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Development of a prediction model for long-term quality of life in critically ill patients

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ABSTRACT

Purpose: We developed a prediction model for quality of life (QOL) 1 year after intensive care unit (ICU) discharge based upon data available at the first ICU day to improve decision-making.
Methods: The database of a 1-year prospective study concerning long-term outcome and QOL (assessed by EuroQol-5D) in critically ill adult patients consecutively admitted to the ICU of a university hospital was used. Cases with missing data were excluded. Utility indices at baseline (UIb) and at 1 year (UI1y) were surrogates for QOL. For 1-year non-survivors UI1y was set at zero. The grouped lasso technique selected the most important variables in the prediction model. R^2 and adjusted R^2 were calculated.
Results: 1831 of 1953 cases (93.8%) were complete. UI1y depended significantly on: UIb ($P < 0.001$); solid tumor ($P < 0.001$); age ($P < 0.001$); activity of daily living ($P < 0.001$); imaging ($P < 0.001$); APACHE II-score ($P = 0.001$); ≥80 years ($P = 0.001$); mechanical ventilation ($P = 0.006$); hematological patient ($P = 0.007$); SOFA-score ($P = 0.008$); tracheotomy ($P = 0.018$); admission diagnosis surgical $P < 0.001$ (versus medical); and comorbidity ($P = 0.049$). Only baseline health status and surgical patients were positively associated with UI1y. R^2 was 0.3875 and adjusted R^2 0.3807.
Conclusion: Although only 40% of variability in long-term QOL could be explained, this prediction model can be helpful in decision-making.

1. Introduction

Uncertainty about outcomes in critically ill patients admitted to the intensive care unit (ICU) is heavy to bear for patients and family. In general, patients and family only associate outcome with survival and often, unrealistic expectations at long-term are hoped for [1]. The true burden of disease and its long-term consequences on physical, mental and cognitive functioning may be underestimated [2,3], as well as the possibility to return to former daily life and overall quality of life (QOL) [4].

It is the important task of critical care physicians to inform patients and family in a reliable way about these outcomes. However, for critical care physicians too, uncertainty concerning long-term functionality and QOL is difficult to handle [5]. Major reductions in long-term QOL were seen in cases of severe acute respiratory distress syndrome, prolonged mechanical ventilation, trauma, and severe sepsis [6]. Still, long-term QOL remains difficult to predict for the individual patient and patients and families frequently are not well briefed about expected long-term survival and functionality despite explicit wishes to have this information [7].

Accurate prediction models can guide physicians in their handling, communication, and decision-making. Prediction models in critical care do exist but their role in decision-making is however limited [8]. Severity of illness and organ failure scores mainly focus on estimation

Abbreviations: ICU, intensive care unit; QOL, quality of life; D1, first ICU day = first 24 h of ICU admission; ADL, activities of daily living; S, surgical; M, medical; B, burns; T, trauma; sub, subgroup; APACHE II score, Acute Physiology and Chronic Health Evaluation score; SOFA score, Sequential Organ Failure Assessment score; TISS-28 score, Therapeutic Intervention Scoring System-28 score; NEMS-score, Nine Equivalent of Nursing Manpower Use score; DNR-code, do-not-resuscitate code; MV, mechanical ventilation; VP, vasopressors; RRT, renal replacement therapy; LOS, length of stay; EQ-5D, EuroQOL-5D; UI, utility index; VAS, visual analogue scale; UIb, utility index at baseline; UI1y, utility index at 1 year after ICU discharge; VASb, visual analogue scale at baseline; VAS1y, visual analogue scale at 1 year after ICU discharge; lasso, least absolute shrinkage and selection operator.

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of short- term mortality risk [9-15]. Some prediction models may focus on very specific patient populations or problems and are not generalizable to a broad patient application in critical care [7,16-22]. Some models are rather complex [10,23], not accurate enough [24], or ignore that better future treatments may improve prognosis [19]. Although some prediction models focused on long-term mortality [7,25], short-term [24] and long-term functional outcome [16], none of the models estimated long-term QOL in general critically ill patients.

Therefore, it was our aim to develop an easy to use and accurate prediction model for the mean QOL at 1 year after ICU discharge in general critically ill patients based upon data readily available at the first ICU day (D1) (D1 = first 24 h of ICU admission).

2. Material and methods

2.1. Design and setting

The D1-prediction model was retrospectively developed based upon data of a 1-year prospective cohort study. This study focused on long-term outcome and QOL in critically ill adult (≥16 years) patients consecutively admitted to the 22-bed surgical ICU, the 14-bed medical ICU, and the 6-bed burn unit of the Ghent University Hospital, a tertiary care facility in Belgium [26]. In case of multiple ICU admissions, only the first was considered. Patients admitted to the 10-bed cardiac surgical unit after cardiac surgery were not included in the study cohort.

The Ghent University Hospital ICU is a closed ICU where patients are treated by a team of full-time critical care physicians, nurses and physiotherapists.

The original observational study was approved by the local ethical committee (Ethisch Comité Ghent University Hospital; project 2007/423 approved 06 December 2007) (B67020072805), and conducted in accordance with the declaration of Helsinki. A signed informed consent was obtained from every included patient or his legal representative.

2.2. Data collection and definitions

Data collected within the first 24 h of ICU admission included contact information of the patient, proxy, and general practitioner, demographics, hospital days prior to ICU admission, living and work circumstances before ICU admission, functionality as measured by the Katz activities of daily living (ADL) scale [27], hospitalization in the last 6 months, comorbidity as measured by the Charlson comorbidity index [28], main ICU admission diagnosis (surgical, medical, burns, or trauma), admission circumstances (planned-unplanned/during weekend or not), if the patient belonged to 1 or more of the predefined subgroups (sub) (oncological, hematological, liver cirrhosis Child-Pugh B or C, or elderly (≥80 years) patient), Acute Physiology and Chronic Health Evaluation (APACHE II) score [9], Sequential Organ Failure Assessment (SOFA) score [13], Therapeutic Intervention Scoring System-28 score (TISS-28 score) [29], Nine Equivalent of Nursing Manpower Use score (NEMS-score) [30], do-not-resuscitate (DNR) codes, need for invasive mechanical ventilation, vasopressors, renal replacement therapy (RRT), medical imaging (regardless of number or type), transfusion with blood products, surgery, or tracheotomy.

During ICU stay SOFA, TISS-28 and NEMS-scores, DNR-codes, need for invasive mechanical ventilation, vasopressors, RRT, medical imaging, transfusion, surgery, or tracheotomy were collected on a daily base. ICU length of stay (LOS), hospital LOS, vital status at ICU and hospital discharge, and 1 year following ICU discharge were collected for each patient.

2.3. Quality of life assessments

QOL was assessed by means of the EuroQoL-5D (EQ-5D) [31]. This questionnaire is validated and found suitable for measuring QOL in the critically ill population [32]. It measures health in five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, moderate problems or severe problems. Therefore, patients can be classified into 1 of 243 (3^5) possible health states.

We converted each health state into the corresponding utility index (UI), indicating the preference of being in a health status [33]. UI can range from −0.1584 (severe problems on all dimensions) to 1.000 (no problems on all dimensions). UI = 0.0000 equals dead. In 17 of the 243 possible health states the corresponding UI goes below zero, indicating a health state assumed to be worse than dead. The patient will then have severe problems in at least 3 or 4 or in all 5 dimensions, mainly in the pain/discomfort and anxiety/depression dimensions.

Another part of the EQ-5D is the visual analogue scale (VAS), where patients can rate their perceived overall health between 0 and 100.

QOL was assessed at baseline (defined as QOL 2 weeks before ICU admission) and at strictly 1 year after ICU discharge. Following ICU admission and study inclusion, a face-to-face interview to assess baseline QOL was done as soon as possible. This interview was preferably taken from the patient, or if deemed impossible, from the proxy. One year after ICU discharge, patients were sent the EQ-5D by regular mail. Patients or relatives were contacted by phone to assess the 1-year QOL if the questionnaire was not returned within one month. Eventually, the general practitioner was contacted concerning survival status of the patient.

UI at baseline (UIb) and UI at 1 year after ICU discharge (UI1y) were used as surrogate for QOL at that time point. VASb and VAS1y expressed perceived QOL at baseline and 1 year after ICU discharge. UI1y and VAS1y for non-survivors were set at zero to avoid survival bias.

2.4. Statistical analysis

For the development of the D1-prediction model, three different multivariate linear regression models, respectively Model I, II, and III, were fitted with UI1y as primary outcome. Model I assessed the bivariate association between UIb and UI1y. Model II ("full" model) included all possible available D1 predictors in the linear regression analysis. Model III ("reduced" model) included only predictors in the linear regression, which were selected by the grouped lasso technique.

Lasso (least absolute shrinkage and selection operator) is a regression analysis method that performs both variable selection and regularization in order to enhance the prediction accuracy and interpretability of the statistical model it produces. The grouped lasso technique allows predefined groups of covariates, such as all variables encoding a categorical covariate, to be selected into or out of a model together. This technique was applied to identify the optimal number and most important predictors for UI1y in the D1 linear regression model in order to simplify the model, and to cope with the categorical variables [34,35].

Only complete cases (= patients without missing data) were included in the statistical analysis. The number of included cases varied relative to the considered model.

For each respective model, the R^2 (= proportion of explained variance), adjusted R^2 (= proportion of explained variance, taking into account the number of variables), and the root of the cross-validated prediction error were calculated. By using (10-fold) cross-validation, the root of the cross-validated prediction error gives an honest reflection of the predictive capability of the considered model by splitting the data into a training set and test set 10 times enabling prediction of the test data based on solely the training data.

The F-test compared the fit of the reduced Model III with the full Model II. Descriptive statistics were done with IBM SPSS Statistics software version 23. Linear regression analysis for the development of the D1-model was done with the R 3.2.2 software package [36]. The grouped lasso technique was executed using the "grpreg" routine available in the "grpreg" package [37].

3. Results

A total of 1953 patients (847 surgical, 895 medical, 48 burn, 163 trauma) were included in the original observational study. Respectively 1867 (95.6%), 1809 (92.6%), and 1831 (93.8%) of the 1953 cases were complete and included for development of respectively models I, II, and III. Demographics, admission characteristics, organ failures and outcomes for all cases and for the subsets of complete cases per model are described in Table 1. Results were very similar between the different models, which is a strong indication that there were no systematic differences in the subsets of included cases per model. Missingness of variables is described in Table 2.

Development of the D1-prediction model was based upon all 32 variables (10 continuous, 16 binary, 6 categorical) readily available at D1 of ICU admission (Table 3).

For each respective model the R^2, adjusted R^2, and the root of the cross-validated prediction error were calculated (Table 4).

Model I revealed a positive association between UIb and UI1y. UIb could explain 20% of variability in UI1y (Table 4).

Model II ("full" model) held all possible 32 D1-predictors (Table 3). The multivariate linear regression analysis (data not shown) revealed the following significant D1-predictors (significance level 0.10) for UI1y (in order of decreasing importance): UIb, main ICU diagnosis, sub oncological, ADL, age, APACHE II, D1.medical imaging, sub elderly, sub hematological, D1.surgery, origin of ICU admission, D1.SOFA, D1.MV, D1.tracheotomy, origin of hospital admission and Charlson co-morbidity index. UIb was positively associated with UI1y. The model could explain 40% of the variability in UI1y (Table 4). Variable selection was difficult because of the many correlations between the different covariates (data not shown).

The grouped lasso technique revealed 17 possible D1-predictors to be included in Model III ("reduced" model) (Fig. 1). We excluded one

Table 2
Description of missingness.

Variable	Number missing (N) (Total 1953 cases)	Proportion missing (%)
Number of cases with at least 1 variable missing	144	7.37
UI1y	72	3.69
VASb	39	2.00
UIb	28	1.43
Sub oncological	20	1.02
Sub hematological	1	0.05
BMI	27	1.38
APACHE II	5	0.26
Baseline job	24	1.23
D1.TISS-28 score	1	0.05
D1.NEMS-score	1	0.05
D1.medical imaging	1	0.05
D1.transfusion	1	0.05

Abbreviations:
N = number; UI1y = utility index at 1 year after ICU discharge; VASb = visual analogue scale at baseline; UIb = utility index at baseline; sub = predefined subgroup of a specific patient population; BMI = body mass index; APACHE II = Acute Physiology and Chronic Health Evaluation score; D1 = describes variable at D1 (D1 = first 24 h of ICU admission); TISS-28 score = Therapeutic Intervention Scoring System 28-score; NEMS-score = Nine Equivalent of Nursing Manpower Use score.

Table 1
Demographics, ICU admission, D1 characteristics, and outcomes*.

Complete cases included, N (%)	1953 cases	Model I	Model II	Model III
	1953 (100%)	1867 (95.6%)	1809 (92.6%)	1831 (93.8%)
Baseline characteristics				
Male gender, N (%)	1211 (62.0)	1152 (61.7)	1120 (61.9)	1133 (61.9)
Age (years)	57.2 ± 16.8	57.6 ± 16.7	57.5 ± 16.6	57.5 ± 16.7
BMI (kg/m^2)	25.6 ± 5.4	25.6 ± 5.3	25.6 ± 5.3	25.6 ± 5.3
Charlson co-morbidity index	2.5 ± 2.7	2.5 ± 2.7	2.5 ± 2.7	2.5 ± 2.7
Previous hospitalization in past 6 months, N (%)	843 (43.2)	813 (43.5)	784 (43.3)	794 (43.4)
Living at home before ICU admission, N (%)	1891 (96.8)	1808 (96.8)	1754 (97.0)	1773 (96.8)
ADL at baseline, N (%)				
No limitations	1162 (59.5)	1099 (58.9)	1080 (59.7)	1089 (59.7)
Moderate limitations	625 (32.0)	609 (32.6)	576 (31.8)	587 (32.1)
Chair bound	96 (4.9)	94 (5.0)	91 (5.0)	92 (5.0)
Bedridden	70 (3.6)	65 (3.5)	62 (3.4)	63 (3.4)
UIb	0.62 ± 0.33 (a)	0.62 ± 0.33	0.63 ± 0.33	0.62 ± 0.33
VASb	65.6 ± 20.0 (b)	65.7 ± 19.9	65.8 ± 19.9	65.7 ± 19.9
ICU admission characteristics				
ICU admission during weekend, N (%)	564 (28.9)	535 (28.7)	512 (28.3)	522 (28.5)
ICU admission unplanned, N (%)	1430 (73.2)	1364 (73.1)	1318 (72.9)	1333 (72.8)
Hospital days prior ICU admission (days)	3.1 ± 14.0	2.9 ± 11.7	2.7 ± 9.8	2.7 ± 9.8
ICU-D1 characteristics				
APACHE II	16.9 ± 8.2 (c)	17.0 ± 8.2	16.9 ± 8.1	16.9 ± 8.1
SOFA score	4.6 ± 3.8	4.6 ± 3.8	4.6 ± 3.7	4.6 ± 3.8
Need for mechanical ventilation, N (%)	606 (31.0)	572 (30.6)	557 (30.8)	564 (30.8)
Need for vasopressor therapy, N (%)	390 (20.0)	371 (19.9)	361 (20.0)	364 (19.9)
Need for RRT, N (%)	43 (2.2)	43 (2.3)	39 (2.2)	40 (2.2)
Need for tracheotomy, N (%)	35 (1.8)	35 (1.9)	34 (1.9)	35 (1.9)
Outcomes				
ICU-LOS (days)	6.5 ± 10.5	6.5 ± 10.3	6.5 ± 10.4	6.5 ± 10.3
ICU mortality, N (%)	168 (8.6)	160 (8.6)	151 (8.3)	152 (8.3)
Hospital-LOS (days)	29.3 ± 42.4	29.0 ± 40.7	28.7 ± 40.4	28.6 ± 40.3
Hospital mortality, (%)	285 (14.6)	275 (14.7)	259 (14.3)	262 (14.3)
UI1y*	0.46 ± 0.38 (d)	0.46 ± 0.38	0.47 ± 0.38	0.46 ± 0.38
1-year mortality, N (%)	515 (26.4)	504 (27.0)	477 (26.4)	483 (26.4)

Abbreviations:
D1 = first 24 h of ICU admission; ± = mean and standard deviation; ICU = intensive care unit; N = number; BMI = body mass index; ADL = activities of daily living; UIb = utility index at baseline; VASb = visual analogue scale at baseline; APACHE; II = Acute Physiology and Chronic Health Evaluation score; SOFA = sequential organ failure assessment; RRT = renal replacement therapy; LOS = length of stay; UI1y = utility index at 1 year after ICU discharge; * = based upon 1953 cases in database unless indicated otherwise; (a) = 28/1953 missing data (1.43%); (b) = 39/1953 missing data (2.00%); (c) = 5/1953 missing data (0.26%); (d) = 72/1953 missing data (3.7%), *UI1y for non-survivors = 0.

Table 3
All 32 possible D1-variables to predict UI1y.

Variable	Description
10 continuous variables	UIb, VASb, age, BMI, Charlson co-morbidity index, hospital days prior ICU admission, APACHE II, D1.SOFA, D1.TISS-28, D1.NEMS
16 binary variables (only 1 dummy possible for each binary variable in the D1-model: 0/1*)	Sub oncological, sub hematological, sub cirrhosis, sub elderly (≥80 years), gender, previous hospitalization in the past 6 months, admission during weekend, admission unplanned, D1.DNR, D1.MV, D1.VP, D1.RRT, D1.surgery, D1.medical imaging, D1.tracheotomy, D1.transfusion
6 categorical variables (>1 dummy for each categorical variable in the D1-model)	Living situation at baseline (reference = 1/at home with 2 dummies: 2/special care facility; 3/other); ADL (reference = 1/no limitations with 3 dummies: 2/moderate limitations, 3/chair bound, 4/bedridden); origin of hospital admission (reference = 1/home with 5 dummies: 2/emergency department, 3/other hospital, 4/psychiatric institution, 5/special care facility, 6/other); origin of ICU admission (reference = 1/emergency department with 8 dummies: 2/hospital ward, 3/high-care unit, 4/coronary care unit, 5/operation theatre, 6/catheterization room, 7/recovery room, 8/other hospital, 9/other); baseline work (reference = 1/student with 5 dummies: 2/at work, 3/unemployed, 4/housekeeping, 5/invalidity, 6/retired); main ICU diagnosis (reference = 1/medical with 3 dummies: 2/surgical, 3/burns, 4/trauma)

Abbreviations:
D1 = first 24 h of ICU admission; UI1y = utility index at 1 year after ICU discharge; UIb = utility index at baseline; VASb = visual analogue scale at baseline; BMI = body mass index; APACHE II = Acute Physiology and Chronic Health Evaluation score; D1. = describes variable at D1; SOFA = Sequential Organ Failure Assessment (SOFA) score; TISS-28 = Therapeutic Intervention Scoring System 28 score; NEMS-score = Nine Equivalent of Nursing Manpower Use score; sub = predefined subgroup of a specific patient population; DNR = do-not-resuscitate score; MV = mechanical ventilation; VP = vasopressors; RRT = renal replacement therapy; ADL = activities of daily living; ICU = intensive care unit; *0/1 = either the variable is present (1) or not (0).

D1-predictor (D1.NEMS) because of lack of significance (coefficient estimate 0.00006, standard error = 0.0018, p = 0.973) and finally, 16 selected D1-predictors were included in Model III. Multivariate regression analysis is shown in Table 5. Finally, D1-prediction of mean UI1y based upon Model III can be obtained by:

$$\begin{aligned}\text{Mean UI1y} = {} & 0.56 + 0.0009 * \text{VASb} + 0.3017 * \text{UIb} - 0.1190 \\ & * \text{sub oncological} - 0.1077 * \text{sub hematological} - 0.1035 \\ & * \text{sub elderly} - 0.0023 * \text{age} - 0.0931 * \text{ADL2} - 0.1794 \\ & * \text{ADL3} - 0.1186 * \text{ADL4} - 0.0067 * \text{Charlson} - 0.0047 \\ & * \text{APACHE II} + 0.1102 * \text{main ICU diagnosis2} + 0.0346 \\ & * \text{main ICU diagnosis3} - 0.0151 \\ & * \text{main ICU diagnosis4} - 0.0092 * \text{D1.SOFA} - 0.0728 \\ & * \text{D1.DNR} - 0.0530 * \text{D1.mechanical ventilation} - 0.0329 \\ & * \text{D1.vasopressors} - 0.0689 \\ & * \text{D1.medical imaging} - 0.1238 * \text{D1.tracheotomy}.\end{aligned}$$

Only UIb, VASb, and surgical or burn patients (versus medical patients) were positively associated with UI1y.

Explanation of variability in UI1y and cross-validated prediction error of Model III were comparable or even better than these of Model II (Table 4). By using cross-validation, the latter provides an honest reflection of the uncertainty for making new predictions using the corresponding model. The F-test revealed no significant better fit for the full Model II compared to the reduced Model III ($P = 0.432$).

4. Discussion

We fitted 3 different linear regression models to develop an easy to use and accurate prediction model for the mean QOL at 1 year after ICU discharge in general critically ill patients based upon data readily available at the first ICU day. Model I, which positively related UIb and UI1y could only explain 20% of the variability in UI1y. Both models II, which held all 32 possible D1-predictors, and III, with a reduced amount of the most important and powerful D1-predictors, explained 40% of variability in mean UI1y. As this latter D1-prediction model was less complex, had a better performance and fit, and could easily be implemented in an electronic patient data file, we preferred this "reduced" D1-prediction model for prediction of UI1y.

For centuries, humans have tried to predict the future. In medicine, the data rich environment of critical care has led the way in outcome prediction because of its usefulness in improving decision-making under uncertainty, especially when the stakes are so high. However, ICU risk predicting systems lack patient-centeredness and often fail to predict long-term mortality and long-term functional outcomes [38]. Even until recent, estimation of long-term QOL was considered too challenging to be reliably used in medical decision-making as QOL was thought to be too personal and too subjective [39].

A prediction model for long-term QOL based upon readily available data in an early stage of ICU admission could therefore help critical care physicians to identify those patients who will return to their baseline functionality, or those who will need a long revalidation. It could also help to inform patients and families in a reliable way, to triage patients for ICU admission, to guide in treatment decisions, and it could eventually help to transform future healthcare by making better prospects of recovery and better allocation of resources [40,41].

Still, prediction models have not gained much acceptance in clinical practice, mainly because of complex algorithms that hamper implementation in daily practice, and because of concerns of being wrong [24]. Our reduced D1-prediction model could explain 40% of variability of UI1y. This is acceptable but nevertheless, a higher accuracy would be

Table 4
Fitting of the 3 different D1-prediction models to predict UI1y.

Model	Description	Number of D1-variables included (N)	Number of complete cases included (of 1953 cases) (N) (%)*	R^2	Adjusted R^2	Root of cross-validated prediction error
I	Bivariate association between UIb-UI1y	1	1867 (95.6%)	0.2050	0.2050	NA
II	Full model	32	1809 (92.6%)	0.3980	0.3800	0.3068
III	Reduced model	16	1831 (93.8%)	0.3875	0.3807	0.3026

Abbreviations:
D1 = first 24 h of ICU admission; UI1y = utility index at 1 year after ICU discharge; R^2 = proportion of explained variance; adjusted R^2 = proportion of explained variance, taking into account the number of variables; N = number; UIb = utility index at baseline; NA = not applicable; * = cases with partial information (=missing of at least 1 variable in at least 1 case) were excluded for the development of the respective model.

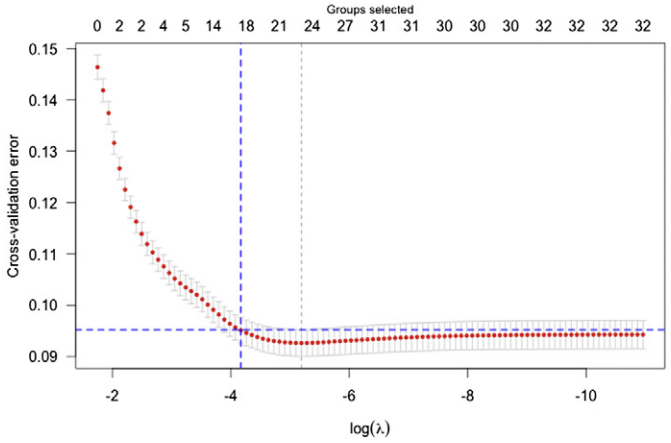

Fig. 1. Grouped lasso technique to select D1-variables in Model III. Description: X-axis (above): all 32 D1-variables; X-axis (under): logarithm of penalty parameter λ. Y-axis: cross-validated prediction error (red dots) with error-bar (± standard error of the cross-validated prediction error). Cross-section of X-axes and Y-axis (light grey dotted line) revealed that the lowest value of the cross-validated prediction error was reached when 24 of all 32 D1-variables were selected in the prediction model. Subsequently, the one-standard-error rule was applied in order to select the λ-value where the corresponding cross-validated prediction error is within 1 standard error of the optimal (lowest) cross-validated prediction error. This was done to avoid too many D1-variables in the prediction model. Cross-section of X-axes and Y-axis (blue dotted line) after applying of the one-standard-error rule revealed that the optimal number of D1-variables in the prediction model was 17 out of all 32 D1-variables. Abbreviations D1 = first 24 h of ICU admission; log = logarithm; λ = penalty parameter.

better. Still, model III, as it is based upon readily available data within the first 24 h of ICU admission, and as it is easy to use within an electronic patient data file, could be considered as a helpful tool for a more systematic approach of integration of all D1-variables of the individual critically ill patient.

Although it is not defined to what level model predictions could be helpful and beyond the scope of our study, it certainly might facilitate decisions, which otherwise should have been taken based upon subjective evaluation alone [42]. The D1-prediction model will never replace clinician's judgments, but rather inform and reinforce these judgments, as recommendations for further care highly correlate with physician's estimations of a good long-term QOL [7,8,16,43]. Further research should focus on refining of this QOL prediction model.

Within our QOL prediction model, we were able to identify 16 D1-variables that had great impact on long-term outcome. Baseline QOL and functionality appeared to be strong positive predictors for long-term QOL. This is in accordance with the findings of Veerbeeck [24] and Heyland [16] who respectively demonstrated that a good baseline neurological status in stroke patients and good baseline functionality in elderly patients had a great impact on long-term ADL and functionality.

We also found that the predicted UI1y for surgical patients was significantly higher versus medical patients ($P < 0.001$). This was in contrast to burn patient ($P = 0.484$) or trauma (0.618) patients, for whom we could not demonstrate any significant difference in UI1y versus medical patients.

The study has several strengths. First, to the best of our knowledge, this is the first simple D1-prediction model which has an acceptable accuracy and which focus on long-term QOL in general critically ill patients. Second, it is original and deals with a very important issue nowadays in critical care. It might have several consequences on resources allocation and anticipates a clear discussion with patients and family members regarding prognosis and preparation for outcomes. Third, the prediction model was developed upon prospectively accurately collected data. Fourth, there was no selection bias in the database, because of the consecutive and prospective enrollment of patients and the high long-term follow-up rate for mortality and QOL. Fifth, the D1-model is not too complex and can aid in decision-making early in ICU stay. Sixth, the database held data concerning baseline condition and QOL, which is of importance in outcome studies and in developing objective prediction models, but still is exceptionally assessed [6]. The high impact of UIb on UI1y illustrates the requirement of knowledge of baseline condition to make any prediction on outcome at long-term. Seventh, we used a grouped lasso technique, which is an objective selection and shrinkage estimation method for linear regression models [34,35]. We preferred this technique above the widely used stepwise selection method – where prediction accuracy only improves when covariates have a strong relationship with the outcome - to select the optimal

Table 5
Model III: multivariate regression analysis.

D1 variables	Estimate	SE	*t*-Value	*P*-Value	95% CI
VASb	0.0009	0.0004	1.956	0.051	−0.000 to 0.002
UIb	0.3017	0.0325	9.277	<0.001	0.238 to 0.365
Sub oncological	−0.1190	0.0232	−5.120	<0.001	−0.165 to −0.073
Sub hematological	−0.1077	0.0402	−2.679	0.007	−0.187 to −0.029
Sub elderly (≥80 yrs)	−0.1035	0.0318	−3.259	0.001	−0.166 to −0.041
Age	−0.0023	0.0005	−4.330	<0.001	−0.003 to −0.001
ADL, reference = no limitations					
Moderate limitations	−0.0931	0.0198	−4.712	<0.001	−0.132 to −0.054
Chair bound	−0.1794	0.0384	−4.675	<0.001	−0.255 to −0.104
Bedridden	−0.1186	0.0456	−2.601	0.009	−0.021 to −0.029
Charlson co-morbidity index	−0.0067	0.0034	−1.969	0.049	−0.013 to −0.000
APACHE II	−0.0047	0.0014	−3.289	0.001	−0.007 to −0.002
Main ICU diagnosis, reference = medical					
Surgical	0.1102	0.0172	6.423	<0.001	0.076 to 0.144
Burns	0.0346	0.0495	0.700	0.484	−0.063 to 0.132
Trauma	−0.0151	0.0302	−0.499	0.618	−0.074 to 0.044
D1.SOFA	−0.0092	0.0035	−2.656	0.008	−0.016 to −0.002
D1.DNR	−0.0728	0.0480	−1.517	0.129	−0.167 to 0.021
D1.mechanical ventilation	−0.0530	0.0192	−2.761	0.006	−0.091 to −0.015
D1.vasopressors	−0.0329	0.0258	−1.273	0.203	−0.084 to 0.018
D1.medical imaging	−0.0689	0.0191	−3.603	<0.001	−0.106 to −0.031
D1.tracheotomy	−0.1238	0.0525	−2.360	0.018	−0.227 to −0.021

Abbreviations:
D1 = first 24 h of ICU admission; SE = standard error; CI = confidence interval; VASb = visual analogue scale at baseline; UIb = utility index at baseline; sub = predefined subgroup of a specific patient population; ADL = activities of daily living; APACHE II = Acute Physiology and Chronic Health Evaluation score; ICU = intensive care unit; D1. = describes variable at D1; SOFA = Sequential Organ Failure Assessment (SOFA) score; DNR = do-not-resuscitate score.

number and most important predictors for UI1y in the D1 linear regression model in order to simplify the model, and to cope with the categorical variables.

Our study also has some limitations. First, the D1-model was developed based upon a single-center dataset. Second, the model was not externally validated, nor was it validated into clinical practice. Implementation studies are needed to investigate the added value of our model in decision-making compared to clinical expertise alone [24]. Third, the model could only explain 40% of variability of UI1y. This could be considered as not accurately enough. However, at this moment, it should be seen as a unique help in informing patients and families, in decision-making and in advanced care planning.

5. Conclusion

We developed an easy to use prediction model for the mean QOL at 1 year after ICU discharge in general critically ill patients based upon data readily available at the first ICU day. Although only 40% of the variability in long-term QOL could be explained, this prediction model can be a helpful tool in decision-making, in good and informative communication towards patients and families, in resource allocation, and in advanced care planning. Further research should now focus on prospective and multicenter validation and refining of this QOL prediction model.

Conflict of interest

None.

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