

The impact of transthoracic echocardiography on the shortterm prognosis of elderly patients in the intensive care unit: a retrospective analysis based on the MIMIC-III database

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Background: Elderly patients in the intensive care unit (ICU) often suffer from cardiac function impairment. Real-time monitoring of cardiac function and structural changes has important clinical significance. Transthoracic echocardiography (TTE) is a convenient, intuitive, and non-invasive real-time examination of the heart, and it has been widely used for intensive care patients. This study aims to analyze the impact of TTE on the prognosis of elderly patients in ICU.

Methods: Data from elderly patients in the ICU was obtained from the MIMIC-III 1.4 database, and they were divided into a TTE examination group and a non-TTE examination group. The baseline data of the two groups were compared, and multiple regression analysis, propensity score (PS), compatibility analysis, and other methods were used to analyze the influence of TTE on the prognosis of elderly patients in ICU.

Results: A total of 8,952 elderly cases were included, comprising 3,280 cases (36.6%) in the TTE group and 5,672 cases (63.4%) in the non-TTE group. The SAPS score (20.34 \pm 5.34 vs. 18.74 \pm 5.2, t=13.889, P<0.001) and SOFA score (5.10 \pm 3.38 vs. 3.82 \pm 2.81, t=19.250, P<0.001) of patients in the TTE group were higher than those of non-TTE group. The rate of patients in the TTE group receiving mechanical ventilation (52.10% vs. 34.80%) and vasoactive drugs (29.30% vs. 15.00%) was significantly higher than that in the non-TTE group. In the PS score compatibility cohort, the 28-day mortality rate of patients in the TTE group was 23.4%, and the 28-day mortality rate of patients in the non-TTE group was 28.7%. The adjusted odd ratio (OR) value was 0.76 (95% CI: 0.65–0.87, P<0.001). Analysis of secondary endpoints showed that patients in the TTE group did not use mechanical ventilation and hypertension drugs for a longer period of time than those in the non-TTE group, and the TTE group patients had significantly more fluid input in the first three days after admission to the ICU than in the non-TTE group.

Conclusions: TTE examination can reduce the 28-day mortality risk of elderly critically ill patients.

Keywords: Echocardiography; elderly; critical care; prognosis

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Introduction

Elderly patients often present to the intensive care unit (ICU) with serious and complicated conditions, and the prognosis is often poor. In fact, there is a certain controversy about the admission of elderly patients to the ICU, because studies have shown that more than half of the elderly patients admitted to the ICU are at the end of life (1). One study found that compared with staying in a standard ward, staying in an ICU did not improve the 6-month survival rate of elderly patients over 80 years old (2). Later, Guidet et al. found in a randomized controlled study that compared with standard treatment, admission to the ICU for elderly patients over the age of 75 did not reduce the 6-month mortality rate (3). In another study of health economics, the hospital mortality of non-elderly (18-65 years old) patients, elderly (65-80 years old) patients, and advanced age (>85 years old) patients increased sequentially, and the total medical expenses and daily average increased in turn (4). In addition to the economic costs and the lack of impact on the prognosis, many meaningless ICU treatments may cause a scarcity of medical resources, and other patients who need to be admitted to the ICU are delayed (5). Elderly patients admitted to the ICU often have heart disease or other heart-related problems, leading to frequent decline or deterioration of heart function in elderly patients, which increases hospital mortality and is not conducive to long-term prognosis (6). In clinical practice, doctors often perform transthoracic ultrasound examinations on these patients, as often as once a day to monitor changes in their condition. Transthoracic echocardiography (TTE) is a simple, non-invasive test that can determine whether there are abnormalities in the structure and function of the heart in elderly patients (7). Using TTE, the doctor can judge the severity of the patient's condition and adjust the treatment plan in time. However, there is no relevant research to evaluate the rationality of TTE for middleaged and elderly patients in ICU, and some doctors have not actively adjusted the treatment plan based on the results of ultrasound examination (8). In fact, many ICU doctors are not very familiar with the relevant guidelines, even if the guidelines may not clearly stipulate this issue (9,10). For patients who are not selected for non-cardiac surgery, studies have found that preoperative echocardiography cannot reduce mortality and reduce hospital stay (11). There are also research results that show that TTE parameters cannot improve the APACHE II score for predicting the risk of death in critically ill patients (12).

The purpose of this study is to observe whether the TTE examination has an impact on the short-term prognosis and related indicators of elderly patients admitted to the ICU through retrospective analysis, so as to provide certainty for the rational application of TTE in clinical practice, reducing the excessive use of TTE, and optimizing the allocation of medical resources.

We present the following article in accordance with the STROBE reporting checklist (available at https://dx.doi. org/10.21037/apm-21-1713).

Methods

Study population

The subjects of this study are elderly patients admitted to the ICU. Inclusion criteria: (I) age ≥ 65 years; (II) first admission to ICU (for elderly patients who have been admitted to ICU multiple times, only the first admission data is collected); (III) stay time in ICU ≥ 24 h. Exclusion criteria: (I) loss of key data, such as the first sequential organ failure score (SOFA), the first simplified acute physiology score I (SAPS I), etc.; (II) lost to follow-up. All patients' information in the MIMIC-III database is anonymous, and informed consent is not required; this study is eligible for exemption after being reviewed by the Ethics Committee of Shanxi Provincial People's Hospital. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

Data source

The data for this study was obtained from the MIMIC-III database. The MIMIC-III database is an open critical medicine database jointly released by the Massachusetts Institute of Technology Computational Physiology Laboratory, Beth Israel Dikon Medical Center and Philips Medical under the funding of the National Institutes of Health. The latest version is MIMIC-III v1.4 (13). The database collected hospitalization information of more than 50,000 patients admitted to the ICU of Beth Israel Dikang Medical Center from June 2001 to October 2012. The data includes vital signs, medications, laboratory tests results, clinical observation results, records drawn by nursing staff, fluid balance, program codes, diagnostic codes, imaging reports, hospital stay and survival data, etc. Data acquisition process and permission: The data extraction and analysis work in this study was completed by Dr. Wang.

After completing the Cooperative Organization Training Initiative (CTCI) course, the access to the database was approved by the review committee of Beth Israel Dikang Medical Center and Massachusetts Institute of Technology. At the same time, Dr. Chen passed the test to protect human research participants and obtained the right to download and use the database.

Data extraction

SQL language was used to extract the following data from MIMIC-III database: age, gender, weight, white blood cell count (WBC), hemoglobin (Hb), platelet count (PLT), blood urea nitrogen (BUN), blood creatinine (SCr), blood glucose (Glu), blood electrolytes (K⁺, Na⁺, Ca²⁺), blood HCO₃, sequential organ failure score (SOFA), ICU hospital stay, ICU deaths, other ICU data, comorbidities [hypertension, coronary heart disease, chronic obstruction pulmonary disease (COPD), and chronic kidney disease (CKD)], whether mechanical ventilation, vasoactive drugs and renal replacement therapy (RRT) were used during ICU hospitalization, and whether they were complicated by ventilator-associated pneumonia (VAP), urinary tract infection (UTI), diabetic ketoacidosis (DKA), acute myocardial infarction (AMI), etc. All laboratory test parameters are extracted from the data generated within the first 24 hours after the patient enters the ICU (i.e., the baseline value) and the extreme values during the ICU hospitalization period [i.e., the maximum value (max) and minimum value (min)].

Outcome

The primary endpoint observed in this study is the mortality rate within 28 days after the patient was admitted to the ICU. Secondary endpoints include the number of days of non-mechanical ventilation within 28 days after the patient was admitted to the ICU, the number of days without vasoactive drugs, the maximum dose of norepinephrine, the fluid input volume in the first three days after the patient was admitted to the ICU, and the decrease of serum lactic and creatinine. Calculation of the decrease in lactate and creatinine: For patients undergoing TTE examination, we used the latest test result before TTE examination; for patients who did not undergo TTE examination, the first test after admission to the ICU minus the result of the first test results 48 h after 7655

this test.

Statistical analysis

SPSS software (version 23.0, IBM, Chicago, USA) was used to perform statistical analysis on all research data. Continuous variables are tested for normality first. If they are normally distributed, they are expressed as the mean ± standard deviation (x \pm SD). The comparison between the two groups uses independent student *t*-test; if they are nonnormally distributed, then expressed as median (quartile) [M(OL, OU)] and the Wilcoxon ran sum test was used for comparison between the two groups. Categorical variables are expressed as percentages (%), and the χ^2 test is used for comparison between the two groups. Multivariate logistic regression analysis was used to analyze the risk factors related to death of elderly patients within 28 days of admission to the ICU. Doubly robust estimation was used to infer the relationship between the use of TTE and patient endpoint events (14). The gradient boosted model (GBM) was used to estimate the propensity score (PS) of patients undergoing TTE examination, so as to minimize the imbalance of variables between the TTE group and the non-TTE group. Using PS as the weight, the inverse probabilities weighting (IPW) model was used to generate a weighted cohort (15). P<0.05 indicates that the difference is statistically significant.

Results

General information

According to the inclusion and exclusion criteria, we extracted 8,952 elderly cases from the MIMIC-III database (Figure 1), and divided them into TTE and non-TTE groups. There were 3,280 cases (36.6%) in the TTE group, of which 1,729 were women (52.71%); there were 5,672 cases (63.4%) in the non-TTE group, of which 2,955 cases (52.1%) were women. The SAPS score (20.34±5.34 vs. 18.74±5.2, t=13.889, P<0.001) and SOFA score (5.10±3.38 vs. 3.82±2.81, t=19.250, P<0.001) of patients in the TTE group were higher than those of non-TTE group. The percentage of patients in the TTE group receiving mechanical ventilation (52.10% vs. 34.80%) and vasoactive drugs (29.30% vs. 15.00%) was significantly higher than that in the non-TTE group. These results suggest that patients undergoing TTE examination are more severely ill than those who are not undergoing TTE examination (For



Figure 1 Flowchart of cases enrollment with brief criteria. TTE, transthoracic echocardiography.

detailed information, see Table 1).

Double robust analysis

The results of PS analysis using GBM based on covariates are shown in Figure 2. The contribution of different covariates to the PS score can be observed in Figure 2. In this study, the covariates that have a greater contribution to PS include chronic heart failure (CHF), creatine kinase (CK), troponin, occupancy ICU hours, PO2, etc. In clinical practice, these indicators often prompt doctors to perform TTE examinations on patients. Based on this result, IPW was used to standardize the difference between the TTE group and the non-TTE group (15). The results are shown in Table 1. By comparing the patient cohorts derived from PS score compatibility, it was found that there are still differences in many indicators between the two groups of patients, but the results have been reversed. For example, in the original cohort, the ratio of CHF patients in the TTE group was higher than in the non-TTE group. However, in the new cohort, the rate of CHF patients in the non-TTE group was higher than in the TTE group. Similar variables include creatine kinase (CK), and troponin. Further regression analysis adjusted these variables with differences between groups.

Endpoint analysis

The doubly robustness estimation showed that patients in the TTE examination group had a lower risk of death within 28 after admission to the ICU than in the non-TTE group. In the PS score compatibility cohort, the 28-day mortality rate of patients in the TTE group was 23.4%, and the 28-day mortality rate of patients in the non-TTE group was 28.7%. The adjusted OR value was 0.76 (95% CI: 0.65–0.87, P<0.001). Similarly, the analysis results of the other three models are consistent with this, suggesting that TTE examination is beneficial to reduce the risk of death at 28 days (Table 2). Analysis of secondary endpoints showed that patients in the TTE group did not use mechanical ventilation and vasoactive drugs for a longer period of time than those in the non-TTE group, and the patients in the TTE group had significantly more fluid input in the first three days after admission to the ICU than patients in non-TTE group, but the former dopamine use rate and the former norepinephrine maximum use speed were higher in the TTE group. Other secondary endpoints were not statistically different between the two groups (Table 3).

Discussion

Due to advances in science and technology, increasingly precise, minimally invasive and even non-invasive examination methods are used in clinical practice. However, what follows is overuse of certain examinations and treatments, which on the one hand causes a significant increase in economic costs, and on the other hand wastes time costs (16-18). In most countries in the world, medical resources are still scarce resources, and medical costs remain a heavy burden (19-21). It is important to clarify

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Table 1 Comparison of the basic demographics, comorbidity conditions, and day of ICU admissions between the original cohort and the adjusted (weighted) cohort

Covariate	Original cohort			PS matching cohort			Missing
	Non-TTE (n=5,672)	TTE (n=3,280)	SMD	Non-TTE (N=2,029)	TTE (N=2,029)	SMD	data
Age (years)	78.21 (8.13)	78.33 (8.10)	0.015	78.97 (8.08)	78.26 (8.20)	0.087	0%
Gender (female)	52.10%	52.70%	0.01	50.70%	52.30%	0.032	0%
MICU	65.30%	74.40%	0.2	70.80%	71.80%	0.022	0%
Weight (kg)	74.53 (24.04)	77.42 (24.11)	0.12	76.26 (26.91)	75.05 (19.51)	0.052	11%
SAPS score	18.74 (5.20)	20.34 (5.34)	0.303	20.10 (5.11)	19.52 (5.07)	0.114	0%
SOFA score	3.82 (2.81)	5.10 (3.48)	0.404	4.67 (3.16)	4.41 (3.07)	0.085	0%
Elixhauser score	8.00 (7.30)	11.43 (7.94)	0.449	10.48 (7.53)	9.74 (7.55)	0.097	0%
MV use (1st 24 hs)	34.80%	52.10%	0.354	46.10%	43.80%	0.047	0%
VP use (1st 24 hs)	15.00%	29.30%	0.349	24.00%	22.50%	0.036	0%
Sedative use (1st 24 hs)	25.50%	35.70%	0.221	32.00%	30.00%	0.044	0%
CHF	21.10%	48.60%	0.604	41.20%	34.00%	0.15	0%
AFIB	27.70%	44.20%	0.35	41.50%	37.60%	0.08	0%
Renal	14.20%	18.90%	0.127	19.80%	16.10%	0.097	0%
Liver	3.70%	4.30%	0.033	4.50%	3.80%	0.035	0%
COPD	16.80%	21.10%	0.111	21.00%	18.90%	0.054	0%
CAD	19.10%	24.10%	0.123	22.80%	23.20%	0.008	0%
Stroke	14.80%	15.20%	0.011	15.70%	16.20%	0.013	0%
Malignancy	27.60%	22.30%	0.124	24.30%	23.20%	0.025	0%
Day of ICU admission			0.12			0.049	0%
Sunday	12.50%	13.00%		13.60%	12.80%		
Monday	13.30%	14.80%		14.00%	14.30%		
Tuesday	14.80%	15.70%		15.10%	15.90%		
Wednesday	14.60%	15.40%		15.20%	14.90%		
Thursday	15.10%	16.40%		15.30%	15.10%		
Friday	17.10%	13.80%		14.50%	15.60%		
Saturday	12.70%	10.90%		12.40%	11.40%		
Vital signs							
MAP (mean, sd)	82.43 (18.83)	80.88 (19.67)	0.08	81.27 (19.31)	81.89 (19.04)	0.033	1.70%
Heart rate (bpm, mean, sd)	86.07 (18.75)	89.54 (21.41)	0.172	88.48 (20.26)	88.10 (19.69)	0.019	1.70%
Temperature (°C) (mean, sd)	36.62 (0.92)	36.62 (1.48)	0.002	36.59 (0.98)	36.64 (1.67)	0.041	2.10%
CVP (mmH ₂ O, mean, sd)	10.15 (6.71)	13.92 (24.27)	0.212	10.74 (7.34)	11.74 (17.65)	0.074	78.809
WBC (×10 ⁹ /L, mean, sd)	12.57 (17.15)	13.26 (13.85)	0.044	13.11 (16.05)	12.92 (15.07)	0.012	6.40%
Hemoglobin (g/L, mean, sd)	10.71 (1.88)	10.72 (1.92)	0.007	10.69 (1.88)	10.76 (1.89)	0.034	6.30%

Table 1 (continued)

Table 1 (continued)

Ocurrists	Original cohort			PS matching cohort			Missing
Covariate	Non-TTE (n=5,672)	TTE (n=3,280)	SMD	Non-TTE (N=2,029)	TTE (N=2,029)	SMD	data
Platelet (×10 ⁹ /L, mean, sd)	228.60 (114.45)	222.98 (115.23)	0.049	224.35 (115.78)	227.56 (114.17)	0.028	6.30%
Sodium (mmol/L, mean, sd)	139.27 (5.83)	138.97 (5.58)	0.052	139.29 (5.45)	139.16 (5.63)	0.024	5%
Potassium (mmol/L, mean, sd)	4.09 (0.71)	4.14 (0.75)	0.073	4.13 (0.72)	4.11 (0.73)	0.036	4.80%
Bicarbonate (bicarbonate, mean, sd)	23.74 (4.68)	23.30 (5.33)	0.088	23.53 (5.10)	23.53 (5.08)	0.001	5.30%
Chloride (bicarbonate, mean, sd)	105.65 (6.83)	105.04 (6.74)	0.089	105.43 (6.77)	105.29 (6.66)	0.02	5.10%
BUN (bicarbonate, mean, sd)	29.05 (22.51)	34.11 (24.51)	0.215	33.21 (24.20)	31.45 (23.38)	0.074	5.30%
Lactate (mmol/L, mean, sd)	2.36 (2.00)	2.39 (2.11)	0.019	2.33 (1.86)	2.36 (2.06)	0.017	58.90%
Creatinine (µmol/L, mean, sd)	1.34 (1.22)	1.62 (1.42)	0.213	1.52 (1.31)	1.50 (1.37)	0.01	5.20%
PH (mean, sd)	7.37 (0.10)	7.35 (0.10)	0.133	7.36 (0.11)	7.36 (0.11)	0.018	49.30%
PO ₂ (mmHg, mean, sd)	158.51 (109.68)	136.60 (96.33)	0.212	142.39 (101.70)	147.38 (104.25)	0.048	52.20%
PCO_2 (mmHg, mean, sd)	42.24 (13.32)	42.78 (14.04)	0.04	42.85 (14.05)	42.35 (13.84)	0.036	52.20%
BNP (tested)	0.80%	4.50%	0.231	2.00%	1.10%	0.068	0%
Troponin (tested)	19.00%	46.50%	0.611	40.20%	32.60%	0.157	0%
CK (tested)	35.50%	66.20%	0.645	62.20%	54.20%	0.162	0%

ICU, intensive care unit; PS, propensity score; TTE, transthoracic echocardiography; SAPS, simplified acute physiology score; SOFA, sequential organ failure score; MV, mechanical ventilation; VP, vasopressor; CHF, chronic heart failure; COPD, chronic obstruction pulmonary disease; WBC, white blood cell; BUN, blood urea nitrogen; CK, creatinine kinase.



Figure 2 Relative influence factor of covariates. The relative influence factor measures how discriminative the 40 covariates of the propensity score model are when predicting the likelihood of echocardiogram performance.

the practical application value of auxiliary examinations for patients. First, patients who should be examined have sufficient reason to get timely examinations. Second, unnecessary examinations and occupying medical resources should be avoided, which can also reduce the economic burden of the country, society and individuals. In a multi-institution (three tertiary, four community) study, Sinvani *et al.* found that elderly patients undergoing cardiac ultrasonography before surgery led to prolonged preoperative waiting time, but did not reduce mortality (18). While coronary angiography in patients with stable angina pectoris cannot improve mortality, the use of intravascular ultrasound to guide drug-eluting stent implantation can further reduce patient mortality (22). Therefore, any new technology must be continuously tested in clinical practice to determine the application value of the technology in clinical practice, especially for different patients. It cannot be taken for granted that the examination must be beneficial to the diagnosis and treatment of patients.

The MIMIC-III database was established by MIT and other units based on the electronic medical record system.

 Table 2 Primary outcome analysis

Variable	OR	959	- P value		
Vallable	Un	2.50%	97.50%		
Doubly robust with all covariates	0.65	0.53	0.81	<0.001	
Propensity score IPW	0.83	0.77	0.89	<0.001	
Propensity score matching	0.76	0.65	0.87	<0.001	
Multivariate	0.67	0.55	0.83	<0.001	

OR, odd ratio.

Table 3 Secondary outcome analysis with propensity scores matched cohorts

It is a continuously supplemented dynamic data system that reflects the diagnosis and treatment process of critically ill patients in the real world. It has become a resource that researchers in critical care medicine often utilize (23), and many important discoveries have been made and analyses have been conducted using this database (24-27). Based on the latest version of the database, we retrospectively analyzed the impact of TTE on the short-term prognosis of elderly patients admitted to the ICU. The results suggest that timely TTE examination can reduce the 28day mortality risk of elderly critically ill patients. According to the analysis results of the PS compatibility cohort, this benefit may be related to several factors. First, in the compatibility cohort, the SAPS and SOFA scores of patients in the non-TTE group were higher than those in the TTE group, suggesting that the former is more ill than the latter, but the difference was adjusted in regression analysis; secondly, it may be due to the fact that doctors gave more fluid input and used more vasoactive drugs to patients in the TTE group based on the results of the TTE examination. Of course, further research is warranted to confirm whether these measures contributed to the decreased mortality rate of patients in the TTE group compared to that in the non-TTE group. Fluid therapy for critically ill patients has always been the focus of critical care medicine. Excessive fluid load, sodium load, and chlorine load increase the risk

Secondary outcomes	Non-Echo (n=2,029)	Echo (n=2,029)	SMD	P value 0.022	
Ventilation free days in 28 days	19.17 (12.45)	20.63 (25.79)	0.072		
Vasopressor free days in 28 days	19.81 (12.60)	21.38 (15.15)	0.113	<0.001	
Dobutamine use	1.10%	2.10%	0.079	0.016	
IV fluid day 1 (mL)	1,235.91 (2,832.91)	1,469.66 (3,112.82)	0.079	0.012	
IV fluid day 2 (mL)	475.71 (2,030.06)	671.76 (2,384.52)	0.089	0.005	
IV fluid day 3 (mL)	78.18 (1,804.90)	335.55 (2,220.60)	0.127	0.0001	
SOFA reduction day 2	0.46 (4.21)	0.36 (2.91)	0.029	0.379	
SOFA reduction day 3	0.70 (4.20)	0.50 (2.88)	0.055	0.077	
Norepinephrine (maximum dosage mg/min)	0.56 (2.11)	0.77 (2.52)	0.088	0.004	
Serum lactate reduction (48 hours)	0.35 (1.96)	0.04 (1.60)	0.171	0.683	
Serum creatinine reduction (48 hours)	0.14 (0.61)	0.10 (0.61)	0.055	0.326	
Serum lactate reduction (24 hours)	0.37 (1.73)	-0.02 (1.44)	0.251	0.353	
Serum creatinine reduction (24 hours)	0.07 (0.52)	0.07 (0.46)	0.003	0.953	

SOFA, sequential organ failure score.

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of death (28,29). However, in clinical practice, doctors' concern about excess fluid may lead to insufficient fluid infusion in some critically ill patients. A study by Marik *et al.* found that for patients with severe sepsis and septic shock, the actual volume of fluid input was significantly lower than the volume recommended by the guidelines; on the other hand, the input of more than 5,000 mL of fluid on the first day of admission to the ICU significantly increase the risk of death and cost of hospitalization (30).

According to our results, we believe that when elderly patients are admitted to the ICU, TTE examinations should be performed in a timely manner according to the patient's specific condition, especially when the effective circulating blood volume of the patient is insufficient. Depending on the examination results and the specific condition of the patient, appropriate vasoactive drugs and fluid treatments should be given in time. Clinicians should not worry too much about the patient's cardiopulmonary function, leading to insufficient fluid administration. This situation requires special attention in elderly patients with cardiopulmonary diseases.

This study has some limitations: First, although this study is based on real-world data with a large sample size, the data comes from a single medical center, which may have various biases such as medical level, habits, and population; secondly, this study is a retrospective analysis, and due to the lack of key information and other reasons in the data extraction process, a large number of patient data may be excluded, and there may be selection bias; in addition, although TTE is non-invasive and convenient, its reproducibility is relatively poor. The consistency of TTE examination in this study cannot be evaluated, and there may be measurement bias. Therefore, we suggest designing a prospective, multi-center study based on similar studies to further observe the impact of TTE on elderly patients with severe illness.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi. org/10.21037/apm-21-1713). The authors have no conflicts

of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All patients' information in the MIMIC-III database is anonymous, and informed consent is not required; this study is eligible for exemption after being reviewed by the Ethics Committee of Shanxi Provincial People's Hospital. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).

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