An Utstein-based model score to predict survival to hospital admission: The UB-ROSC score

Enrico Baldi [a,b,*,1], Maria Luce Caputo [a,c,1], Simone Savastano [d], Roman Burkart [e], Catherine Klersy [f], Claudio Benvenuti [e], Vito Sgromo [g], Alessandra Palo [g], Roberto Cianella [h], Elisa Cacciatore [a], Luigi Oltrona Visconti [d], Gaetano Maria De Ferrari [a,b], Angelo Auricchio [c]

[a] Department of Molecular Medicine, Section of Cardiology, University of Pavia, Pavia, Italy
[b] Cardiac Intensive Care Unit, Arrhythmia and Electrophysiology and Experimental Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[c] Cardiocentro Ticino, Lugano, Switzerland
[d] Division of Cardiology, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[e] Fondazione TicinoCuore, Lugano, Switzerland
[f] Service of Clinical Epidemiology and Biometry, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[g] AREU Azienda Regionale Emergenza Urgenza, AAT Pavia c/o Fondazione IRCCS Policlinico San Matteo, Pavia, Italy
[h] Federazione Cantonale Ticinese Servizi Autoambulanze, Lugano, Switzerland

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ABSTRACT

Aims: To develop and validate a multi-parametric practical score to predict the probability of survival to hospital admission of an out-of-hospital cardiac arrest (OHCA) victim by using Utstein Style-based variables.

Methods: All consecutive OHCA cases occurring from 2015 to 2017 in two regions, Pavia Province (Italy) and Canton Ticino (Switzerland) were included. We used random effect logistic regression to model survival to hospital admission after an OHCA. We computed the model area under the ROC curve (AUC ROC) for discrimination and we performed both internal and external validation by considering all OHCAs occurring in the aforementioned regions in 2018. The Utstein-Based ROSC (UB-ROSC) score was derived by using the coefficients estimated in the regression model. The score value was obtained adding the pertinent score components calculated for each variable. The score was then plotted against the probability of survival to hospital admission.

Results: 1962 OHCAs were included (62% male, mean age 73 $\pm$ 16 years). Age, aetiology, location, witnessed OHCA, bystander CPR, EMS arrival time and shockable rhythm were independently associated with survival to hospital admission. The model showed excellent discrimination (AUC 0.83, 95%CI 0.81–0.85) for predicting survival to hospital admission, also at internal cross-validation (AUC 0.82, 95%CI 0.80–0.84). The model maintained good discrimination after external validation by using the 2018 OHCA cohort (AUC 0.77, 95%CI 0.74–0.80).

Conclusions: UB-ROSC score is a novel score that predicts the probability of survival to hospital admission of an OHCA victim. UB-ROSC shall help in setting realistic expectations about sustained ROSC achievement during resuscitation manoeuvres.

1. Introduction

Out-of-hospital cardiac arrest (OHCA) is the most frequent cause of death in the industrialized world [1,2]. OHCA outcome significantly varies across different countries [3]; it is influenced by numerous underlying independent variables related to the patient's characteristics, e.g. age, comorbidity, and the circumstances in which the event occurred (aetiology, witnessed or not, public or private location, etc.) [4] as well as by modifiable factors, including bystander cardiopulmonary resuscitation (CPR), use of automated external defibrillators (AED) and the intervention time of emergency medical services (EMS) [5,6]. Similarly to survival, also the probability of return of spontaneous circulation (ROSC) significantly varies across geographies [3]. Prompt initiation of CPR manoeuvres after OHCA has an immediate impact on both ROSC achievement and outcome. ROSC in field can be temporarily or permanently achieved, bearing in mind that the most important one in OHCA management is a sustained ROSC. The development of a user-friendly and generally applicable tool to predict the resuscitation success, indicated by a sustained ROSC leading to hospital admission after arrival of the EMS team, would be of major clinical relevance. Such a score – made up off different independent variables which are readily

* Corresponding author at: c/o Fondazione IRCCS Policlinico San Matteo, Viale Golgi 19, 27100 Pavia, Italy.
E-mail address: enrico.baldi@unipv.it (E. Baldi).
[1] These authors contributed equally.

available to the EMS team – could support the decision for aggressive therapy, provide medical personnel and family members with reasonable expectation of immediate outcome as well as improve general termination-of-resuscitation rules beyond those currently available [7–11].

Recommended guidelines for uniform OHCA data reporting have been developed as the Utstein Style [12,13]; thus, a basis for comparison has been created by providing clear data definitions. Utstein Style data reporting already contains key prognostic variables associated with survival or death following cardiac arrest, but to our knowledge, there has been no effort to develop a predictive score of sustained ROSC using these variables.

Therefore, the aim of our study was to develop and validate a multiparametric score to predict the probability of sustained ROSC and survival to hospital admission of OHCA victims by using the Utstein templates for patient data collection.

2. Methods

2.1. Population

All consecutive patients suffering OHCAs of any aetiology between January 1st, 2015 and December 31st, 2017 in the province of Pavia, Northern Italy, and in the Canton of Ticino, Southern Switzerland, were included in the study. Patients declared dead before ambulance arrival, with a "do not resuscitate" order, and/or with incomplete or unknown data were excluded from further analysis. A second cohort of consecutive patients from the same centers admitted between January 1st, 2018 and December 31st, 2018 was also enrolled for external validation using the same inclusion/exclusion criteria.

2.2. Study design and setting

This is a prospectively designed development of a multiparametric practical score to predict the probability of survival to hospital admission of OHCA victims by using Utstein templates for patient data collection in 2 large regional registries. Both the province of Pavia and the Canton of Ticino have a prospectively designed registry of cardiac arrest, i.e. the Cardiac Arrest Registry of the Province of Pavia (Pavia CARe), and the Ticino Region Cardiac Arrest Registry (TiReCa). Both registries follow the Utstein recommendations for data collection [12,13], as previously described [14,15], periodically reviewed for quality assessment by an internal commission, and were approved by the local ethical committees.

2.3. EMS and resuscitation network in the province of Pavia

The province of Pavia is a region of 2965 km^2 with several rural and a few urban areas with a total population of 548,722 inhabitants (as per December 31st, 2014). A national emergency telephone number, 112, is connected to the regional EMS dispatching centre. The local EMS dispatcher coordinates 33 ambulances staffed with Basic Life Support — Defibrillation (BLS-D) trained personnel, and 5 ALS-trained staffed vehicles. In case of suspected OHCA, the EMS dispatcher activates one or two emergency vehicles of which at least one with a physician on board and assists the calling bystander during chest compressions (telephone CPR).

2.4. EMS and resuscitation network in the Canton of Ticino

The Swiss Canton of Ticino has a population of 350,363 inhabitants (as per December 31st, 2014). It covers a territory of >2800 km^2 in the southern part of Switzerland. The population is distributed among some cities (population ranging from 5000 to 70,000 inhabitants) and few hundreds of rural municipalities. A national emergency telephone number — 144, is connected to each of the six regional EMS dispatching

centres operating in the Canton of Ticino, which in turn coordinate seven EMS services, all with ALS-trained staffed vehicles. When a cardiac arrest is suspected, a telephone assisted CPR is initiated until the arrival of an ambulance. The EMS dispatchers send the ambulance and, in parallel, alert the traditional first-responders represented by police officers and fire brigade, all trained in BLS-D and equipped with AEDs. If the OHCA condition is regarded as safe, the lay responders' network is also activated and automatically managed by a mobile application [16]. Their training includes the standard Swiss Resuscitation Council Basic Life Support (SRC BLS)/AED course for lay rescuers which complies with the recommendations of the European Resuscitation Council. Each EMS service individually collects data about OHCA interventions in the registry pursuant the Utstein methodology. An internal commission then periodically performs a quality assessment review of the data. None of 2 EMS systems have had or has rules for termination of resuscitation (TOR). The decision to terminate resuscitation is always at discretion of the pre-hospital team/physician until arrival at emergency room. However, patient's characteristics (e.g. age, comorbidities, etc.), OHCA circumstances (e.g. presence of witness, bystander CPR, etc.), and additional resuscitation elements (e.g. cardiac rhythm, end-tidal CO_2 value before and during CPR, duration of resuscitation effort, etc.) may guide a TOR decision.

2.5. Definition of survival to hospital admission (sustained ROSC)

The survival to hospital admission of the patient was defined as a patient in whom a ROSC was sustained until arrival at the emergency department and transfer of care to medical staff at the receiving hospital. This definition corresponds to the Utstein recommendations' core outcome — "Survived event" [13].

2.6. Predictors identification for survival to hospital admission

Age, aetiology, OHCA location site, witnessed OHCA, bystander CPR, time of EMS arrival and presenting rhythm are all Utstein variables readily available at EMS arrival being considered of prognostic relevance according to recent literature [13,17–23].

2.7. Statistical analysis

Each and every analysis was performed by using Stata 15.1 (StataCorp, College Station, TX, USA). Variables are given as mean and standard deviation (SD), or the median and 25th–75th percentiles if continuous, and with counts and percent if categorical. Comparisons were made by means of the Mann Whitney U test or Fisher exact test. A random effect logistic regression, with a random effect for center, was used to develop the model for sustained ROSC. Odds ratios (OR) and their 95% confidence intervals (95%CI) were computed. The model area under the ROC curve (AUC ROC) was computed for discrimination. Model sensitivity (to identify survivors) and specificity (to identify non-survivors) with predictive values for a probability of hospital survival >50% was estimated, and model calibration was graphically assessed. A 10-fold cross validation to obtain optimism corrected AUC-ROC was used (internal validation). The coefficients estimated from the model, multiplied by 10 and rounded to the closest integer were used to compute a prediction score; the score was then plotted against the probability of survival to hospital admission to provide an easy to use nomogram. The score was then applied to the validation cohort, and the area under the ROC curve (95%CI) against survival to hospital admission was computed for external validation.

3. Results

Overall, 3186 patients suffered from an OHCA during the study period. Of these, 1109 (34.8%) were declared dead before ambulance arrival or had a "do not resuscitate" order, 115 patients (3.6%) had

incomplete data thus, being excluded from any subsequent analysis. The demographic characteristics of the 1962 OHCA victims (1383 cases in the province of Pavia and 579 cases in the Canton of Ticino) representing the derivation cohort, and circumstances of the arrest are presented in Table 1. Although the population groups from the two centers differed statistically in most of the variables, some of them could be considered modestly different from the clinical standpoint. Indeed, the age was similar (Ticino: 71.1 yrs old vs Pavia: 73.4 yrs old, $p < 0.001$) as well as time to EMS arrival (Ticino: 11.3 min. vs. Pavia: 11.6 min, $p = 0.09$). On the other hand, there were more males in Ticino (66.6%) compared to Pavia (60.5%, $p < 0.01$), OHCA was less frequently due to a cardiac cause in Ticino (77.9%) vs Pavia (92.8%, $p < 0.001$) and occurred less frequently at home in the Ticino cohort (69.1%) compared to the Pavia cohort (79.6%, $p < 0.001$). A non-shockable rhythm was more frequent in the Pavia cohort (81.6% vs. 74.8%, $p < 0.001$), most likely due to a less frequent bystander CPR (33.8% vs. 71.2%, $p < 0.001$) thus, resulting in a lower survival to hospital admission (16.9% vs. 33.5%, $p < 0.001$).

3.1. Predictors of survival to hospital admission

The multivariable logistic model for survival to hospital admission, including all the acknowledged prognostic factors from the literature, is summarized in Table 2. The model shows an AUC of 0.83 (95%CI 0.81–0.85; Fig. 1), and a good calibration (Fig. 1). Excellent discrimination was found at the internal validation (AUC 0.82, 95%CI 0.80–0.84, after 10-fold cross-validation). All variables were independently associated with survival to hospital admission. The coefficients derived from the model, and simplified, were used to calculate a prediction score, the proposed Utstein-based ROSC score (UB-ROSC), that can be easily computed by summing up the pertinent score components reported in Table 2, last column. It varies from −50 to +44. The probabilities of survival to hospital admission (with 95%CI) are tabulated (left panel)

and plotted as a nomogram (right panel) in Fig. 2. A score of 0 corresponds to a 50% probability of survival to hospital admission. The calculation of two simulated cases (red & green dots) is shown in the figure legend.

3.2. External validation of the UB-ROSC score

The UB-ROSC score was further validated in a cohort composed of 747 OHCAs patients enrolled in 2018, 537 in the Pavia registry and 210 in the Ticino registry (Table 1, validation cohort). In this external validation, the model maintained a discrimination value of 0.77 (95% CI 0.74–0.80) for predicting survival to hospital admission as compared to the 0.82 obtained from the internal validation (see above).

4. Discussion

To the best of our knowledge, the Utstein-based ROSC (UB-ROSC) score, is the first available score predicting sustained ROSC and survival to hospital admission of patients after having suffered an OHCA. The UB-ROSC score shows excellent discrimination capability and already accounts for a random effect related to center, thus making it a score to be used in-field, and possibly supporting resuscitation-related decisions such as considering termination of resuscitation manoeuvres.

Resuscitation termination rules are still matter of debate. Previous studies suggested some resuscitation termination rules capable to identify patient without a chance of survival; however the generalisability of these rules has been significantly questioned [7–11,24,25]. Indeed, it is unlikely to be able to achieve a positive predictive value of 100%, and even a small chance of survival shall not be a-priori neglected. However, it is important to emphasize that a low UB-ROSC score should never lead to withhold resuscitation, since a resuscitation attempt should be performed in all patients, even with a minimal probability of survival. The utility of UB-ROSC is instead to help in setting realistic expectations about the likelihood of achieving sustained ROSC during resuscitation manoeuvres. This knowledge is important for paramedics, rescue teams and even more so for family members. The awareness and understanding that the circumstances of OHCA and the demographic characteristics of the cardiac arrest victim play a significant role in the possibility of survival to hospital admission is particular relevant for acceptance of poor outcome by family members; despite that, it is particularly important to make every effort to save patients' lives.

The UB-ROSC score shares some important prognostic elements with the ACLS score proposed by Eisenberg et al. [26], and with the ROSC After Cardiac Arrest (RACA) score by Gräsner et al. [23], but is significantly different in the way it was designed to predict outcome at variance with the other two. All three scores have been developed to formulate a prediction of the probability of the patient surviving based on variables that are both predictive of survival and readily available at the scene of the emergency. Both the ACLS score and the UB-ROSC score are operational scores whereas the RACA score is not meant to be used as a practical score by the EMS personnel at arrival on the scene. The RACA score was on the other hand developed as an instrument to facilitate the comparison of different ROSC percentages in studies performed in different conditions and enrolling patients with different characteristics. Therefore, it is useful to enable comparison between different EMS systems, educational levels, technical equipment, and therapeutic interventions, but it cannot be used to help EMS personnel to assess survival probability of OHCA victims in a real-life scenario [23]. The ACLS was developed as a score predictive of outcome (specifically, discharge alive from hospital) following OHCA [26], whereas UB-ROSC is a score predictive of sustained ROSC and survival to hospital admission. Although the development and use of an practical score predicting OHCA patients' survival following hospital treatment would represent the best score possible; in daily practice it fails short because it includes the uncertainties and weakness of each ring of the so-called "chain-of-survival" [27]. Endpoints such as 'hospital discharge'

Table 1
Characteristics of the derivation and validation cohorts.

Variable	Derivation cohort (year 2015–2017)	Validation cohort (year 2018)
Patients included	1962	747
Male gender	1223 (62.3)	442 (59.2)
Age, mean ± SD	72.7 ± 15.7	73.7 ± 16.1
Age ≥ 80	786 (40.1)	347 (46.4)
Aetiology		
Cardiac	1734 (88.4)	623 (83.4)
Trauma	83 (4.2)	37 (4.9)
Drowning	6 (0.3)	7 (0.9)
Respiratory	91 (4.6)	52 (7)
Other non-cardiac	48 (2.5)	28 (3.8)
Witness		
None	540 (27.5)	224 (30)
Bystander	1137 (58)	414 (55.4)
EMS	285 (14.5)	109 (14.6)
Location		
Home	1501 (76.5)	556 (74.4)
Nursing home	149 (7.6)	77 (10.3)
Work place	26 (1.3)	9 (1.2)
School	1 (0.1)	0 (0)
Street	176 (9)	57 (7.6)
Public building	72 (3.6)	35 (4.7)
Sport	37 (1.9)	13 (1.8)
Rhythm		
Not Shockable	1562 (79.6)	641 (82.2)
Shockable	400 (20.4)	133 (17.8)
Bystander CPR		
Yes	879 (44.8)	327 (43.8)
No	1083 (55.2)	420 (56.2)
Time to EMS arrival, mean in minutes (IQR)	11.5 (7.9–14)	13.8 (8–15)
Survival to hospital admission	428 (21.8)	197 (26.4)

Table 2
Multivariable logistic model for survival to hospital admission and score computation.

Candidate predictors[*]	Survival to hospital admission (%)	OR (95%CI)	p	Score component
Sex				
Female	141 (19.1)	1.00		0
Male	287 (23.5)	0.74 (0.56–0.99)	0.044	−3
Age				
<80	345 (29.3)	1.00		0
≥80	83 (10.5)	0.39 (0.29–0.54)	<0.001	−9
Aetiology			<0.001	
Cardiac	359 (20.7)	1.00		0
Trauma	11 (13.3)	0.72 (0.35–1.52)	0.394	−3
Drowning	1 (16.7)	1.09 (0.10–11.77)	0.945	1
Respiratory	46 (50.5)	6.72 (4.03–11.20)	<0.001	19
Other non-cardiac	11 (22.9)	0.95 (0.44–2.05)	0.906	0
Location			0.014	
At home	292 (19.5)	1.00		0
Nursing home	16 (10.7)	0.51 (0.27–0.95)	0.035	−7
Workplace	12 (46.2)	1.90 (0.76–4.77)	0.173	6
School	1 (100)	1.00		0
Street	54 (30.7)	1.50 (0.96–2.35)	0.075	4
Public building	35 (48.6)	1.70 (0.95–3.02)	0.072	5
Sport	18 (48.7)	2.00 (0.91–4.42)	0.087	7
Bystander and CPR			<0.001	
No witnessed, no CPR	30 (9.6)	1.0		0
No witnessed, yes CPR	31 (13.7)	0.59 (0.32–1.09)	0.091	−5
Witnessed, no CPR	66 (13.2)	1.19 (0.72–1.97)	0.502	2
Witnessed, yes CPR	200 (31.4)	1.51 (0.93–2.44)	0.094	4
EMS witnessed	101 (35.4)	3.61 (2.18–5.96)	<0.001	13
Rhythm			<0.001	
Not Shockable	201 (12.9)	1.00		0
Shockable	227 (56.8)	8.18 (6.08–11.02)		21
Time arrival EMS			<0.001	
≤10 min	247 (25.3)	1.00		0
11–15 min	130 (19.9)	0.69 (0.52–0.92)	0.012	−4
≥15 min	51 (15.4)	0.49 (0.33–0.72)	<0.001	−7
Constant		0.20 (0.10–0.39)		−16

Model performance	Model statistics
Model p	<0.001
AUC ROC (95%CI)	0.83 (0.81–0.85)
Model sensitivity	50.2 (45.4–55.1)
Model specificity	92.9 (91.5–94.1)
Model positive predictive value of a probability of survival > 50%	66.4 (60.9–71.5)
Model negative predictive value of a probability of survival > 50%	87 (85.3–88.6)
10-fold cross validation AUC ROC (95%CI)	0.82 (0.80–0.84)
Validation in 2018 cohort	0.77 (0.74–0.80)

[*] All variables were significantly associated with survival to hospital admission at the univariable analysis.
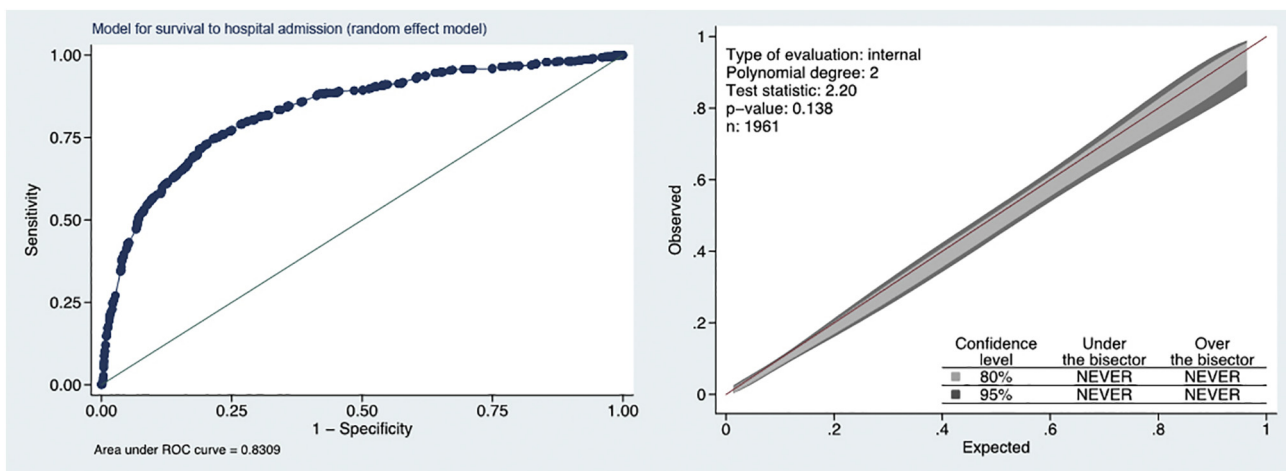

Fig. 1. Left panel: Receiver Operating Characteristic (ROC) curve of RACA score; the naïve area under the curve of 0.83 corresponds to an excellent discrimination of the model in the overall population. Right panel: Calibration curve for the model in the overall population. The bisecting line corresponds to perfect calibration of the model (perfect agreement between observed deaths and predicted deaths). The line is entirely included in the shaded area corresponding to the 80% and 95% confidence intervals for the observed-predicted relationship, denoting that the model is well calibrated (there is neither over nor underestimation of the mortality).
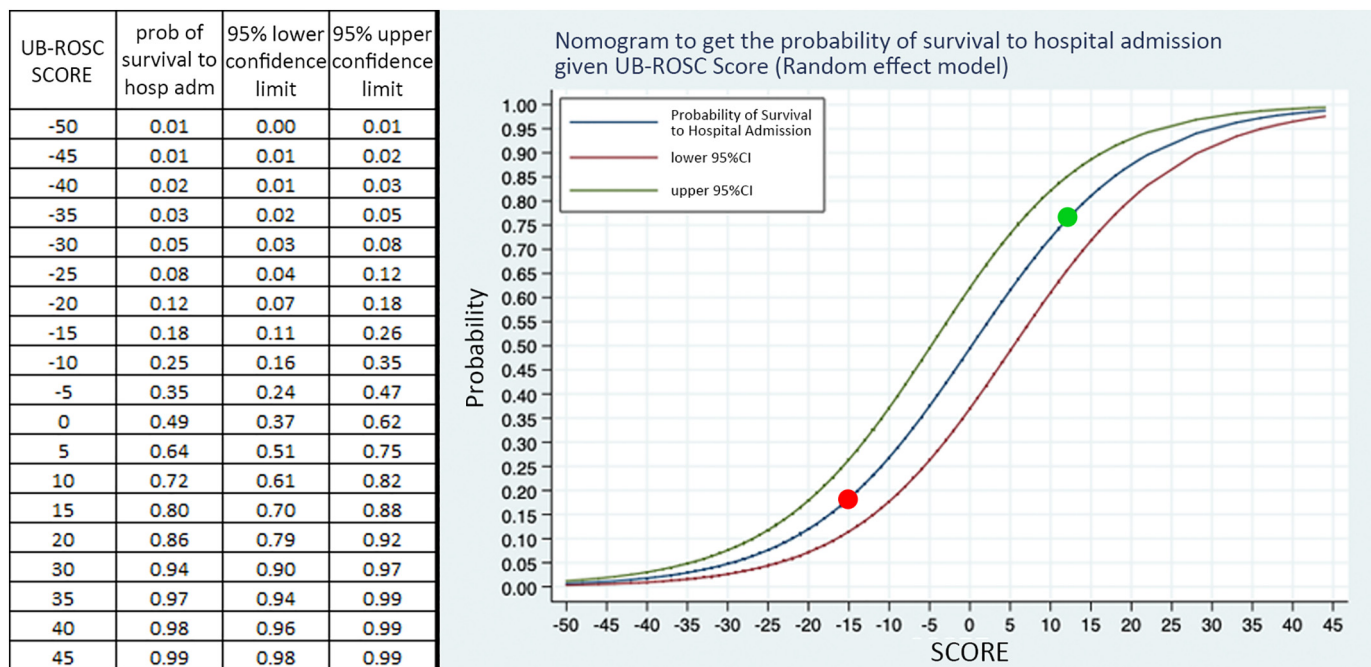
UB-ROSC SCORE	prob of survival to hosp adm	95% lower confidence limit	95% upper confidence limit
-50	0.01	0.00	0.01
-45	0.01	0.01	0.02
-40	0.02	0.01	0.03
-35	0.03	0.02	0.05
-30	0.05	0.03	0.08
-25	0.08	0.04	0.12
-20	0.12	0.07	0.18
-15	0.18	0.11	0.26
-10	0.25	0.16	0.35
-5	0.35	0.24	0.47
0	0.49	0.37	0.62
5	0.64	0.51	0.75
10	0.72	0.61	0.82
15	0.80	0.70	0.88
20	0.86	0.79	0.92
30	0.94	0.90	0.97
35	0.97	0.94	0.99
40	0.98	0.96	0.99
45	0.99	0.98	0.99

Fig. 2. Table (with 95%CI) (left panel) and nomogram of the probabilities of survival to hospital admission (right panel) associated to the different UB-ROSC score values. The red dot corresponds to a simulated case of female patient (0), aged 87 (-9), who suffered an OHCA of respiratory aetiology ($+19$) in a nursing home (-7); the OHCA was witnessed by bystanders but CPR was not initiated ($+2$), the EMS arrival time was 12 min (-4) and the first rhythm was not shockable (0). Considering the constant (-16) the UB-ROSC score is $0 - 9 + 19 - 7 + 2 - 4 + 0 - 16 = -15$, which correspond to an 18% probability of survival to hospital admission. The green dot corresponds to a simulated case of a male patient (-3), aged 57 (0), who suffered an OHCA of cardiac aetiology (0) on the work place ($+6$); the OHCA was witnessed by bystanders and CPR was initiated before EMS arrival ($+4$), the EMS arrival time was 9 min ($+0$) and the first rhythm was a shockable one ($+21$). Considering the constant (-16) the UB-ROSC score is $-3 + 0 + 0 + 6 + 4 + 0 + 21 - 16 = +12$, which corresponds to a 76% probability of survival to hospital admission. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

and 'survival after 1 year' are clinically more relevant, but are also affected by the type, quality, and extent of post-resuscitation care that is often not standardized, and may therefore not be appropriate as a primary endpoint for scoring systems that are mainly based on preclinical data collection. Furthermore, the ACLS score may require frequent adjustments and repeated reassessments when in-hospital management strategies change, e.g. temperature management recommendation [28], percutaneous revascularization in the setting of acute myocardial infarction [29], etc., or novel approaches become available. In contrast, the UB-ROSC score considers a very well-defined and critical phase of an OHCA, i.e. the pre-hospital phase. Achieving a sustained ROSC is already a major step toward good cardio-circulatory and possibly neurological outcome.

As the RACA score, also the UB-ROSC score considers resuscitation success in the pre-hospital phase of resuscitation. The RACA score predicted endpoint is ROSC in field, defined as a palpable pulse for ≥20 s. On the other hand, UB-ROSC considers only sustained ROSC as outcome allowing admission of the patient to the hospital as a clinically more relevant endpoint.

The ACLS score considered four key variables for predicting discharge alive following cardiac arrest: arrest witnessed (A), cardiac rhythm (C), lay bystander cardiopulmonary resuscitation (L) and response time of paramedic unit (speed, S). In a similar manner, UB-ROSC included prognostic variables readily available, but increased the number of prognostic variables including variables that, over the last 2 decades, have been consistently demonstrated to be associated with outcome [17–23]. These include patients' age and sex, aetiology of cardiac arrest, OHCA location. Notably, all variables considered in the UB-ROSC score are part of the uniform and modern reporting of data from OHCA developed as the Utstein Style [13]. Most of the prognostic variables included in the UB-ROSC score are similar but not identical as RACA score since this latter does not use Utstein Style variables, for both OHCA aetiology and location, thus requiring off-line adaptation.

In addition to being easier to apply, compared to RACA, the UB-ROSC performed much better. The discrimination power of UB-ROSC score was as high as 0.82 after internal and 0.77 after external validation, thus, markedly greater than the 0.71 value reported in the original publication by Gräsner et al. [23] or found in recent external validations, including our own [30–32]. Indeed, using this same data set, we found an AUC of 0.76 for the RACA score [30].

To allow an easy and simple calculation of the score by EMS personnel during a mission, a free mobile application for iOs system "UB-ROSC score" has been developed; the score is also calculable at http://www.sanmatteo.org/site/home/ub-rosc-score.html.

4.1. Limitations

Our study has some limitations. A first limitation is related to classification of OHCA aetiology, which was not based on the latest Utstein revision released in 2015. Since the study period started on January 1st, 2015, our registries could not be aligned with that revision. Therefore, to limit recording errors, we maintained the 2004 categorization for the entire cohort. Although the model maintained a good performance both after internal validation on the 2015–2017 cohort and external validation on the 2018 cohort, further validation in independent cohorts is warranted for confirmation. The transferability of our results to other EMS organization that do not include a physician-staffed rescue team may be considered another limitation. Although validation in different geographical realties is highly needed, it is unlikely that the ROSC probability is lower when paramedics alone are performing advanced CPR whereas time to hospital transportation is possibly related to pre-hospital survival. Finally, as stated in the methods, none of the 2 EMS systems has ever applied a decision algorithm for resuscitation termination. This decision has always been left to the intervening physician discretion. For this reason, it cannot be ruled out that the discrimination ability of our score has been affected by a bias of self-fulfilling prophecy.

However, UB-ROSC considered a derivation and validation cohort in which patient's clinical characteristics and most likely, physician decision for resuscitation termination, were similar thus, possibly mitigating this issue.

5. Conclusions

The UB-ROSC score is a novel score to be used in-field and predicts the probability of survival to hospital admission of OHCA victims. UB-ROSC is not a score to withhold resuscitation. UB-ROSC shall help in setting realistic expectations about sustained ROSC achievement during resuscitation manoeuvres, an important target for paramedics, rescue teams and even more so for family members.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2020.01.032.

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