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Development of an electronic Poor Outcome Screening (ePOS) Score to identify critically ill patients with potential palliative care needs

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ABSTRACT

Purpose: To develop and validate an electronic poor outcome screening (ePOS) score to identify critically ill patients with potentially unmet palliative care (PC) needs at 48 hours after ICU admission.
Materials and Methods: Retrospective single-centre cohort study of 1'772 critically ill adult patients admitted to a tertiary academic ICU in Switzerland between 2017 and 2018. We used data available from electronic health records (EHR) in the first 48 hours and least absolute shrinkage and selection operator (LASSO) logistic regression to develop a prediction model and generate a score to predict the risk of all cause 6-month mortality.
Results: Within 6 months of the ICU admission, 598 patients (33.7%) had died. At a cut-off of 20 points, the ePOS score (range 0-46 points) had a sensitivity of 0.81 (95% CI 0.78 to 0.84) and a specificity of 0.51 (0.48 to 0.54) for predicting 6-month mortality and showed good discriminatory performance (AUROC 0.72, 0.67 to 0.77).
Conclusions: The ePOS score can easily be implemented in EHR and can be used for automated screening and stratification of ICU patients, pinpointing those in whom a comprehensive PC assessment should be performed. However, it should not replace clinical judgement.

1. Background

Changing population demographics and improvements in medical therapy have resulted in a growing proportion of elderly and multimorbid patients being admitted to the intensive care unit (ICU) [1,2]. These patients not only are at high risk of dying [3-5] but are also likely to suffer from poor long-term outcomes [6-8] such as functional and cognitive impairment, psychological distress, and substantial 6-month mortality – a composite that has previously been coined "poor outcome phenotype" [9]. Therefore, these patients often present with complex palliative care (PC) needs and might benefit from specialized PC consultation, which has been shown to reduce ICU length of stay (LOS), ICU readmissions, costs, and psychological distress among family members and to improve symptom control [10-13]. However, identifying critically ill patients with potential PC needs is notoriously difficult [9] and physicians' prognostication is often inaccurate. Therefore, many patients with substantial PC needs will go unrecognized if they are not assessed systematically.

The use of "trigger criteria" and screening tools for rapid, structured evaluation of potential PC needs in the ICU has increased over time [15-18] and has been linked to improved outcomes [10]. However, multiple factors like the use of subjective criteria and the need for manual chart review preclude the implementation of currently available PC screening tools in clinical practice outside a research setting [14]. Furthermore, published trigger criteria vary substantially between studies and health care settings and are often poorly defined. The latter is partly due to the absence of a gold standard to measure PC needs and a consensus as to

Abbreviations: APACHE, Acute Physiology And Chronic Health Evaluation; AUROC, Area Under The Receiver Operating Characteristic; CENTRAL, Cochrane Central Register Of Controlled Trials; CI, Confidence Interval; DNR, Do-Not-Resuscitate; EHR, Electronic Health Records; ePOS, electronic Poor Outcome Screening; ICU, Intensive Care Unit; IDCL, Institutional Data Coordination Lab; IQR, Interquartile Range; LASSO, Least Absolute Shrinkage And Selection Operator; LOS, Length Of Stay; NPV, Negative Predictive Value; PPV, Positive Predictive Value; RRT, Renal Replacement Therapy; SAPS, Simplified Acute Physiology Score; STROBE, Strengthening The Reporting Of Observational Studies In Epidemiology; TRIPOD, Transparent Reporting Of A Multivariable Prediction Model For Individual Prognosis Or Diagnosis.

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when PC should be implemented. Nevertheless, a life expectancy of less than 6 months is commonly considered highly specific for palliative care needs [15].

An ideal screening tool should be objective, applicable to different healthcare systems and be able to discern patients requiring primary-level vs. specialty-level PC [14] after a brief period of intensive care. Automatized trigger identification using electronic health records (EHR) has been recommended for this purpose [16] and is the preferred approach of ICU specialist for integrating PC in the ICU [17]. However, yet, there are no EHR-based PC screening tools that overcome the above-mentioned limitations.

Therefore, we sought to develop the electronic poor outcome screening (ePOS) score, an EHR-based screening tool to predict 6-month mortality as a proxy to identify patients with a "poor outcome phenotype" in the ICU [9,18].

2. Methods

2.1. Study design

This retrospective single-centre cohort study was conducted at the University Hospital of Bern, Switzerland. The study protocol was approved by the responsible research ethics committee (KEK Project-ID 2019-01070) who waived the need for informed consent due to the retrospective study design. The results are reported in adherence to the Strengthening The Reporting of OBservational Studies in Epidemiology (STROBE) [19] and Transparent Reporting of a multivariable prediction model for Individual Prognosis Or Diagnosis (TRIPOD) reporting guidelines [20].

2.2. Patients and setting

Data from all adult patients (≥ 18 years) admitted to the ICU between January 1st, 2017 and December 31st, 2018 were considered for this study. We excluded patients admitted for evaluation of organ donation and patients with an ICU LOS < 48 hours to select patients in whom a trial of full ICU treatment was deemed appropriate, while excluding patients with futile prognosis and imminent death, as well as patients with quick recovery. The department of intensive care medicine at the University Hospital in Bern is the sole provider of intensive care for adults in the hospital and is a 60-bed mixed medical-surgical tertiary ICU with an intensive care specialist on site 24 hours per day. Specialized palliative care consultations by an interprofessional team (physician and nurse) are available upon request during daytime (Monday to Friday) and 24/7 by telephone. No standardized procedure for palliative care referrals is currently in place.

2.3. Source of data

All data were provided by data scientists at the institutional Data Coordination Lab (IDCL) and were downloaded from electronic health records linked to the national death registry. In case of multiple ICU admissions, only data from the first admission was considered. Data from patients who refused the institutional general consent and patients with residency outside of Switzerland or with unknown vital status at 6 months were excluded from the dataset.

2.4. Outcomes

The primary outcome was all-cause mortality at 6 months (180 days) after the index ICU admission. We have chosen this outcome as a proxy to identify a poor outcome phenotype and to avoid discharge bias [21] as many of our ICU patients are discharged to other ICUs or hospitals after the initial stabilization phase. Vital status was ascertained using the data linkage with the national death registry for all participants, and last follow-up of vital status was performed on January 31st, 2020. Secondary outcomes included ICU LOS, organ support, ICU mortality, hospital mortality, 1-year mortality, specialized palliative care consultations during the index hospitalization, modification of life sustaining treatment orders, hospital discharge destination, and ICU- or unplanned hospital re-admissions during the 12-month follow-up period.

2.5. Statistical analysis

Statistical analysis was performed with R version 3.6.1. Continuous variables are summarized as median with interquartile ranges [IQR] and compared using Mann–Whitney U test. Categorical variables are described by counts and percentages and compared using $\chi 2$ or Fisher's exact tests.

2.6. Predictor variables for poor outcome phenotype

First, we conducted a systematic literature search in Ovid Medline, Embase and CENTRAL (Cochrane Central Register of Controlled Trials) to identify common categories and predictors used to trigger palliative care consultations in adult critically ill patients and to study any type of validation of trigger criteria in previous studies. Keywords and free-text words for 1) intensive care/critical care, 2) palliative care/supportive care, 3) trigger/scores and 4) validation were used. Based on the results of the literature review and medical knowledge, we selected and defined commonly used trigger categories and translated them into searchable and/or extractable terms and physiological variables available in the EHR at 48 hours after ICU admission. The initial set of predictor variables included patient data from categories known to be associated with a poor outcome phenotype such as acute severe illness [22], poor functional status [23,24] and progressive illness or declining health trajectory [9,22,25]. Variables with more than 20% missing data were removed from the database. These variables were: presence or absence of demetia, advanced medical directives, serum albumin and bilirubin levels. A comprehensive list of potential predictor variables can be found in the Appendix (Table S1). As there is no integrated national health database in Switzerland, data on prior hospitalizations and re-admissions was only available for the University hospital of Bern (the major ICU in the region) and do not include admissions to other hospitals. However, the hospital database is linked with the national death registry and, therefore, vital status was available for all patients.

2.7. Missing data

Missing data in predictor variables were imputed assuming data to be missing at random and using single imputation by chained equations. Binary variables, categorical variables with more than two levels and continuous variables were imputed using logistic regression, polytomous regression and predictive mean matching, respectively.

2.8. Model development

We used LASSO (least absolute shrinkage and selection operator) logistic regression to predict 6-month mortality as a function of the covariates of the patients. The lambda penalty parameter in the loss function was estimated using 5-fold cross-validation. Alpha was set to 1 throughout. To assess the performance of the obtained prediction model, we characterized the overall accuracy and the discriminatory power of the model by calculating the Brier score and the area under the receiver operating characteristic (AUROC) curve, respectively. Then, we evaluated the model calibration by using calibration curves and performing Hosmer-Lemeshow goodness of fit test. The internal validity of the model was assessed using 1,000 bootstrap samples, where samples were drawn with replacement from the derivation sample. The bootstrapping method was chosen due to the relatively small dataset. Imputation was not included in the bootstrapping step. The bootstrap-corrected performance estimates were calculated by subtracting the optimism from the performance of the original model (in-sample

estimates are generally too high – too optimistic – so bootstrap samples are used to estimate how overly-optimistic the model is and correct the statistics). The 95% confidence intervals (CI) for the bootstrapped performance measures were derived using the percentile method.

2.9. Score development

From the prediction model described above, we created the *electronic poor outcome screening (ePOS) score* by using the regression coefficient-based scoring method. Continuous variables were converted to factors with cut-off values chosen a priori using clinical knowledge, as using continuous variables would result in a score that is not necessarily an integer, which makes score calculation more difficult. On entering variables into a penalised logistic regression model (LASSO), all variables are retained within the final model, although with very small coefficients in some cases. We converted the penalised regression coefficients into a prognostic index by multiplying each beta-coefficient by 10 and rounding to the closest integer [26]. This step effectively removes the predictors with very small effects from the score. Adding up the converted coefficients yields the score of increasing risk of 6-month mortality. The discriminatory power of the score was assessed by calculating the AUROC curve. The validity of this measure was assessed by performing internal validation as described above. Finally, we analysed the distribution of the scores among all patients and divided the cohort into a low- and high-risk group. The reference point (cut-off) was chosen to maximize sensitivity while maintaining a minimum specificity of 0.5, to identify all patients at high risk of a poor outcome. This approach allowed to create a score for automated screening of ICU patients, pinpointing those in whom a comprehensive assessment of potential palliative care needs should be performed. To determine the accuracy of this method we estimated sensitivity, specificity, positive and negative predictive values, and likelihood ratios.

3. Results

3.1. Patient characteristics

We identified 1,792 patients with an ICU length of stay of 48 hours or more. After excluding six patients admitted for evaluation of organ donation and 14 patients with unknown vital status at 6 months, 1,772 patients (67.1% males and 32.9% females) remained in the dataset (Fig. 1). The majority (69.0%) were medical admissions and the median [IQR] age was 66 [54 - 74] years. At 6 months after ICU admission, 598 (33.7%) patients had died. Patient characteristics at baseline are presented in Table 1, stratified by survivors and non-survivors at 6 months after ICU admission. Non-survivors were significantly older than survivors (median age 70 [61 - 77] vs. 63 [52 - 72] years, $p < 0.001$), had higher comorbidity scores and were also more likely to have a dependent functional status at hospital admission. At ICU admission, non-survivors had higher illness severity scores, were more often admitted from a hospital ward, had higher blood lactate and serum creatinine levels, and were more frequently treated with vasopressors or inotropes. Most patients had no initial treatment limitation (97.7% of survivors and 91.3% of non-survivors) and only a minority had a documented advanced medical directive (2.4% of survivors and 7.4% of non-survivors) at ICU admission. However, non-survivors had more documented Do-Not-Resuscitate (DNR) orders ($n = 49$, 8.2%) compared to survivors ($n = 33$, 2.8%) (Table 1). Additional patient characteristics are presented in the appendix (Table S2).

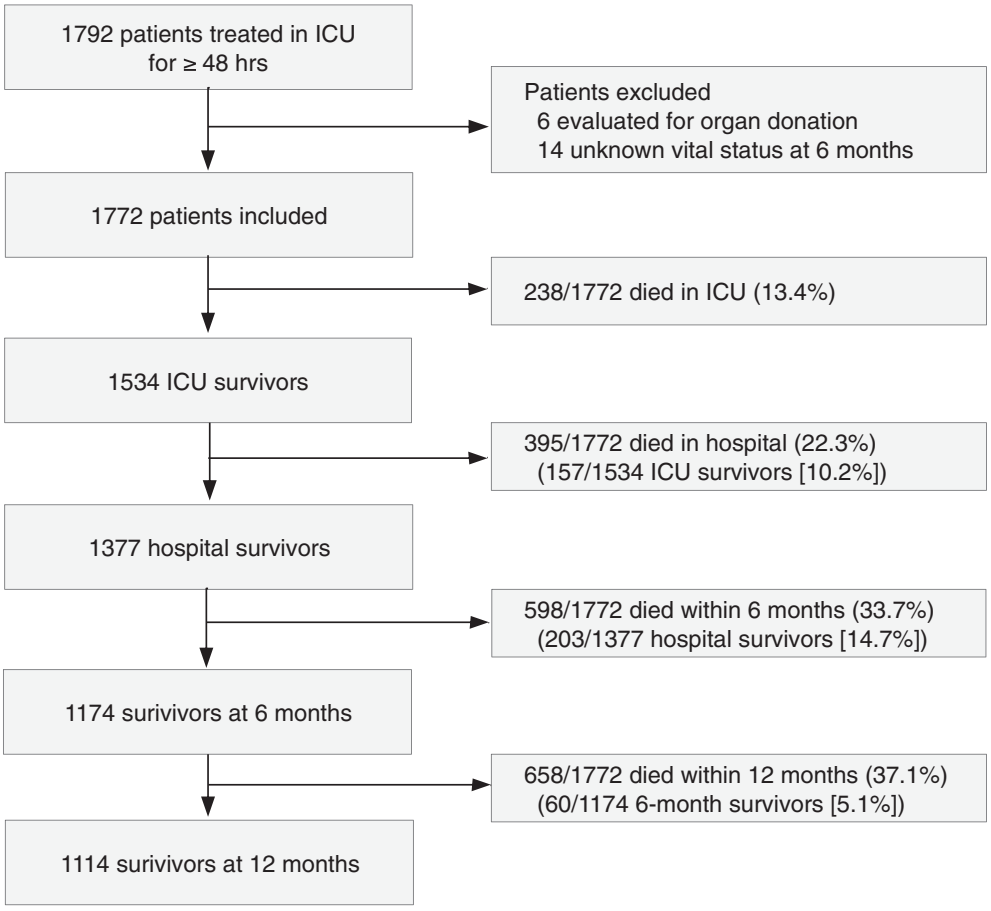

Fig. 1. Flow of participants through the study

Table 1
Patient characteristics at ICU admission, stratified by 6-month survivors vs. non-survivors

	All patients (n = 1772)	Survivors (n = 1174)	Non-Survivors (n = 598)	P-Value
Age, years	66 [54 - 74]	63 [52 - 72]	70 [61 - 77]	<0.001
Male gender	1189 (67.1%)	793 (67.5%)	396 (66.2%)	0.61
BMI, kg/m2 (n = 1134)	26 [22 - 30]	26 [22 - 30]	25 [22 - 29]	0.48
APACHE II score (n = 1459)	27 [21 - 33]	25 [20 - 31]	30 [25 - 35]	<0.001
Place of residency before admission				0.07
Home	1509 (85.2%)	1013 (86.3%)	496 (82.9%)	
Long-term care facility	164 (9.3%)	98 (8.3%)	66 (11.0%)	
Unknown	99 (5.6%)	63 (5.4%)	36 (6.0%)	
Functional status before admission				0.006
Independent	1487 (83.9%)	1006 (85.7%)	481 (80.4%)	
Dependent	285 (16.1%)	168 (14.3%)	117 (19.6%)	
Weighted Charlson score[1]				0.67
0 points	333 (18.8%)	226 (19.3%)	107 (17.9%)	
1-2 points	563 (31.8%)	366 (31.2%)	197 (32.9%)	
>2 points	876 (49.4%)	582 (49.6%)	294 (49.2%)	
Hospital admissions within the last 6 months				0.03
None	1336 (75.4%)	905 (77.1%)	431 (72.1%)	
1-2 admissions	350 (19.8%)	221 (18.8%)	129 (21.6%)	
>2 admissions	86 (4.9%)	48 (4.1%)	38 (6.4%)	
ICU Admission type				0.002
Medical	1222 (69.0%)	777 (66.2%)	445 (74.4%)	
Surgical, elective	222 (12.5%)	163 (13.9%)	59 (9.9%)	
Surgical, emergency	328 (18.5%)	234 (19.9%)	94 (15.7%)	
ICU admission diagnosis				<0.001
Trauma +/- head injury	142 (8.0%)	118 (10.1%)	24 (4.0%)	
Cardiac arrest	174 (9.8%)	86 (7.3%)	88 (14.7%)	
Cardiovascular disease	176 (9.9%)	107 (9.1%)	69 (11.5%)	
Non-traumatic cerebral pathology (incl. intracranial bleeding)	333 (18.8%)	202 (17.2%)	131 (21.9%)	
Respiratory failure	266 (15.0%)	173 (14.7%)	93 (15.6%)	
Sepsis	94 (5.3%)	59 (5.0%)	35 (5.9%)	
Other	587 (33.1%)	429 (36.5%)	158 (26.4%)	
Treatment limitations present at ICU admission				<0.001
No limitation	1686 (95.1%)	1140 (97.1%)	546 (91.3%)	
No escalation of treatment	4 (0.2%)	1 (0.1%)	3 (0.5%)	
DNR	82 (4.6%)	33 (2.8%)	49 (8.2%)	
Documented medical directive	72 (4.1%)	28 (2.4%)	44 (7.4%)	<0.001
Vasopressors / inotropes administered at ICU admission				
Dobutamine	253 (14.3%)	151 (12.9%)	102 (17.1%)	0.021
Noradrenaline	999 (56.4%)	612 (52.1%)	387 (64.7%)	<0.001
Adrenaline	348 (19.6%)	209 (17.8%)	139 (23.2%)	0.008

[1] The Charlson Comorbidity Index (CCI) predicts one-year mortality in patients with multiple comorbidities. Comorbidities are weighted from 1 to 6 for mortality risk and disease severity, and then summed to form the total CCI score. Numbers are reported as count (%) or median [interquartile range]. BMI: Body mass index. APACHE: Acute Physiology And Chronic Health Evaluation. ICU: Intensive Care Unit. DNR: Do Not Resuscitate

3.2. Process of care

A total of 1478 (83.4%) patients (79.3% survivors vs. 91.5% non-survivors; p<0.001), received mechanical ventilation at some point during the ICU stay (Table 2). Tracheostomy was performed in 146 (8.2%) patients after a median of 7 [4.3 - 9.5] days. During the ICU stay, vasoactive drugs were administered in 1279 (72.2%) patients (66.7% survivors vs. 82.9% non-survivors; p<0.001), and renal replacement therapy (RRT) was used in 297 (16.8%) patients (12.9% survivors vs. 24.4% non-survivors; p<0.001). Treatment limitations during the ICU stay were established in 459 (25.9%) patients (6.5% survivors vs. 64.0% non-survivors; p<0.001). Overall, only 36 (2.0%) patients were referred to a specialized palliative care physician.

3.3. Outcomes

At 6 months after ICU admission, 598/1772 (33.7%) patients had died (Table 2, Fig. 1). ICU mortality was 13.4%, with a median ICU LOS of 4.2 [2.9 – 8.0] days. One or more re-admissions to our ICU during the index hospitalization occurred in 190/1534 (12.4%) ICU survivors. Hospital mortality was 22.3% and hospital LOS was 13.0 [6.0 – 23.0] days; 45.2% of hospital survivors were discharged to another hospital, 32.5% were discharged to a rehabilitation facility and 19.2% were discharged home. Thirty-six hospital survivors (2.6%) were discharged to a long-term care facility. 12 months after the index ICU admission, overall mortality was 37.1%.

3.4. Prediction model and score development

Of the potential predictor variables available at 48 hours after ICU admission (Table S1), 14 variables remained in the final model. The association between these predictor variables and 6-month mortality is presented in Table S3 (Appendix). The validated AUROC for the model was 0.72 (95% CI 0.69 to 0.74) and the Brier score was 0.19 (95% CI 0.19 to 0.20), indicating good discriminatory and prediction performance, respectively. For derivation of the ePOS score, each coefficient was rounded to the nearest integer, resulting in the score points presented in Table 3. At 48 hours after ICU admission, the ePOS score, ranging from 1 to 46 points, can be used to define high vs low risk of 6-month mortality (Fig. S1 and Table S4). The validated AUROC for the ePOS score using the cut-off value of 20 points was 0.72 (95% CI 0.67 to 0.77), with a sensitivity of 0.81 (95% CI 0.78 to 0.84) and specificity of 0.51 (95% CI 0.48 to 0.54), respectively. The positive (PPV) and negative predictive value (NPV) were 0.46 (95% CI 0.43 to 0.49) and 0.84 (95% CI 0.81 to 0.87) respectively (Table S5). High-risk patients (ePOS score > 20) had a 6-month mortality of 45.8% compared to 15.8% in low-risk patients (ePOS score < 20 points, p-value < 0.001) (Table S6).

Table 2
Process of care and patient outcomes, stratified by 6-month survivors vs. non-survivors

	All patients (n = 1772)	Survivors (n = 1174)	Non-survivors (n = 598)	P-Value
Process of care during the index ICU admission				
Vasoactive drugs	1279 (72.2%)	783 (66.7%)	496 (82.9%)	<0.001
Mechanical ventilation	1478 (83.4%)	931 (79.3%)	547 (91.5%)	<0.001
Duration of mechanical ventilation, hrs.	65 [36 - 125]	59 [28 - 121]	73 [49 - 134]	<0.001
Renal replacement therapy	297 (16.8%)	151 (12.9%)	146 (24.4%)	<0.001
Tracheostomy performed	146 (8.2%)	100 (8.5%)	46 (7.7%)	0.61
Treatment limitations established in ICU				<0.001
None	1313 (74.1%)	1098 (93.5%)	215 (36.0%)	
DNR	180 (10.2%)	57 (4.9%)	123 (20.6%)	
No escalation of treatment	91 (5.1%)	19 (1.6%)	72 (12.0%)	
Withdrawal	181 (10.2%)	0 (0.0%)	181 (30.3%)	
Organ donation	7 (0.4%)	0 (0.0%)	7 (1.2%)	
ICU re-admissions during hospitalization[a]	n= 1534	n=1174	n=360	0.20
None	1344 (87.6%)	1037 (88.3%)	307 (85.3%)	
1-2 re-admissions	177 (11.5%)	129 (11.0%)	48 (13.3%)	
>2 re-admissions	13 (0.9%)	8 (0.7%)	5 (1.4%)	
Palliative care consultation during hospitalization				<0.001
Yes	36 (2.0%)	4 (0.3%)	32 (5.4%)	
No	1736 (98.0%)	1170 (99.7%)	566 (94.6%)	
Hospital outcomes				
Hospital mortality [b]	395 (22.3%)	0 (0.0%)	395 (66.1%)	<0.001
Hospital LOS, days [b]	13.0 [6.0 - 23.0]	15.0 [8.0 - 25.0]	8.9 [3.8 - 18.0]	<0.001
ICU Mortality [b]	238 (13.4%)	0 (0.0%)	238 (39.8%)	<0.001
ICU LOS, days [b]	4.2 [2.9 - 8.0]	4.5 [2.9 - 8.3]	4.1 [2.8 - 7.5]	0.047
Hospital discharge destination				<0.001
Home	264 (14.9%)	243 (20.7%)	21 (3.5%)	
Other hospital	622 (35.1%)	483 (41.1%)	139 (23.2%)	
Long-term care facility	36 (2.0%)	26 (2.2%)	10 (1.7%)	
Rehabilitation facility	448 (25.3%)	417 (35.5%)	31 (5.2%)	
Other	8 (0.5%)	5 (0.4%)	3 (0.5%)	
ICU re-admissions within 12 months [c]	n = 1377	n = 1174	n = 203	0.38
None	1173 (85.2%)	1006 (85.7%)	167 (82.3%)	
1-2 re-admissions	186 (13.5%)	154 (13.1%)	32 (15.8%)	
>2 re-admissions	18 (1.3%)	14 (1.2%)	4 (1.9%)	

Numbers are reported as count (%) or median [interquartile range]. ICU: Intensive Care Unit. LOS: Length of stay. ED: Emergency Department. DNR: Do Not Resuscitate. [a)] in ICU survivors. [b)] includes patients discharged to other hospitals [c)] in hospital survivors. ICU readmissions reflect only the proportion of patients readmitted to *our* ICU and do not include patients readmitted to ICUs of other hospitals. Therefore, while the reported mortality rate is accurate, the true ICU readmission rate in our cohort may be slightly higher.

4. Discussion

We developed and validated the electronic poor outcome screening (ePOS) score based on modified PC trigger criteria, patient characteristics and physiological variables that can be automatically extracted from EHR to allow early identification of ICU patients at high risk for poor outcome and potential PC needs. The ePOS score showed good performance in identifying patients at high risk of death at 6 months. High-risk patients (ePOS score > 20) had a 6-month mortality of 45.8% compared to 15.8% in low-risk patients. The ePOS score may be used for automated screening of ICU patients, pinpointing those in whom a comprehensive assessment of PC needs should be performed, thus enabling timely referral to a specialized PC service if required.

In our cohort, long-term mortality was 33.7% at 6 months and 37% at one year. This is in accordance with a large study of 420,187 adult ICU patients reporting that one-third of those admitted to the ICU died during long-term follow-up [27]. At first glance, the individual components of our score do not appear novel. Factors like age, comorbidities, mechanical ventilation, functional status, and illness severity scores are well known to be associated with long-term (6–12 months) mortality in ICU patients [28]. However, previously published trigger criteria are often poorly defined (e.g., "multi-organ" failure, or "prolonged" mechanical ventilation), heterogeneous, and include subjective or composite factors. Therefore, they cannot be readily extracted from EHR without cumbersome manual chart review, which might, in turn, be a major barrier for routine clinical implementation. Furthermore, currently available PC triggers and screening criteria, although selected based on their association with mortality, have not been formally validated. Finally, the novelty of this tool is also the clearly defined and studied timepoint of the screening. Other PC screening tools are often inconsistency regarding the timepoint of screening. Most studies screened at ICU admission, and many screened more than once.

Our aim was to develop and validate a prediction model and a screening score to predict 6-month mortality using only objective, measurable triggers that can be extracted directly from EHR within 48 hours of ICU admission. We have chosen to calculate the score at 48h after ICU admission to allow early identification of patients at high risk for poor outcome, while still permitting clinicians and families to observe the effect of a time-limited treatment, as we explicitly do not intend our score to be used as a triage tool for ICU admission. The ePOS score incorporates patient and illness characteristics, recent hospitalizations, physiological variables, and indicators of worsening functional status. Most variables are routinely collected in EHR, and the ePOS score can, therefore, easily be integrated and calculated automatically by a computer software. Importantly, in contrast to other PC screening tools, we do not provide another simple list of trigger criteria. Instead, the ePOS score combines relevant predictive variables by allocating weighted score points to each factor and provides a clear cut-off value with high sensitivity.

Unlike other studies, we did not incorporate acute illness severity scores like the Simplified Acute Physiology Score [SAPS] or the Acute Physiology And Chronic Health Evaluation [APACHE] scoring system. Such scores are based mainly on acute physiology measures collected at ICU admission and, therefore, lack any information about the response to treatment. Moreover, these scores have not been designed to predict long-term outcomes and they have been developed for the ICU population, and their low precision impedes patient-level use.

Table 3
Final ePOS Score to identify ICU patients at 48 hours after ICU admission at high risk to die within the next 6-months.

Variable	Points
Preadmission functional status and comorbidities	
Age group	
< 60 years	+0
60-69 years	+5
70-79 years	+9
> 79 years	+14
Functional status	
Independent	+0
Partially or fully dependent in one or more daily living activities (toileting, ambulation…)	+3
Malignancy	
none	+0
Active malignancy/cancer	+3
Number of hospital admissions within previous 6 months	
None	+0
1-2 admissions	+2
>2 admissions	+5
ICU admission details	
Time between hospital and ICU admission	
< 24 hours	+0
> 24 hours	+11
ICU admission type	
Surgical (elective or emergency)	+0
Medical	+4
ICU admission diagnosis*	
Cardiovascular disease or respiratory failure	+2
Non-traumatic cerebral pathology (incl. intracranial bleeding)	+7
Cardiac arrest	+7
Other	+0
Organ dysfunction / support present at 48h after ICU admission	
Serum lactate level > 2 mmol/L**	
Yes	+7
No	+0
Invasive mechanical ventilation**	
Yes	+9
No	+0
Vasoactive drugs**	
Yes	+2
No	+0
Renal replacement therapy**	
Yes	+5
No	+0
Total Score (sum)	(0-46 points)

* APACHE diagnostic codes; ** value / administered at 48h after ICU admission

4.1. Implications

Improving the detection of patients with unmet PC needs is a crucial step to overcome inequity in access to PC and to ensure that patients receive the right care at the right time, in accordance with their needs and preferences. Although screening tools and trigger criteria for PC consultation have been published before, a recent survey among ICU physicians showed a low acceptance rate [29] of previously published trigger criteria [22,25,30] and a recent systematic review found that physicians are often unable to identify patients who require PC in the early stage of critical illness [31]. Therefore, automatic and systematic screening and early identification of patients at risk of poor outcome using EHR-based tools like the ePOS score might overcome barriers to clinical implementation and has been recommended in previous reports [18].

The ePOS score is highly sensitive for increased risk of 6-month mortality. However, it is not very specific and – intentionally – does not include subjective clinical judgement. The goal is to improve the *detection* of patients with unmet PC needs using the score. Therefore, a high score should not necessarily lead to immediate referral to a specialist PC service but rather trigger a comprehensive PC needs assessment, including clinical judgement. At this stage, clinicians should differentiate between simple and complex PC needs. The former can be addressed by intensivists while the latter may require specialized PC consultation [32]. Importantly, our score should not be used as a substitute for clinical judgment, but rather as a tool to trigger a palliative care assessment in the ICU early in the course of disease.

4.2. Strengths and limitations

Our study has several strengths. First, we systematically searched the literature for well-established palliative care triggers. Then, we developed a clinically applicable risk score based on objective factors with good discriminatory performance using transparent methodology and clinical data readily available from EHR in most developed healthcare settings. We included only patients with an ICU stay of at least 48 hours and we used only data available in these first 48h for our prediction model. In doing so, we were able to exclude unambiguous cases with very low and very high risk of ICU mortality such as uncomplicated elective surgical admissions (e.g., uneventful cardiac surgery) and patients with catastrophic events (e.g., large intracranial haemorrhage) in whom treatment was withdrawn within 48 hours. A time-limited trial of full organ support with regular re-evaluation after 48–72 hours has been suggested to improve care of multimorbid patients, allowing for evaluation of the clinical progress before deciding to continue or to withdraw treatment [33,34]. Therefore, unlike most available mortality prediction scores in critical care, we did not only consider data available at the time of ICU admission, but also considered the patients' history before admission as well as the clinical response in the first 48 hours of ICU treatment. Finally, we obtained reliable long-term mortality data for 99.2% of all eligible patients up to one year after ICU admission, and our study provides important cues as to which data from EHR can be used for long-term mortality prediction in critically ill patients. By providing a score and a cut-off value based on a measurable and clinically relevant outcome such as 6-month mortality, we provide a model that can be validated and implemented across different EHR and ICU settings.

Our study has limitations. First, missing data are inevitable with retrospective analyses of patient charts and limitations driven by study design apply. We used established imputation methods to minimize risk of bias. However, several potentially relevant comorbidities, such as dementia and frailty were not recorded in our dataset. In contrast to other predictive tools, our score does not include subjective factors like clinical judgement. This might be considered both a weakness and a strength. We believe the strengths prevail in choosing this approach, because using unbiased data adds objectivity and reproducible accuracy to our score, rendering it transferable to other healthcare settings and provider models. Furthermore, we emphasize that subjective evaluation by clinical staff is still a necessary and recommended step for patients identified by the ePOS score to be at risk for poor outcome. Second, due to a lack of an accepted definition of "palliative care needs", we used 6-month mortality as a proxy for a poor outcome phenotype. However, 6-month mortality represents an objective and measurable outcome that is likely to be associated with substantial palliative care needs [18], although it could theoretically be due to other non-related events post ICU. Third, the single-centre design and the relatively small sample size demands external validation of our findings to determine whether our risk score is generalisable in other settings and populations. Finally, as we only considered the first ICU admission during the index hospitalisation, our risk score may not be valid in case of an ICU re-admission.

5. Conclusion

We developed and validated the electronic poor outcome screening (ePOS) score based on based on modified PC trigger criteria, patient characteristics and physiological data obtained in the first 48 hours after ICU admission. The ePOS score can easily be implemented in EHR and can be used for automated screening and stratification of ICU

patients, pinpointing those in whom a comprehensive assessment of PC needs should be performed. Using the score at 48h after ICU admission allows for early identification of patients at high risk for poor outcome while still permitting clinicians and families to observe the effect of a time-limited period of full ICU treatment. The ePOS score is not intended to be used as a substitute for, but rather as a tool to foster comprehensive palliative care assessements in the ICU early in the course of disease. However, the score should be externally validated. Moreover, future research needs to study which outcomes will benefit most: the family carer's distress, the medical professional's distress, health care resource utilization or quality and goals' concordance of advance directives for future complications or emergency situations.

Ethics approval and consent to participate

The study protocol was reviewed and approved by the responsible regional research ethics committee (KEK, Project ID-2019-01070).

Consent for publication

Not applicable.

Availability of data and materials

The datasets generated and analysed during the current study are not publicly available due to national regulations but de-identified data that underly the reported results will be made available to researchers with a defined protocol and analysis plan, after approval by the University of Bern, Switzerland, and all co-authors (Email to nora.luethi@med.unibe.ch) on reasonable request.

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Declaration of Competing Interest

The authors declare that they have no competing interests. SW, JCS and LC report (full departmental disclosure) departmental grants outside of the submitted work from Orion-Pharma, Abbott-Nutrition-International, Braun-Medical-AG, CSEM-AG, Edwards–Lifesciences- Services-GmbH, Kenta-Biotech-Ltd, Maquet-Critical-Care-AB, Omnicare-Clinical-Research-AG, Nestle, Pierre-Fabre-Pharma-AG, Pfizer, Bard-Medica-S.A., Abbott-AG, Anandic-Medical-Systems, Pan-Gas- AG-Healthcare, Bracco, Hamilton-Medical-AG, Fresenius-Kabi, Getinge-Group-Maquet-AG, Dräger-AG, Teleflex-Medical-GmbH, Glaxo-Smith-Kline, Merck-Sharp-and-Dohme-AG, Eli-Lilly-and-Company, Baxter, Astellas, Astra-Zeneca, CSL-Behring, Novartis, Covidien, and Nycomed. The money was paid into departmental funds. No personal financial gain applied.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jcrc.2022.154007.

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