

Development and clinical empirical validation of the Prognosis Prediction Model of Chronic Critical Illness

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Research

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Abstract

Background A vast number of patients with chronic critical illness (CCI) have died of delayed organ failure in the intensive care unit (ICU). The weak organ function of patients needed appropriate tool to evaluate, which could provide reference for clinical decisions and communication with family members. The objective of this study was to develop and validate a prediction model for accurate, timely, simple, and objective identification of the critical degree of the patients' condition.

Methods This study used a retrospective case-control and a prospective cohort study, with no interventions. Patients identified as CCI from a comprehensive ICU of a large metropolitan public hospital were selected. A total of 344 (case 172; control 172) patients were included to develop the Prognosis Prediction Model of Chronic Critical Illness (PPCCI Model) in this case-control study; 88 (case, 44; control 44) patients were included for the validation cohort in a prospective cohort study. The discrimination of the model was assessed by the area under the curve (AUC) of the receiver operating characteristic (ROC).

Results The model comprised 9 predictors: age, prolonged mechanical ventilation (PMV), sepsis/other serious infections, Glasgow Coma Scale (GCS), mean artery pressure (MAP), heart rate (HR), respiratory rate (RR), oxygenation index (OI), and active bleeding. In both cohorts, the PPCCI Model could better identify the dead CCI patients (development cohort: AUC, 0.934; 95% CI, 0.908–0.960; validation cohort: AUC, 0.965; 95% CI, 0.931–0.999), and showed better discrimination than the Acute Physiology And Chronic Health Evaluation II (APACHE II), Modified Early Warning Score (MEWS), and Sequential Organ Failure Assessment (SOFA).

Conclusions The PPCCI Model can provide a standardized measurement tool for ICU medical staff to evaluate the condition of CCI patients, to facilitate rational allocation of ward-monitoring resources or communicate with family members.

Background

The development of critical care medicine and nursing has benefited and increasingly rescued a vast number of patients from various life-threatening diseases[1]. However, in many patients, health may not be quickly restored, and the long-term prognosis may not be optimistic[2–4]. These patients may be deficient in self-care ability and, thus, may have to undergo long-term ICU stay for treatment and monitoring and constitute the group of patients with chronic critical illness (CCI)[4–6]. The Research Triangle Institute (RTI) International presented a report and defined CCI based on the requirements of the Centers for Medical Care & Medical Services (CMS)[7].

Whether it is patients, family members, or medical staff, several problems remain to be solved in the communication and treatment decision-making of CCI patients[8, 9]. Many patients live in pain and despair[10–12], are unable to participate in their own treatment decisions due to disease restrictions[13, 14], and, thereby, are forced to accept their families' decisions. However, family decision-makers often have unrealistic expectations of outcomes[15]. Doctors may often be more pragmatic than either patients

of family members about expectations of CCI, but possibly encounter challenges in communicating the expected disease outcomes, long-term rehabilitation care plan, or treatment cessation[16, 17]. An effective evaluation tool can identify high-risk CCI patients at earlier timepoints to facilitate advanced interventions to protect patient organ function[3]. Similarly, the tool could accurately identify low-risk and medium-risk patients to facilitate early caregiver intervention in patient rehabilitation[18]. There are several critical illness assessment tools, such as the Acute Physiology And Chronic Health Evaluation II (APACHE II)[19], Modified Early Warning Score (MEWS)[20, 21], and Sequential Organ Failure Assessment (SOFA)[22, 23]. APACHE II is unsuitable to evaluate patient condition and mortality risk in long-term hospitalization[24]; MEWS is more appropriate for evaluating patients in the general ward[20]; and both APACHE II and SOFA require blood tests, which prolongs evaluation.

We sought to develop and validate a new model that can not only obtain data quickly and easily without increasing patient discomfort and economic burden, but also evaluate risk with high sensitivity, specificity, and accuracy.

Methods

Design

This observational study comprised two stages: first, we collected and analyzed data from a development cohort and developed the proposed model based on a retrospective case–control study. Second, we tested the model in the clinical setting of a prospective cohort study. Before study initiation, we unified the research purpose, disease definition, inclusion and exclusion criteria, variable names, units, and judgments. We extracted data on demographic variables and potential independent predictors from medical records of the study center during hospitalization. Data collection and collation were undertaken by three investigators. In case of abnormal data, such as, variable had different data in the same period, or data inconsistent with the patient's progress, even might affect the research results, we would timely check and solve to avoid information bias. Patients or their legal guardians provided written informed consent for study participation.

Setting and patient selection

All study participants were from a comprehensive ICU of a large metropolitan public hospital. The inclusion criteria were: hospitalization for 8 or more critical care days with at least one clinical condition, including prolonged mechanical ventilation (PMV); tracheostomy; sepsis, and other severe infections[25]; wounds; multiorgan failure (at least two failures: heart, liver, kidney, respiratory), or brain hemorrhage/traumatic brain injury (TBI)[26]. The exclusion criteria were: poor prognosis, such as end-stage cancer, end-stage multiorgan failure, etc., at the time of ICU admission; age below 18 years; family decision to abandon active treatment; poisoning or other diseases with unclear diagnosis; adverse events leading to changes in disease or death; and patients with missing data or refusal of consent for study participation.

Outcomes and predictor variables

Death or survival during hospitalization were the main outcomes. We identified 27 potential independent predictors, including gender, age, underlying diseases, surgery, congenital diseases, pressure injury, PMV, sepsis/other serious infections, artificial airway, urinary catheter/cystostomy, deep vein catheterization, abdominal/pelvic drainage tube, pleural catheter, intracerebral/intraspinal drainage tube, other drainage tubes, Glasgow Coma Scale (GCS), body temperature, mean arterial pressure (MAP), heart rate (HR), respiratory rate (RR), oxygenation index (OI), arrhythmia, random blood glucose, 24-hour urinary volume (including ultrafiltration volume), jaundice, active bleeding, and degree of edema.

Data collection

Development cohort

In development cohort, we included CCI patients treated in the ICU between January 2012 and December 2017. A case-control study was undertaken with deceased patients as the case (death, n = 172) group. The control group was randomly sampled at a ratio of 1: 1 according to the sample size of the case group. The random sampling method for the control group was as follows: we generated a corresponding random number for each research object; then ranked the random number in ascending order; and selected the smallest 172 numbers. Patients without exacerbations, who were transferred out of the ICU, or discharged were included in the control (survival, n = 172) group. Patients with persistent abnormalities in variables due to repeated illness were included in the control group upon eventual improvement and transfer out of the ICU.

The timepoint of data collection for predictive variables in the case group was the first time that the variable appeared abnormal, showed a critical value, or worsened after 8 days in the ICU. Predictive variables included GCS less than 15 points, MAP greater than 109 or less than 70 mm Hg, HR greater than 100 or less than 60 times/min, RR less than 12 or more than 24 cycles/min, and OI less than 400 mm Hg, etc. For consistency of the control group data, the time of data collection was specified as 06:00 on the 9th day in the ICU. However, not all data points could be collected, and we needed to supplement these data with records of the same variable that first appeared after the data-collection timepoint.

Validation cohort

The validation cohort included CCI patients treated at the hospital between January 2018 and March 2019. After ICU admission for more than 8 days, we ascertained whether patients were eligible for study inclusion. The prospective case-control (case, n = 44; control, n = 44) study followed the same inclusion and exclusion criteria as in the development cohort, with 1:1 random sampling and the data collection timepoint of predictive variables was consistent between the development and validation cohorts for both case and control groups.

Statistical analysis

Data were validated by two researchers after independent entry. Descriptive statistics are presented using mean and SD for continuous variables with normal distribution or median and interquartile range (IQR) for variables with abnormal distribution. Categorical variables are presented as frequency and

proportions. In the development cohort, Variables were evaluated for their association with hospital mortality using the chi-square, independent t , or Mann–Whitney U test, as appropriate ($p < 0.1$). Furthermore, variables with clinical relevance were considered for further binary logistic regression analysis, where we used the Forward: Conditional method to develop a model with death or survival as the dependent variable, with an entry probability of 0.05. Similarly, we evaluated whether the model lacked a degree of fit according to Hosmer–Lemeshow goodness-of-fit statistics ($p > 0.05$) and chi square value. We used APACHE II, MEWS, and SOFA to score the previous development and subsequent validation cohorts, and evaluated the prediction efficiency and stability of the model with AUC[27].

All statistical analyses were conducted in IBM® SPSS® Statistics (Version 26, Property of IBM Corp. © Copyright IBM Corporation and its licensors 1989, 2019).

Results

We screened 11,785 ICU patients from January 2012 to December 2017, including 1755 CCI patients. The development cohort included 1244 (case, 172; control 1072) eligible CCI patients; 2312 ICU patients were admitted from January 2018 to March 2019, including 344 CCI patients. The validation cohort included 235 CCI patients (case, 44; control, 191).

Model development

A total of 344 patients were included in the development cohort, 172 in the case group and 172 in the control group. Table 1 presents baseline data and predictors for these patients, and shows the results of univariate analysis of their correlation with mortality.

Table 1
Univariate Analysis of Risk Variables and Mortality in Development Cohort

Variable	Alive, (n = 172)	Dead, (n = 172)	t/Z/ χ^2	P
Age (yr), Median (IQR)	58.5, (44.8–70.3)	72.5, (55.0–82.0)	5.862	< 0.001
Gender (male), n (%)	118 (68.6)	121 (70.3)	0.123	0.725
PMV, n (%)	68, (39.5%)	146, (84.9%)	75.230	< 0.001
Sepsis/other serious infections, n (%)	99, (57.6%)	126, (73.3%)	9.366	0.002
Underlying diseases, n (%)	65, (37.8%)	112, (65.1%)	25.708	< 0.001
Congenital diseases, n (%)	1, (0.006%)	2, (0.012%)	< 0.001	1.000
Surgery, n (%)	52, (30.2%)	50, (29.1%)	0.056	0.813
GCS, n (%)				
15	85, (49.4%)	22, (12.8%)	-9.285	< 0.001
13–14	4, (2.3%)	1, (0.6%)		
9–12	18, (10.5%)	15, (8.7%)		
3–8	65, (37.8%)	134, (77.9%)		
Body temperature (°C), Median (IQR)	37.20, (36.70–37.83)	37.55, (36.88–38.40)	3.538	< 0.001
MAP (mm Hg), Mean (SD)	89.2 (13.5)	76.1 (23.8)	6.24	< 0.001
HR (times/min), Median (IQR)	85.0, (72.8–98.3)	105.0, (86.8–122.0)	6.823	< 0.001
RR (cycles/min), Median (IQR)	20.0, (19.0–22.3)	23, (18.8–27.0)	3.496	< 0.001
OI (mm Hg), Median (IQR)	300.00, (248.36–375.13)	180.00, (125.80–268.85)	-9.327	< 0.001
Arrhythmia, n (%)	19, (11.0%)	44, (25.6%)	22.423	< 0.001
Random blood glucose (mmol/L), Median (IQR)	7.24, (6.18–9.21)	7.94, (6.12–11.03)	1.569	0.117

IQR = inter quartile range

Variable	Alive, (n = 172)	Dead, (n = 172)	t/Z/ χ^2	P
Pressure Injury, n (%)	23, (13.4%)	33, (19.2%)	2.133	0.144
Artificial airway, n (%)	120, (69.8%)	166, (96.5%)	43.881	< 0.001
Urinary catheter/Cystostomy, n (%)	160, (93.0%)	165, (95.9%)	1.393	0.238
Deep vein catheterization, n (%)	87, (50.6%)	112, (65.1%)	7.451	0.006
Abdominal/pelvic drainage tube, n (%)	10, (5.8%)	6, (3.5%)	1.049	0.306
Pleural catheter, n (%)	14, (8.1%)	11, (6.4%)	0.388	0.533
Intracerebral/Intraspinal drainage tube, n (%)	24, (14.0%)	17, (9.9%)	1.357	0.244
Other drainage tubes, n (%)	7, (4.1%)	2, (1.2%)	1.826	0.177
24-hour urine volume (including ultrafiltration volume, ml) \leq 400 ml, n (%)	0, (0%)	7, (4.1%)	5.250	0.022
Jaundice, n (%)	7, (4.1%)	5, (2.9%)	0.345	0.557
Active bleeding, n (%)	12, (7.0%)	44, (25.6%)	21.841	< 0.001
The degree of edema, n (%)				
None	138, (80.2%)	80, (46.5%)	54.941	< 0.001
Mild	26, (15.1%)	34, (19.8%)		
Moderate	6, (3.5%)	31, (18.0%)		
Severe	2, (1.2%)	27, (15.7%)		
IQR = inter quartile range				

Although the result of random blood glucose on univariate analysis indicated $p > 0.1$, we included it in subsequent analysis because of the important relationship between mortality and blood glucose[28]. Through collinearity diagnosis, we determined there was no synergistic effect among variables. After assigning values to 16 variables on univariate analysis ($p < 0.1$) and random blood glucose, we eliminated the variables through binary logistic regression analysis to construct the final model. The final model contained 9 predictive variables, such as age, PMV, sepsis/other series infections, GCS, map, HR, RR, OI, and active bleeding (Table 2). The chi square value of the Hosmer–Lemeshow goodness-of-fit statistics is 8.938, $p = 0.348$, which showed that the model had good goodness of fit. Furthermore, the variables of the PCCI Model showed good accuracy and stability in the training of ANN (case, AUC = 0.957; control, AUC = 0.957).

Table 2
Binary Logistic Regression Analysis of Risk Variables Screened in Development Cohort

	B	S.E	Wals	df	Sig.	OR	OR 95% CI
Age	0.459	0.162	8.042	1	0.005	1.582	1.152–2.172
PMV	1.489	0.359	17.179	1	<0.001	4.433	2.192–8.963
Sepsis/other serious infections	1.065	0.384	7.681	1	0.006	2.899	1.366–6.156
GCS	0.767	0.146	27.446	1	<0.001	2.154	1.616–2.870
MAP	1.498	0.372	16.196	1	<0.001	4.472	2.156–9.276
HR	0.903	0.195	21.466	1	<0.001	2.467	1.684–3.615
RR	1.213	0.347	12.233	1	<0.001	3.364	1.705–6.639
OI	0.623	0.244	6.504	1	0.011	1.865	1.155–3.012
Active bleeding	1.111	0.500	4.928	1	0.026	3.036	1.139–8.094
constant	-6.654	0.818	66.207	1	<0.001	0.001	
OR = odds ratio.							

For ease of use in clinical practice, we rounded the β coefficients to one decimal place and assigned them to each corresponding variable to develop a simple scoring rule – Prognosis Prediction of Chronic Critical Illness (PPCCI) Model.

PPCCI Model Score = age assignment \times 0.5 + PMV assignment \times 1.5 + Sepsis/other serious infections assignment \times 1.1 + GCS assignment \times 0.8 + MAP assignment \times 1.5 + HR assignment \times 0.9 + RR assignment \times 1.2 + OI assignment \times 0.6 + Active bleeding assignment \times 1.1

Model validation

A total of 88 patients (case, 44; control, 44) were included in the validation cohort. Before validation, we verified whether the development and validation cohorts were conditionally consistent through a univariate analysis of patient characteristics and risk variables, and results showed no significant between-group differences in patient characteristics and risk variables (Table 3).

Table 3
Comparison of Patient Characteristics and Risk Variables between Development Cohort and Validation Cohort

variable	Development (n = 344)	Validation (n = 88)	t/Z/ χ^2	P
Age (yr), Median (IQR)	64.0, (49.0–77.0)	67.0, (54.5–76.3)	1.215	0.224
Gender (male), n (%)	239 (69.5%)	63 (71.6%)	0.149	0.700
PMV, n (%)	214, (62.2%)	49, (55.7%)	1.254	0.263
Sepsis/other serious infections, n (%)	225, (65.4%)	49, (55.7%)	2.857	0.091
Underlying diseases, n (%)	177, (51.5%)	46, (52.3%)	0.019	0.891
Congenital diseases, n (%)	3, (0.9%)	0, (0%)	0.026	0.873
Surgery, n (%)	102, (29.7%)	34, (38.6%)	2.623	0.105
GCS, n (%)				
15	107, (31.1%)	23, (26.1%)	3.968	0.265
13–14	5, (1.5%)	0, (0%)		
9–12	33, (9.6%)	12, (13.6%)		
3–8	199, (57.8%)	53, (60.2%)		
Body temperature (°C), Median (IQR)	37.30, (36.80–38.20)	37.40, (36.80–38.10)	0.355	0.723
MAP (mm Hg), Mean (SD)	82.6 (20.4)	81.3 (17.9)	0.549	0.583
HR (times/minute), Median (IQR)	93.0, (77.0–110.0)	92.0, (81.8–102.0)	-0.136	0.892
RR (times/minute), Median (IQR)	21.0, (19.0–24.0)	21.0, (19.0–23.3)	0.293	0.769
OI (mm Hg), Median (IQR)	249.44, (161.72–324.24)	270.14, (172.00–336.36)	-0.074	0.941
Arrhythmia, n (%)	63, (18.3%)	17, (19.3%)	0.047	0.829
Random blood glucose (mmol/L), Median (IQR)				
3.9–7.2	150, (43.6%)	31, (35.2%)	3.139	0.371
7.3–11.1	120, (34.9%)	32, (36.4%)		
2.9–3.8 or 11.2–13.9	39, (11.3%)	15, (17.0%)		

variable	Development (n = 344)	Validation (n = 88)	t/Z/ χ^2	P
≤ 2.8 or ≥ 14.0	35, (10.2%)	10, (11.4%)		
Pressure Injury, n (%)	56, (16.3%)	8, (9.1%)	2.869	0.090
Artificial airway, n (%)	286, (83.1%)	72, (81.8%)	0.086	0.769
Urinary catheter/Cystostomy, n (%)	325, (94.5%)	83, (94.3%)	< 0.001	1.000
Deep vein catheterization, n (%)	199, (57.8%)	42, (47.7%)	2.911	0.088
Abdominal/pelvic drainage tube, n (%)	16, (4.7%)	5, (5.7%)	0.015	0.902
Pleural catheter, n (%)	25, (7.30%)	8, (9.10%)	0.330	0.566
Intracerebral/Intraspinal drainage tube, n (%)	41, (11.9%)	9, (10.2%)	0.196	0.658
Other drainage tubes, n (%)	9, (2.6%)	4, (4.5%)	0.355	0.551
24-hour urine volume (including ultrafiltration volume, ml) ≤ 400 ml, n (%)	7, (2.0%)	1, (1.1%)	0.013	0.909
Jaundice, n (%)	12, (3.5%)	4, (4.5%)	0.023	0.879
Active bleeding, n (%)	56, (16.3%)	16, (18.2%)	0.183	0.669
The degree of edema, n (%)				
None	218, (63.4%)	53, (60.2%)	6.052	0.109
Mild	60, (17.4%)	13, (14.8%)		
Moderate	37, (10.8%)	7, (8.0%)		
Severe	29, (8.4%)	15, (17.0%)		

Sensitivity analyses

Based on the scatterplot and linear correlation coefficient, we confirmed that the PPCCI Model had strong linear correlation with APACHE II, MEWS, and SOFA. The ROC curve of the development cohort and validation cohort (Figs. 1 and 2) showed that the discrimination of PPCCI Model was better than that of APACHE II, MEWS, and SOFA ($p < 0.05$). The PPCCI Model could better identify deceased CCI patients (development cohort: AUC, 0.934; 95% CI, 0.908–0.960; validation cohort: AUC, 0.965; 95%CI, 0.931–0.999). The order of prediction efficiency from strong to weak was PPCCI Model, SOFA, MEWS, and APACHE II.

The PPCCI Model score ranges from 0 to 20.8. We used the quartile to grade the risk of the model: low < 4.7; medium 4.7–6.6; high 6.7–9.2, and extremely high ≥ 9.3 . In both cohorts, Kruskal-Wallis H test showed significant difference in the mortality among risk stratifications ($p < 0.001$). According to the proportion of death cases in each risk stratification, we found that the mortality rate of patients increased with higher risk stratification. The higher the score, the higher the mortality.

Discussion

We developed and validated a clinical prediction model, which can predict outcomes of patients with CCI by scoring. The PPCCI Model has a good performance in terms of accuracy and stability of prediction in the development cohort cases, and similar prediction performance in the validation cohort. This model uses data that can be obtained accurately, timely, easily, and objectively in the clinic, without increased patient discomfort and costs.

The prediction efficiency of PPCCI Model is superior to APACHE II, MEWS, and SOFA in both the development and validation cohorts. Moreover, the PPCCI Model has its advantages. APACHE II and SOFA[29] require invasive procedures such as arterial blood gas analysis, renal function, electrolytes, and blood routine tests for each evaluation. However, the PPCCI Model shortens the time to assess the prognosis of CCI patients without increasing patient discomfort and medical costs. Except for the arterial blood, the predictive variables of the PPCCI Model are noninvasive and fast, which can be used to quantify the disease status of patients with CCI at any time. This advantage of the PPCCI Model makes it feasible to obtain all data in a much shorter time than APACHE II and SOFA. Moreover, it reduces the discomfort, medical cost, and workload of medical staff in patients who need long-term treatment.

There are some details about variables selection. First, RTI defines PMV time as mechanical ventilation time of more than 96 hours[7]. Second, The diagnosis of "sepsis/other series infections" is actually a complex and time-consuming process. We just intercepted the diagnostic results and did not shorten the diagnosis time of this indicator in the true sense. When using the PPCCI Model to evaluate the patient's condition, the patient has already been diagnosed with "sepsis/other series infections".

The ultimate goal of CCI patient care is to return to social normalcy and regain self-care capabilities. However, patients are usually faced with the long-term isolation and the threat of cross-infection with drug-resistant bacteria[30]. In addition to screening high-risk and very high-risk patients, the PPCCI Model could be used for identifying low-risk patients, who are likely to recover their ability of self-care with the help of rehabilitation team, community medical staffs, and even family members in more active rehabilitation environments[31]. By transferring patients based on scoring, we can reduce the economic burden on the patients' families and the national medical burden, and improve the use efficiency of ICU beds. Moreover, through the model, primary medical institutions can judge whether the patient's condition is deteriorating or they need to be referred to the higher level medical institutions.

The risk stratification of the PPCCI Model would be really helpful for medical staffs to discuss with families about patients' conditions and the ethical issues of treatment cessation. For example, patients

with extremely high-risk in this study had a mortality rate of 100%, and the failure of organ function was usually irreversible. However, A study showed that less than 40% of the patients who need ICU care for more than 2 weeks had discussed with doctors about the prognosis or their idea of advanced life support[32]; more than half of the family members said they could not understand patient diagnoses, prognosis, or treatment.

Limitations

This study had several limitations. First, due to the limited time and energy of researchers, this was a single-center study, and the final conclusion of the model may be biased by the sample size. Second, retrospective data were used in development cohort; therefore, the accuracy is lower than that of prospective research. Some cases lacked data and were excluded from the study, which might have led to biased results. However, we collected more than 1 year of prospective clinical case data in the validation cohort to verify the impact of the retrospective study. Even in prospective studies, incomplete data of some patients is inevitable. Third, the knowledge and experience of the surveyor affected the final measurement results. Over the course of the study, we strengthened the training of surveyor. Fourth, although we put forward the risk stratification of CCI, we did not propose evidence-based interventions, which need to be explored in the future research. Finally, this tool could not completely replace the clinician's judgment[33].

Conclusions

In summary, the PPCCI Model can provide a standardized measurement tool for medical staff to evaluate the condition of CCI patients. So that, we can attempt to rationally allocate ward-monitoring resources or discuss palliative care with family members[34, 35]. The model can provide basis for clinical medical staff to undertake corresponding treatment and nursing based on patient condition[36]. There is a need to explore whether the PPCCI Model is suitable for the evaluation of CCI patients in primary hospitals, communities, and even at home to provide objective basis for the evaluation and referral of patients.

Abbreviations

CCI: Chronic critical illness; ICU: Intensive care unit; PPCCI Model: Prognosis Prediction Model of Chronic Critical Illness; AUC: Area under the curve; ROC: Receiver operating characteristic; PMV: Prolonged mechanical ventilation; GCS: Glasgow Coma Scale; MAP: Mean artery pressure; HR: Heart rate; RR: Respiratory rate; OI: Oxygenation index; APACHE II: Acute Physiology And Chronic Health Evaluation II; MEWS: Modified Early Warning Score; SOFA: Sequential Organ Failure Assessment; RTI: Research Triangle Institute; CMS: Centers for Medical Care & Medical Services; TBI: Traumatic brain injury; IQR: Interquartile range.

Declarations

Ethics approval and consent to participate

Ethical review was approved by Ethics Committee of the First Affiliated Hospital of Fujian Medical University. (No.: MRCTA, ECFAH of FMU [2018] 137)

Consent for publication

Not applicable.

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

RH, YW and LZ were responsible for the conception and design of the work; WKX performed the data analysis; LZ were responsible for drafting of the manuscript; RH and YW made critical revisions to the manuscript for important intellectual content; LZ were responsible for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved. LZ, WKX, YW and WYL organised the data collection. All authors read and approved the final manuscript.

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Figures

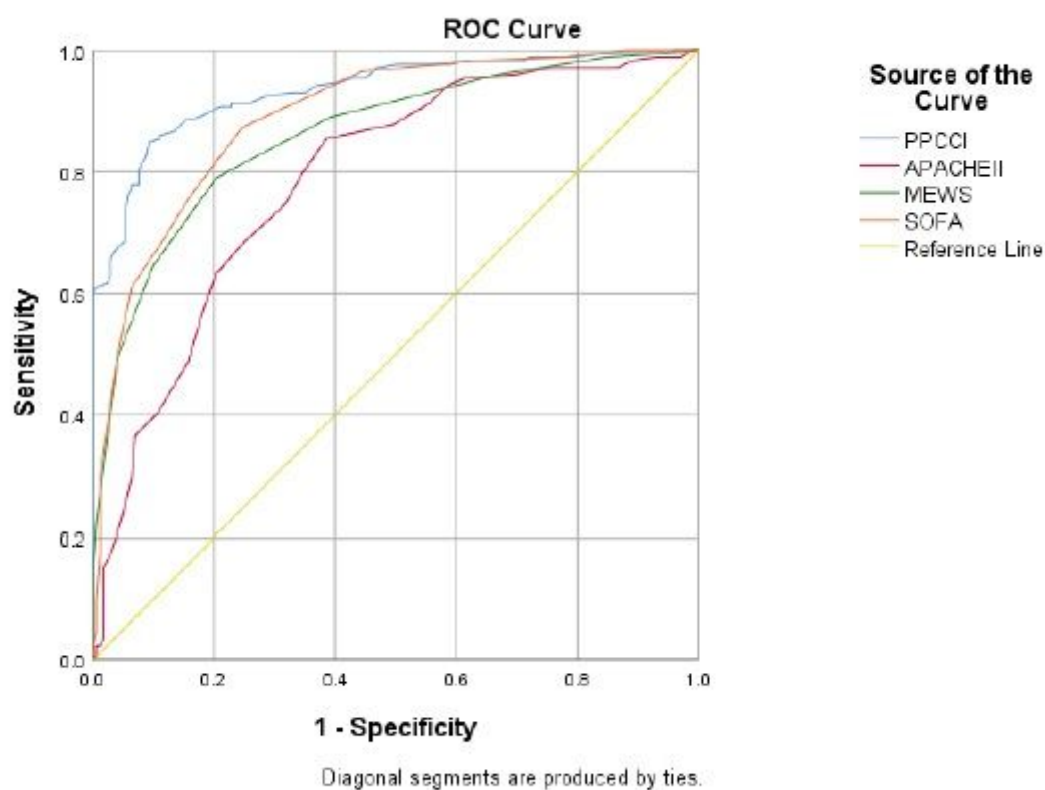


Figure 1

ROC curve of development cohort scoring with four scoring tools

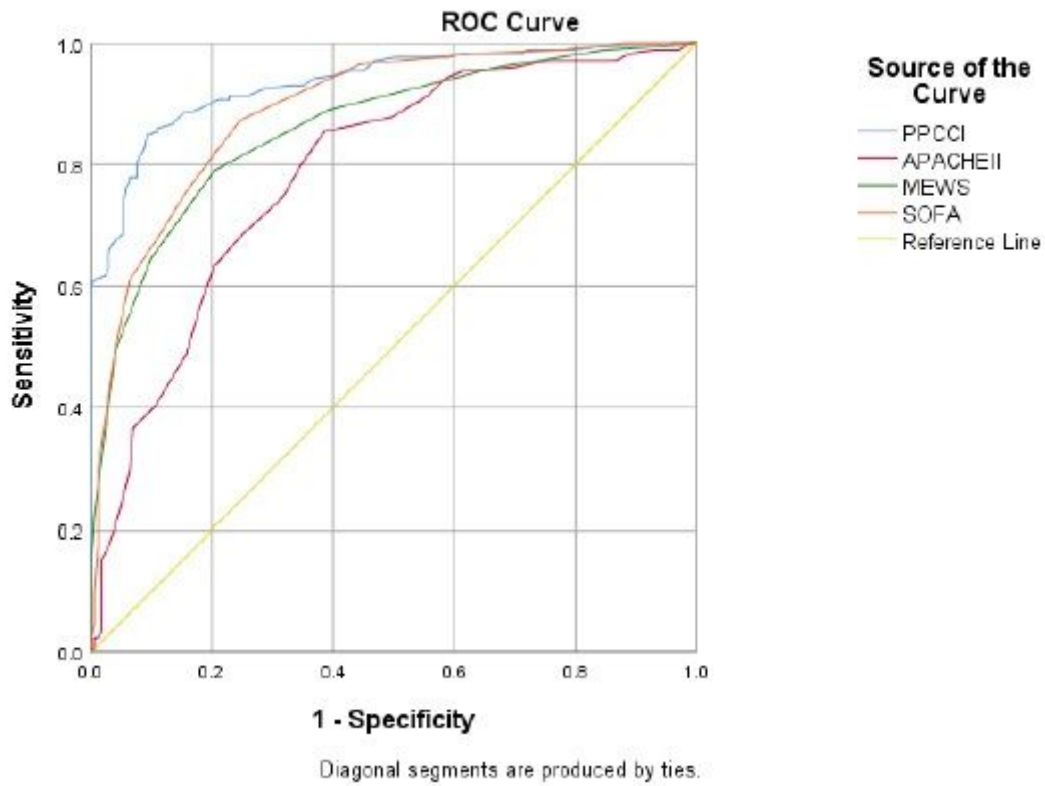


Figure 1

ROC curve of development cohort scoring with four scoring tools

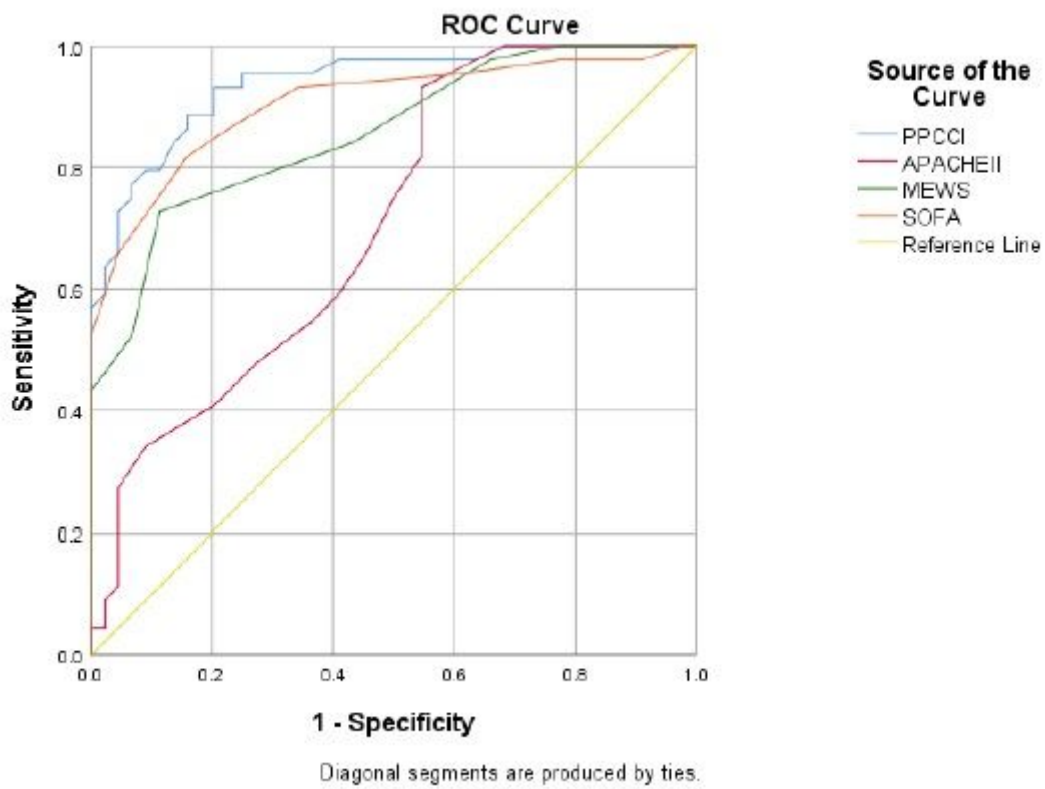


Figure 2

ROC curve of validation cohort scoring with four scoring tools

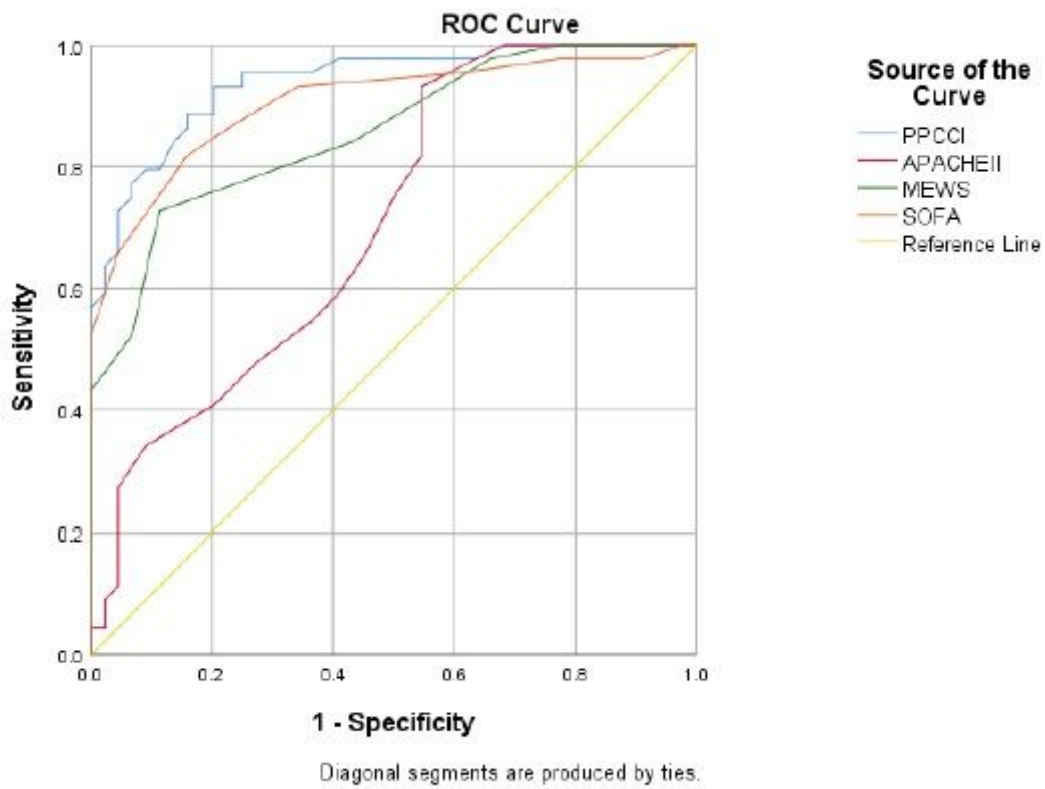


Figure 2

ROC curve of validation cohort scoring with four scoring tools