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Original Article

Feasibility of using the predisposition, insult/infection, physiological response, and organ dysfunction concept of sepsis to predict the risk of deterioration and unplanned intensive care unit transfer after emergency department admission

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Abstract

Background: Recognizing patients at risk for deterioration and in need of critical care after emergency department (ED) admission may prevent unplanned intensive care unit (ICU) transfers and decrease the number of deaths in the hospital. The objective of this research was to study if the predisposition, insult, response, and organ dysfunction (PIRO) concept of sepsis can be used to predict the risk of unplanned ICU transfer after ED admission.

Methods: The ICU transfer group included 313 patients with unplanned transfer to the ICU within 48 hours of ED admission, and the control (non-transfer) group included 736 randomly sampled patients who were not transferred to the ICU. Two-thirds of the total 1049 patients in this study were randomly assigned to a derivation group, which was used to develop the PIRO model, and the remaining patients were assigned to a validation group.

Results: Independent predictors of deterioration within 48 hours after ED admission were identified by the PIRO concept. PIRO scores were higher in the ICU transfer group than in the non-transfer group, both in the derivation group [median (mean ± SD), 5 (5.7 ± 3.7) vs. 2 (2.5 ± 2.5); $p < 0.001$], and in the validation group [median (mean ± SD), 6 (6.0 ± 3.4) vs. 2 (2.4 ± 2.6); $p < 0.001$]. The proportion of ICU transfer patients with a PIRO score of 0−3, 4−6, 7−9, and ≥10 was 14.1%, 46.5%, 57.3%, and 83.8% in the derivation group ($p < 0.001$) and 12.8%, 37.3%, 68.2%, and 70.0% in the validation group ($p < 0.001$), respectively. The proportion of inpatient mortality in patients with a PIRO score of 0−3, 4−6, 7−9, and ≥10 was 2.6%, 10.1%, 23.2%, and 45.9% in the derivation group ($p < 0.001$) and 3.3%, 12.0%, 18.2%, and 20.5% in the validation group ($p < 0.001$), respectively.

Conclusion: The PIRO concept of sepsis may be used in undifferentiated medical ED patients as a prediction system for unplanned ICU transfer after admission.

Keywords: emergencies; intensive care unit; patient transfer; risk factors; sepsis

Conflicts of interest: The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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1. Introduction

The emergency department (ED) is an important source of hospital inpatients, especially those with critical problems. However, the condition of some patients may deteriorate after admission and require an unplanned transfer to the intensive care unit (ICU). Patients with an unplanned ICU transfer after ED admission have a higher rate of mortality than those who are admitted directly to the ICU from the ED.[1–5] Although admissions from the ED account for the majority of unplanned transfers to the ICU,[6] strategies to decrease unplanned ICU transfers after ED admission are lacking. Some researchers have tried to determine the risk of unplanned ICU transfer after ED admission[7,8]; however, these studies were based primarily on administrative data or focused only on certain age groups. The Modified Early Warning Score (MEWS) and its physiologically based derivatives have been validated as predictors of admission, inpatient mortality, and the need for ICU admission in ED patients.[9–13] However, these systems use only vital sign variables and have a lower sensitivity to predict inpatient mortality.[14] In addition, the MEWS is inferior to the Mortality in Emergency Department Sepsis (MEDS) in risk assessment for death in ED patients with sepsis.[15] The MEDS and other scoring systems have been used to identify predictors of death from multiple dimensions, including demographic data, comorbid illnesses, physiological changes, and laboratory abnormalities.[16–18]

The predisposition, insult, response, and organ dysfunction (PIRO) concept was proposed by experts at the International Sepsis Definition Conference in 2001 to describe the phenotypes of sepsis.[19] The PIRO model, with multi-dimensional predictive variables, has been validated in risk staging for sepsis.[20–23] Sharing some common features of clinical presentations with sepsis, diseases other than infections may have risk factors for clinical deterioration and/or mortality from multiple dimensions, similar to the PIRO model for sepsis. This observational study was performed to determine if the PIRO concept of sepsis can be used as a prediction system for unplanned ICU transfer due to clinical deterioration after undifferentiated medical ED admission.

2. Methods

2.1. Setting

This study was conducted in the ED of a suburban teaching hospital. Staffed by full-time emergency physicians (EPs), this ED has historically served approximately 50,000 patients annually with an admission rate of 25%, which accounts for 45% of inpatients in this facility.

2.2. Study design and patients

Patients with non-traumatic conditions who underwent an unplanned transfer to the ICU within 48 hours of ED admission between January 1, 2007 and December 31, 2010, were included in this study (ICU transfer group). Additionally, we randomly sampled patients who were not transferred to the ICU within 48 hours of admission (non-transfer group) to serve as controls. The ratio of controls to cases was approximately 2:1. Patients were included if they were to be admitted to a general ward, but remained in the ED because of a delay in transfer or blocked access. Patients were excluded if they were younger than 18 years of age, were admitted for injuries/intoxications/suicides or obstetric problems, or had critical conditions but initially refused ICU admission. We excluded patients who had signed "do not resuscitate" (DNR) orders, because it may affect the decision of transferring patients to ICU and medical efforts to resuscitate the patients. We also excluded patients who showed no clinical deterioration after admission but were transferred to the ICU for a second opinion of potential risk. Patients who were transferred to the ICU within 48 hours for close monitoring after a major operation or invasive procedure (expected transfer) were also not enrolled in the study. The development of study patients is illustrated in Fig. 1.

Two research nurses with at least 3 years of experience in emergency medicine and critical care, respectively, reviewed the medical records and abstracted the data on a structured data sheet. Another research assistant was responsible for data entry. Each of the research nurses was responsible for different parts of the data abstraction, and one research nurse rechecked the correctness of data entry. A board-certified EP checked the quality of the data sheets and examined the quality of the data by establishing criteria to confirm that the data were logically valid. The research nurses were trained on the objective of the study, the definition of variables, and the technique of reviewing medical records and abstraction of data. Both electronic and written medical records were reviewed to identify the desired information. The research nurses reviewed the diagnoses of outpatient visits and hospitalizations, medication used, and results of examinations to ensure that certain important comorbid illnesses were present.

2.3. Candidate predictor variables

The candidate predictor variables included those of predisposition (P; demographic data, comorbid conditions, and chronic organ insufficiency), insult (I; diseases and organ system), physiological responses to diseases (R; vital sign changes), and organ dysfunction (O). The comorbid conditions were applied in part from the Charlson comorbidity index,[24] and chronic organ insufficiencies were from Acute Physiology and Chronic Health Evaluation (APACHE) scores.[25] We used physiological responses in systemic inflammatory response syndrome as the R variables in our study, but defined a maximum heart rate (HR) $\geq$ 130/minute and a maximum respiratory rate (RR) $\geq$ 30/minute as the thresholds. These threshold values were the same as the highest scores in the MEWS.[9] The acute O variables were introduced from definitions of severe sepsis.[26]

Regarding the reasons for admission, which was used as "Insult" (diseases and organ system) in the PIRO classification, we categorized all patients presenting with infection from

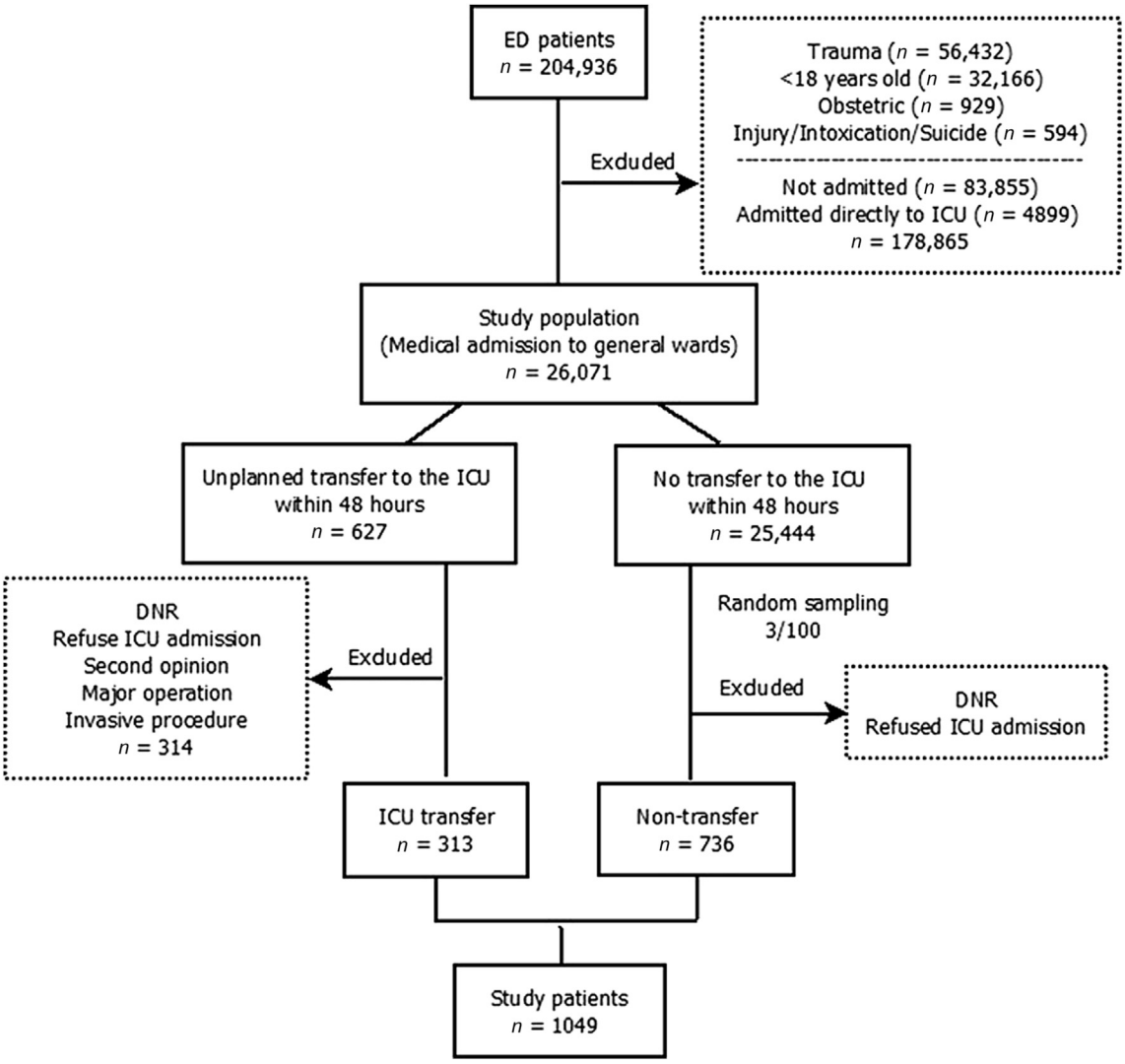

Fig. 1. Development of study patients and group for derivation and validation. DNR = do not resuscitate; ED = emergency department; ICU = intensive care unit.

different sources as "infections" in our study, except that infections from the neurological system were categorized as neurological diseases. Intra-abdominal diseases that had developed to peritonitis and/or presented with toxic signs of infection were also categorized as infections. For patients without infection, the reasons for admission were categorized according to involvement of the organ system.

Vital signs and physiological changes were recorded at four time points: triage, decision of disposition, immediately prior to leaving the ED (or for those deteriorated when they were still in the ED, the last time these signs were recorded prior to deterioration), and time of clinical deterioration. The first three time points were grouped into the period "before deterioration". Only those symptoms/signs that occurred prior to deterioration were used as candidate predictors. Because there were no predetermined criteria for EPs to decide if certain tests (e.g., arterial blood gases, liver enzymes, coagulation tests, or lactate level) would be ordered, results of tests were considered to be negative in our study if they were not ordered.

2.4. Model construction and data analysis

We randomly assigned two-thirds of the study patients to the derivation group, and the remaining one-third were assigned to the internal validation group. Next, we used the derivation group to construct the PIRO model. We first dichotomized all variables with pre-defined thresholds and performed univariate analysis by using Fisher's exact test to assess their statistical differences. Those candidate predictors with $p < 0.1$ were entered in the logistic regression analysis. We followed the study of Howell et al[22] and constructed individual P, I, R, and O models separately by using forward stepwise logistic regression analysis to identify significant predictors. We obtained an individual integer score across each of the independent predictors after dividing the β coefficient from the regression model by 0.5. The total PIRO score was obtained by summation of individual P, I, R, and O integer scores, and this yielded the final PIRO model. Model discrimination was assessed by calculating the area under the receiver operating characteristic curve (AUC). Model

calibration was assessed using the Hosmer−Lemeshow goodness-of-fit test, and then we validated the models with the internal validation group. We arbitrarily categorized the PIRO score into different risk groups. The proportions of ICU transfer patients and inpatient mortality were then analyzed between the PIRO groups.

All data were analyzed using SPSS software for Windows (version 17.0; SPSS Inc., Chicago, IL, USA). A p value < 0.05 was considered statistically significant. This study was approved by the Institutional Review Board of Cheng-Ching General Hospital, Taichung, Taiwan.

3. Results

Of the 204,936 ED visits in the study period, 26,071 patients with non-traumatic conditions were admitted to general wards and fulfilled the inclusion criteria of our study. Data on 627 of these patients with unplanned ICU transfer within 48 hours of admission were extracted; after excluding 314 patients based on our study criteria, 313 patients remained for further analysis (ICU transfer group). We then randomly sampled 736 patients who were admitted to general wards, but not transferred to the ICU within 48 hours of admission (non-transfer group; Fig. 1). Of these 1049 patients, 605 (57.7%) were male, 492 (46.9%) were elderly (>65 years of age), and 202 (19.3%) were >80 years of age. Reasons for admission included infections in 350 patients (33.4%), followed by gastrointestinal diseases [241 patients (23.0%)] and cardiovascular diseases [138 patients (13.2%)]. Most of the patients [901 individuals (85.9%)] were discharged home, but 91 (8.7%) died during this admission.

After random assignment for the 1049 patients with a probability of 0.7 in Bernoulli distribution, 699 patients were assigned to the derivation group, in which the following analyses were performed and models were constructed. The remaining 350 patients were assigned to the validation group. No candidate variables differed between the derivation and validation groups (Table 1).

Patients in the ICU transfer group were older than those in the non-transfer group (64.7 ± 18.2 years vs. 59.0 ± 19.5 years, $p < 0.001$). Patients who were >80 years or had diabetes, coronary artery disease, cerebrovascular disease, dementia, or a cerebral performance category (CPC) score of three or four, had a greater chance of deteriorating clinically and being admitted to the ICU unexpectedly within 48 hours of ED admission. Patients with clinical deterioration and unplanned ICU transfer within 48 hours of admission were also more likely to have a history of respiratory failure, congestive heart failure, severe liver disease, end-stage renal disease, or advanced malignancy or present with neurological disease or infections (Table 2). Immune compromise and cardiovascular presentation were also entered into logistic regression analysis according to our methodology ($p < 0.1$). Patients were more likely to have an unplanned ICU transfer if the maximum RR was ≥30/minute, maximum HR was ≥130/minute, or white blood cell count was abnormal (>12,000/μL or < 4000/μL, or bands >5%). Hypotension, renal dysfunction, respiratory dysfunction, liver dysfunction, hematological dysfunction, or metabolic dysfunction, were also associated with an unplanned ICU transfer (Table 3). Independent predictors of deterioration within 48 hours of ED admission are listed by section of the PIRO model in Table 4.

Table 1
Demographic data and comorbid illnesses.

	Derivation group (n = 699)	Validation group (n = 350)	Combined (n = 1049)	p[a]
Sex				
Male	404 (57.8)	201 (57.4)	605 (57.7)	0.91
Age (y)				0.77
15−44	168 (24.0)	85 (24.3)	253 (24.1)	
45−64	197 (28.2)	107 (30.6)	304 (29.0)	
65−79	194 (27.8)	96 (27.4)	290 (27.6)	
≥80	140 (20.0)	62 (17.7)	202 (19.3)	
Chronic illness				
Diabetes	227 (32.5)	100 (28.6)	327 (31.2)	0.20
Hypertension	320 (45.8)	147 (42.0)	467 (44.5)	0.25
Cerebrovascular disease	129 (18.5)	60 (17.1)	189 (18.0)	0.60
Coronary artery disease	119 (17.0)	48 (13.7)	167 (15.9)	0.17
Alcohol abuse	61 (8.7)	32 (9.1)	93 (8.9)	0.83
Cerebral performance category				0.70
1 or 2	606 (86.7)	303 (86.6)	909 (86.7)	
3 or 4	93 (13.3)	47 (13.4)	140 (13.3)	
Time of arrival				0.96
12:00 AM to 8:00 AM	129 (18.5)	61 (17.4)	190 (18.1)	
8:00 AM to 4:00 PM	326 (46.6)	166 (47.4)	492 (46.9)	
4:00 PM to 12:00 AM	244 (34.9)	123 (35.1)	367 (35.0)	
Diseases and organ system				0.54
Infections	227 (32.5)	123 (35.1)	350 (33.4)	
Gastrointestinal diseases	162 (23.2)	79 (22.6)	241 (23.0)	
Cardiovascular diseases	95 (13.6)	43 (12.3)	138 (13.2)	
Neurological diseases	58 (8.3)	39 (11.1)	97 (9.2)	
Respiratory diseases	39 (5.6)	13 (3.7)	52 (5.0)	
Others	118 (16.9)	53 (15.1)	171 (16.3)	
Outcomes				0.25
Discharged home	594 (85.0)	307 (87.7)	901 (85.9)	
Death	63 (9.0)	28 (8.0)	91 (8.7)	
Transfer to chronic care facility	38 (5.4)	11 (3.1)	49 (4.7)	
Transfer to other hospital	4 (0.6)	4 (1.1)	8 (0.8)	

Data are expressed as n (%) unless otherwise indicated.
[a] Chi-square test.

We constructed individual P, I, R, and O models separately from the corresponding independent predictors and, in turn, the final PIRO model from its individual components. The AUCs in the derivation group and validation group were 0.68 and 0.72 in the P model, 0.62 and 0.64 in the I model, 0.61 and 0.61 in the R model, and 0.67 and 0.68 in the O model, respectively (Table 5). The AUCs in the final PIRO model were higher than those in the individual components and were 0.77 [95% confidence interval (CI), 0.73−0.81] in the derivation group and 0.80 (95% CI, 0.75−0.85) in the validation group. The calibrations (Hosmer−Lemeshow test) in the P, I, R, and O models did not differ between the derivation and validation groups.

The PIRO scores were higher in the ICU transfer group than in the non-transfer group, both in the derivation group, and the validation group, as shown in Table 6. We categorized

Table 2
Univariate analysis of candidate variables: predispositions and insults.

Covariate	ICU transfer (n = 214)		Odds ratio (95% confidence interval)	p[a]
	Covariate Yes	Covariate No		
Demographic				
Age, ≥80 y	55 (39.3)	159 (28.4)	1.4 (1.1−1.8)	0.01
Sex, male	126 (31.2)	88 (29.8)	1.0 (0.8−1.2)	0.74
Comorbid illness				
Diabetes	90 (39.6)	124 (26.3)	1.5 (1.2−1.9)	<0.001
Hypertension	98 (30.6)	116 (30.6)	1.0 (0.8−1.3)	>0.99
Coronary artery disease	46 (38.7)	168 (29.0)	1.3 (1.0−1.7)	0.04
Cerebrovascular disease	52 (40.3)	162 (28.4)	1.4 (1.1−1.8)	0.01
Alcohol abuse	14 (23.0)	200 (31.4)	0.7 (0.5−1.2)	0.19
Dementia	21 (45.7)	193 (29.6)	1.5 (1.1−2.2)	0.03
Cerebral performance category score of 3 or 4	50 (53.8)	164 (27.1)	2.0 (1.6−2.5)	<0.001
Malignancy, advanced	27 (42.2)	187 (29.4)	1.4 (1.0−2.0)	0.05
History of organ failure				
Respiratory failure	16 (57.1)	198 (29.5)	1.9 (1.4−2.7)	0.003
Congestive heart failure	38 (41.8)	176 (28.9)	1.4 (1.1−1.9)	0.02
Severe liver disease	23 (53.5)	191 (29.1)	1.8 (1.4−2.5)	0.002
End-stage renal disease	18 (58.1)	196 (29.3)	2.0 (1.4−2.7)	0.001
Immune compromise	9 (52.9)	205 (30.1)	1.8 (1.1−2.8)	0.06
Diseases and organ system				
Infections	90 (39.6)	124 (26.3)	1.5 (1.2−1.9)	<0.001
Gastrointestinal diseases	47 (29.0)	167 (31.1)	0.9 (0.7−1.2)	0.63
Neurological diseases	31 (53.4)	183 (28.5)	1.9 (1.4−2.5)	<0.001
Cardiovascular diseases	21 (22.1)	193 (32.0)	0.7 (0.5−1.0)	0.06
Respiratory diseases	12 (30.8)	202 (30.6)	1.0 (0.6−1.6)	>0.99

Data are expressed as n (%) unless otherwise indicated.
[a] Fisher's exact test.

the PIRO scores into four risk groups (PIRO score of 0−3, 4−6, 7−9, and ≥10), and the proportion of ICU transfer patients in an individual PIRO risk group increased with higher PIRO scores (χ^2, $p < 0.001$ and $p < 0.001$, in the derivation group and validation group, respectively; Table 7). The correlation coefficient of predicted versus observed unplanned ICU transfer in the individual PIRO risk groups (i.e., in the derivation group and the validation group, respectively), was 0.926 (Fig. 2). The inpatient mortality rates also differed between the PIRO risk groups (χ^2, $p < 0.001$ and $p < 0.001$, in the derivation group and validation group, respectively; Table 7). However, the predictive and observed inpatient mortality (i.e., in the derivation group and the validation group, respectively), varied in patients with a PIRO score of 7−9 and ≥10; the correlation coefficient was 0.673 (Fig. 3).

4. Discussion

Strategies aimed at recognizing patients at risk for deterioration and in need of critical care after ED admission may

Table 3
Univariate analysis of candidate variables: responses and organ dysfunction.

Covariate	ICU transfer (n = 214)	Non-transfer (n = 485)	Odds ratio (95% confidence interval)	p[a]
Physiological responses				
Respiratory rate ≥ 30/min	25 (11.7)	19 (3.9)	3.2 (1.7−6.0)	<0.001
Heart rate ≥ 130/min	33 (15.4)	23 (4.7)	3.7 (2.1−6.4)	<0.001
Body temperature >38°C or <36°C	80 (37.4)	202 (41.6)	0.8 (0.6−1.2)	0.32
Abnormal white blood cell count[b]	86 (40.2)	135 (27.8)	1.7 (1.2−2.4)	0.001
Organ dysfunction				
Hypotension	33 (15.4)	17 (3.5)	5.0 (2.7−9.3)	<0.001
Renal dysfunction	37 (17.3)	33 (6.8)	2.9 (1.7−4.7)	<0.001
Respiratory dysfunction	36 (16.8)	28 (5.8)	3.3 (2.0−5.6)	<0.001
Liver dysfunction	8 (3.7)	3 (0.6)	6.3 (1.6−23.8)	0.005
Hematological dysfunction	31 (14.5)	18 (3.7)	4.4 (2.4−8.1)	<0.001
Metabolic dysfunction	18 (8.4)	6 (1.2)	7.4 (2.9−18.9)	<0.001

Data are expressed as n (%) unless otherwise indicated.
[a] Fisher's exact test.
[b] White blood cell count of >12,000/μL or <4000/μL or bands > 5%.

Table 4
Logistic regression analysis for model construction.

Variable	β	Integer score[a]	Odds ratio (95% confidence interval)	*p*
Predisposition model				
Diabetes	0.47	1	1.6 (1.1−2.3)	0.009
Cerebral performance category score of 3 or 4	1.15	2	3.2 (2.0−5.0)	<0.001
Congestive heart failure	0.50	1	1.7 (1.0−2.7)	0.04
Severe liver disease	1.28	3	3.6 (1.9−6.9)	<0.001
End-stage renal disease	1.10	2	3.0 (1.4−6.4)	0.005
Immune compromise	1.12	2	3.0 (1.1−8.4)	0.03
Insult model				
Infections	0.82	2	2.3 (1.6−3.2)	<0.001
Neurological diseases	1.38	3	4.0 (2.3−7.0)	<0.001
Response model				
Respiratory rate ≥ 30/min	0.99	2	3.1 (1.4−5.1)	<0.001
Heart rate ≥ 130/min	1.13	2	3.1 (1.7−5.5)	<0.001
Abnormal white blood cell count[b]	0.48	1	1.6 (1.1−2.3)	0.006
Organ dysfunctions model				
Hypotension	1.21	2	3.3 (1.7−6.4)	<0.001
Pulmonary dysfunction	1.02	2	2.8 (1.6−4.9)	<0.001
Renal dysfunction	0.83	2	2.3 (1.3−4.0)	0.003
Hematological dysfunction	1.35	3	3.9 (2.0−7.3)	<0.001
Metabolic dysfunction	1.46	3	4.3 (1.6−11.9)	0.005

[a] β coefficient divided by 0.5.
[b] White blood cell count of >12,000/μL or <4000/μL or bands >5%.

prevent unplanned ICU transfers and decrease the number of deaths in the hospital. Our study suggests that the PIRO concept, a multi-dimensional scoring system for sepsis, can be used to predict unplanned ICU transfer within 48 hours of admission in undifferentiated medical ED patients. We successfully developed a prediction score system according to the PIRO concept. The PIRO scores were higher for the ICU transfer patients than for patients in the non-transfer group. PIRO scores increased with the proportions of patients with ICU transfer, and partly with inpatient mortality.

There are several reasons why the PIRO concept, which was initially proposed to build a risk stratification system for patients with sepsis, could be used in this instance. Delgado et al[27] found that respiratory tract infection, urinary tract infection, sepsis, and other acute infections accounted for 26.9% of patients with unplanned ICU transfer within 24 hours of ED admission; in our study, one-third of patients and 43.1% of ICU transfer patients had infections. Kellett and Deane,[17] in their research to develop the Simple Clinical Score, identified 16 independent predictors of 30-day mortality after undifferentiated ED admissions. These variables, similar to those grouped by the PIRO concept, included age, diabetes, residence in a nursing home, prior chronic conditions limiting daily activities, neurological presentations, cardiac presentation, and vital sign changes. These findings also support the proposition that the PIRO concept may fit easily into the undifferentiated ED setting.

The robustness of our study was confirmed in several ways. First, the discrimination ability of the models was good [AUC in the PIRO model of 0.77 (95% CI, 0.73−0.81) in the derivation group and 0.80 (95% CI, 0.75−0.85) in the validation group], and the AUC in the total PIRO model was higher than that in the separate P, I, R, and O models. Second, the calibration of our model was also good with the Hosmer−Lemeshow goodness-of-fit test ($p > 0.05$ in the P, I, R, and O models).

In addition, our models were valid and clinically useful. In both the derivation and validation groups, the median PIRO score was higher in the ICU transfer group than in the non-transfer group. We also found that with a higher PIRO score, the proportions of patients with clinical deterioration, and partly with inpatient mortality, increased. The proportions of

Table 5
Discriminatory ability and calibration of models.

	Derivation group (n = 699)	Validation group (n = 350)	Calibration p[a]
Predisposition model	0.68 (0.63−0.72)	0.72 (0.66−0.79)	0.34
Insult model	0.62 (0.58−0.67)	0.64 (0.58−0.71)	>0.999
Response model	0.61 (0.56−0.66)	0.61 (0.55−0.68)	0.85
Organ dysfunction model	0.67 (0.63−0.72)	0.68 (0.61−0.74)	0.35
PIRO model	0.77 (0.73−0.81)	0.80 (0.75−0.85)	

Data are expressed as area under the receiver operating characteristic curve (95% confidence interval) unless otherwise indicated.
[a] Hosmer−Lemeshow goodness-of-fit test in logistic regression analysis.

Table 6
PIRO score in ICU transfer versus non-transfer group.

PIRO score	ICU transfer	Non-transfer	p[a]
Derivation group	5 (5.7 ± 3.7)	2 (2.5 ± 2.5)	<0.001
Validation group	6 (6.0 ± 3.4)	2 (2.4 ± 2.6)	<0.001

Data are expressed as median (mean ± SD) unless otherwise indicated.
ICU = intensive care unit.
[a] Student t test.

Table 7
Prediction ability of PIRO score in 1049 study patients.

PIRO group	*n* (% in cohort)		ICU transfer, *n* (% in PIRO group)			Inpatient mortality, *n* (% in PIRO group)		
	Derivation	Validation	Derivation	Validation	Combined	Derivation	Validation	Combined
0–3	421 (60.2)	211 (60.3)	62 (14.1)	27 (12.8)	89 (14.1)	11 (2.6)	7 (3.3)	18 (2.8)
4–6	159 (22.7)	75 (21.4)	74 (46.5)	28 (37.3)	102 (43.6)	16 (10.1)	9 (12.0)	25 (10.7)
7–9	82 (11.7)	44 (12.6)	47 (57.3)	30 (68.2)	77 (61.1)	19 (23.2)	8 (18.2)	27 (21.4)
≥10	37 (5.3)	20 (5.7)	31 (83.8)	14 (70.0)	45 (78.9)	17 (45.9)	4 (20.5)	21 (36.8)
p			<0.001[a]	<0.001[a]	<0.001[a]	<0.001[b]	<0.001[b]	<0.001[b]

[a] Chi-square, PIRO score versus intensive care unit transfer.
[b] Chi-square, PIRO score versus inpatient mortality.

ICU transfer patients with a PIRO score of 4–6, 7–9, and ≥10 were approximately 3.1, 4.3, and 5.6 times higher than those with a PIRO score of 0–3, respectively, and the proportions of patients with mortality with a PIRO score of 4–6, 7–9, and ≥10 were approximately 3.8, 7.5, and 12.9 times higher, respectively, than those with a PIRO score of 0–3. The PIRO score assignment in our study can be of value in the original population for risk stratification with such high odds ratios. The predictive and observed deteriorations (unplanned ICU transfers) in the derivation group and validation group, respectively, correlated very well in the different PIRO risk groups (r = 0.926). However, the predictive and observed inpatient mortality varied in patients with a PIRO score of 7–9 (23.2% in the derivation group and 18.2% in the validation group) and of ≥10 (45.9% in the derivation group and 20.5% in the validation group). Caution should be exercised in predicting inpatient mortality by using a model that was developed by using unplanned ICU transfer as the primary endpoint.

A number of studies have suggested that the rapid response system and medical emergency team reduce the occurrence of unplanned admissions to the ICU, as well as the number of unexpected deaths and in-hospital cardiac arrests.[28–30] However, for some patients, the medical emergency team criteria are satisfied but medical emergency team calls are not triggered, which is recognized as the afferent limb failure of the rapid response system.[31,32] Continuous monitoring and patient-centered systems have been recommended to enhance the ability to detect clinical deteriorations and decrease afferent limb failures.[31,33] However, these strategies require resources and are unlikely to be used in every patient admitted to a general ward. We suggest that by using the PIRO score system to identify high-risk patients, these high-technology monitoring systems could be used more efficiently. Electronic medical record systems have been used to predict the risk of deterioration,[33,34] and some include electronic data of vital signs.[35] Further research may be warranted to determine if risk stratification with the PIRO score, plus acquisition of data from the electronic patient record, can be used to build a decision support system for smart disposition of ED patients.

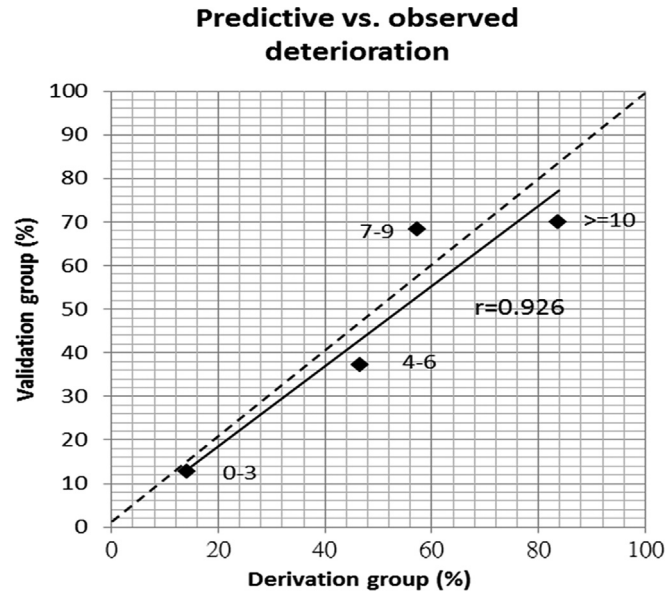

Fig. 2. Predictive versus observed deterioration (%) in different PIRO risk groups (i.e., in the derivation group vs. the validation group). Broken line = reference line. Unbroken line = regression line.

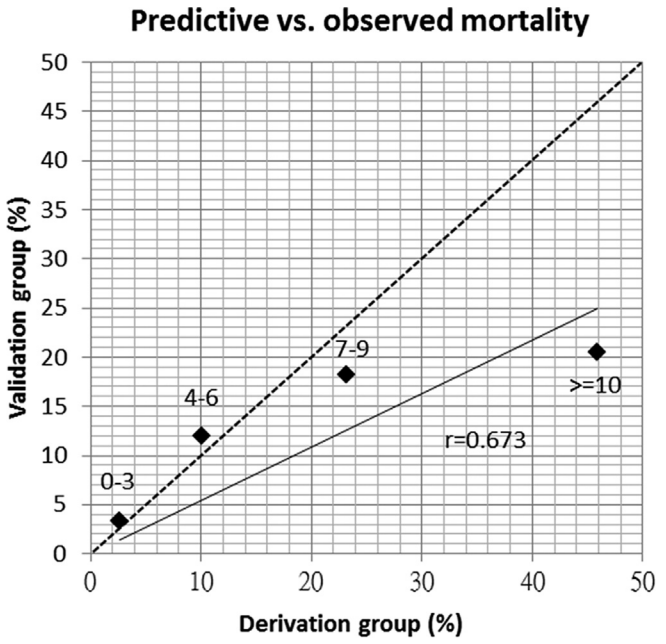

Fig. 3. Predictive versus observed inpatient mortality (%) in different PIRO risk groups (i.e., in the derivation group vs. the validation group). Broken line = reference line. Unbroken line = regression line.

Because our study was a retrospective study conducted at a single institution, there are some limits to the generalization of its results. For argument of different criteria of ICU admission in different facilities, we focused on patients with real clinical deteriorations that led to unplanned ICU transfer, in the hopes that our results would be applicable to other institutions with different resources and admission policies. The methodology of chart review had some common problems of correctness of vital sign measurement, incompleteness of vital sign measurement, and recording of medical events, as well as inconsistent clinical decision criteria for ordering certain examinations and identifying abnormalities during these examinations. However, our study also contributed by including vital signs and laboratory results in the evaluation of the risk of unplanned ICU transfer after ED admission. Future prospective validation research may ameliorate the weakness of a medical record review study, but may also hinder the blindness of outcome assessment, which is important in constructing a clinical prediction rule like that in our study.[36] In addition, selection bias may have occurred in this study, because 33.4% of the patients had an infection. The fact that we categorized all infections from different sources into "infection disease" may explain the high prevalence of infections in this study.

In conclusion, we suggest that the PIRO concept of sepsis may be used to build a prediction system for unplanned ICU transfer after undifferentiated medical ED admissions.

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