however some limitations. Firstly, the AUC of ICU admission prediction was not as good as that of sepsis or septic shock and death. This may be because ICU admission is not objective. The decision for ICU admission always depends on an overall consideration of the disease, patient and families' wish, and medical resources in the treating hospital. Secondly, the

“black box” phenomenon is still a problem [14]. Because no one can oversee how the decision was generated, poor acceptance by the physicians is a great barrier for its promotion. Dissecting the computer’s “decision making process” in the same way as human providers’ decisions may make the “black box” more transparent [14]. Thirdly, the impact of AI prediction on clinical practice was not evaluated. Although it is believed that AI would aid in decision making and reduce human errors, further studies may be necessary to evaluate its impact on physicians’ decisions and patient outcomes. Fourthly, the AI prediction model may not be generalized to other hospitals. Re-training and testing are suggested for applying the AI prediction model to other hospitals. Also, implementation of AI prediction may have ethical and legislative problems. Using AI prediction as an assistive tool may help decrease these concerns from the physicians.

5. Conclusions

We developed the first AI prediction model for adverse outcomes in ED patients with hyperglycemic crises and integrated it in the HIS to provide a real-time decision assistance. Using the AI prediction, ED physicians could get a second opinion from big data in real-time, which may save time in decision making and disposition and may reduce human errors. Further studies about the impact of the AI prediction on clinical practice and patient outcomes are warranted.

Abbreviations

AI: artificial intelligence

HIS: hospital information system

ED: emergency departments

MLP: multilayer perceptron

ICU: intensive care unit

SVM: support vector machine

KNN: K-nearest neighbor

LightGBM: Light Gradient Boosting Machine

AUC: areas under the curve

DKA: Diabetic ketoacidosis

HHS: hyperosmolar hyperglycemic state

ED: emergency department

PHD: predicting the hyperglycemic crisis death

GCS: Glasgow Coma Scale

CI: confidence interval

ML: machine learning

DL: deep learning

EMRs: electronic medical records

CMMC: Chi Mei Medical Center

ICD-9-CM: International Classification of Diseases, Ninth Revision, Clinical Modification

BMI: body mass index

NG: nasogastric tube

Bun: blood urine nitrogen

hs-CRP: high sensitive C-reactive protein

PPV: positive predictive value

NPV: negative predictive value

CDRs: Clinical decision rules

Declarations

Availability of data and materials

The datasets analyzed during this study are available from the corresponding author upon reasonable request.

Ethics approval and consent to participate

This study was approved by the institutional review board of the Chi Mei Medical Center and conducted according to the Helsinki declaration. Informed consent from the patients was waived because this study is retrospective and contains de-identified information, which does not affect the rights and welfare of the patients.

Consent for publication

Not applicable.

Competing interests

All authors denied any competing interests.

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Authors' contributions

CCH (1st author), YK, CFL, and CCH (10th author) designed and conceived this study and wrote the manuscript. CJC and TLL performed the data processing, deployment in AI web service, integration with HIS, testing the application, and launching the application in the HIS. CFL performed model training and testing and statistical analysis. CCH (3rd author), SLH, HJL, and JJW provided professional suggestions and wrote the manuscript. All authors read and approved the final manuscript.

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Tables

Table 1. Characteristics of all the ED patients with hyperglycemic crises in three hospitals between 2009 and 2018

Variable	Total patients (n = 3715)
Age (years)	62.1 ± 18.1
Age subgroup (%)	
20-34	9.4
35-49	15.3
50-64	26.0
≥65	49.3
Sex (%)	
Female	44.6
Male	55.4
Body mass index (kg/m ²)	23.0 ± 4.3
Vital signs at triage	
Glasgow coma scale	12.2 ± 3.2
Systolic blood pressure (mmHg)	137.9 ± 33.7
Heart rate (beats/min)	106.2 ± 23.0
Respiratory rate (breaths/min)	20.1 ± 4.4
Body temperature (°C)	36.7 ± 0.8
Bedridden (%)	57.7
Nasogastric tub feeding (%)	7.2
Past histories (%)	
Hypertension	52.1
Hyperlipidemia	27.9
Malignancy	13.0
Chronic kidney disease	12.2
Laboratory data	
Blood urea nitrogen (mg/dL)	27.5 ± 11.1
White blood cell count (10 ³ /μL)	11.6 ± 6.1
Serum creatinine (mg/dL)	1.9 ± 1.6
Hemoglobin (g/dL)	12.9 ± 2.7
Glucose (mg/dL)	410.5 ± 304.8
High sensitivity C-reactive protein (mg/L)	46.7 ± 76.2
Concomitant infection (%)	43.1
Outcomes <1 month (%)	
Sepsis or septic shock	28.5
ICU admission	5.4
All-cause mortality	10.8

Data are presented as % or mean ± SD. ED, emergency department; ICU, intensive care unit; SD, standard deviation.

Table 2. Evaluation report using the MPL on the adverse outcomes in the testing group of ED patients with hyperglycemic crises

Outcomes <1 month	Number	Negative outcome	Positive outcome	Accuracy	Precision	Sensitivity	Specificity	PPV	NPV	F1	AUC
Sepsis or septic shock	3715	2658	1057	0.736	0.707	0.773	0.722	0.525	0.889	0.711	0.808
ICU admission	3715	3514	201	0.781	0.548	0.533	0.795	0.129	0.109	0.540	0.688
All-cause mortality	3715	3313	402	0.741	0.591	0.633	0.754	0.237	0.945	0.592	0.770

MLP, multilayer perceptron; ED, emergency department; PPV, positive predictive value; NPV, negative predictive value; F1, $2 \times (\text{precision} \times \text{recall} / (\text{precision} + \text{recall}))$; AUC, area under the curve; ICU, intensive care unit.

Table 3. Comparisons of performance among random forest, logistic regression, SVM, KNN, LightGBM, and MLP for adverse outcomes in the ED patients with hyperglycemic crises

Outcomes and algorithms	Accuracy	Precision	Sensitivity	Specificity	PPV	NPV	F1	AUC
Sepsis or septic shock								
Random forest	0.800	0.755	0.703	0.838	0.634	0.877	0.762	0.771
Logistic regression	0.741	0.725	0.852	0.697	0.527	0.922	0.723	0.774
SVM	0.724	0.666	0.565	0.787	0.513	0.820	0.670	0.676
KNN	0.653	0.618	0.612	0.669	0.424	0.813	0.617	0.641
LightGBM	0.800	0.754	0.659	0.856	0.645	0.863	0.756	0.758
MLP	0.736	0.707	0.773	0.722	0.525	0.889	0.711	0.808
ICU admission								
Random forest	0.944	0.598	0.017	0.997	0.250	0.947	0.501	0.507
Logistic regression	0.570	0.540	0.833	0.555	0.096	0.983	0.441	0.694
SVM	0.657	0.532	0.633	0.658	0.095	0.969	0.475	0.646
KNN	0.739	0.515	0.350	0.761	0.077	0.954	0.486	0.556
LightGBM	0.944	0.662	0.050	0.995	0.375	0.949	0.530	0.523
MLP	0.781	0.548	0.533	0.795	0.129	0.109	0.540	0.688
All-cause mortality								
Random forest	0.880	0.606	0.091	0.976	0.314	0.898	0.538	0.533
Logistic regression	0.618	0.589	0.868	0.588	0.204	0.973	0.531	0.728
SVM	0.648	0.576	0.744	0.637	0.200	0.953	0.539	0.690
KNN	0.693	0.549	0.496	0.717	0.176	0.921	0.533	0.607
LightGBM	0.877	0.631	0.165	0.964	0.357	0.905	0.580	0.565
MLP	0.741	0.591	0.633	0.754	0.237	0.945	0.592	0.770

SVM, support vector machine; KNN, K-nearest neighbors; LightGBM, Light Gradient Boosting Machine; MLP, multilayer perceptron; ED, emergency department; PPV, positive predictive value; NPV, negative predictive value; F1, $2 \times (\text{precision} \times \text{recall} / (\text{precision} + \text{recall}))$; AUC, area under the curve; ICU, intensive care unit.

Figures

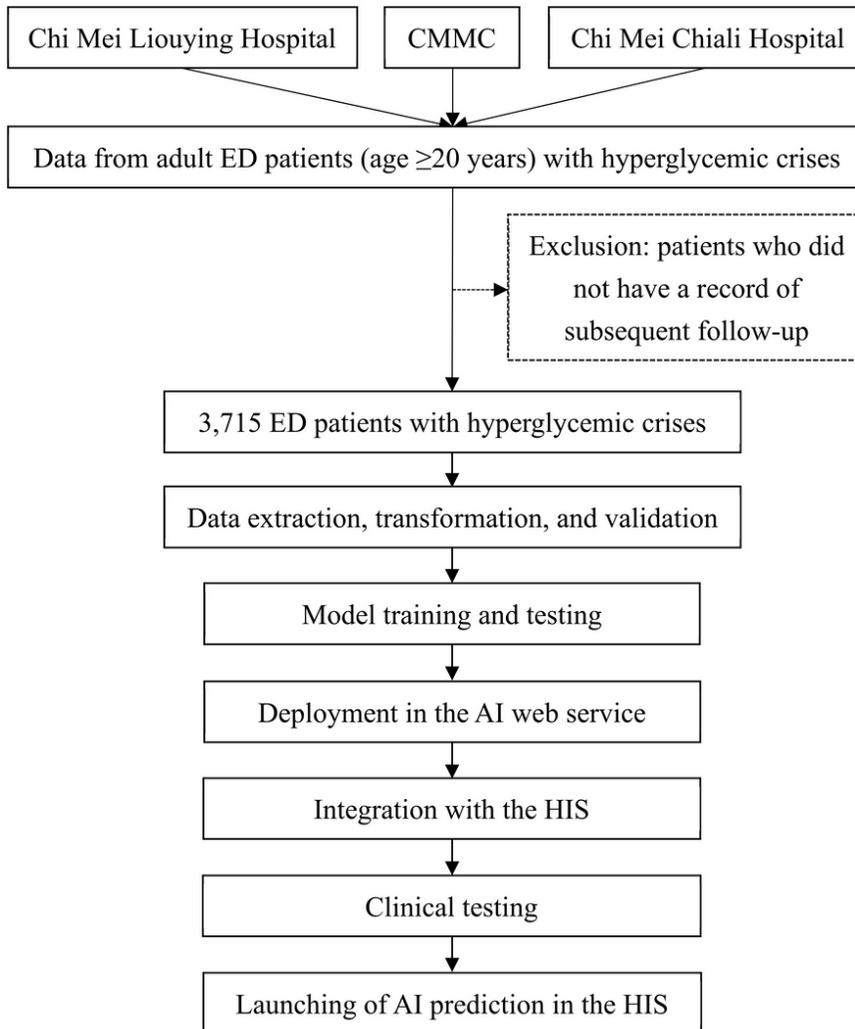


Figure 1

Flowchart of this study. CMMC, Chi Mei Medical Center; ED, emergency department; AI, artificial intelligence; HIS, hospital information system.

Supplementary Files

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