

A machine learning approach to intensive care discharge.

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Abstract

Objective

The primary objective is to work towards a clinical decision support tool that can improve discharge practice on the intensive care unit.

Design

We used two datasets of routinely collected patient data to test and improve upon a set of previously proposed discharge criteria.

Setting

Bristol Royal Infirmary general intensive care unit (GICU).

Patients

Two cohorts derived from historical datasets: 1933 intensive care patients from GICU in Bristol, and 10658 from MIMIC-III (a publicly available intensive care dataset).

Interventions

None.

Results

In both cohorts few successfully discharged patients met the of all the discharge criteria. Both a random forest and a logistic classifier, trained on MIMIC and cross validated on GICU, demonstrated improved performance over the original criteria and generalised well between the cohorts. The classifiers showed good agreement on which features were most predictive of readiness-for-discharge, and these were generally consistent with clinical experience. By weighting the NLD criteria according to feature importance from the logistic model we showed improved performance over the original NLD criteria, while retaining good interpretability.

Conclusions

Our findings constitute a proof of concept for a decision support tool to run alongside a clinical information system, and streamline the process of discharge from the ICU.

Introduction

Demand for intensive care unit (ICU) beds is rising at a time when resource is constrained[1]. In order to optimise the allocation of this resource, patients should be discharged from the ICU as soon as they no longer require the specialist input provided there. The reduced ICU capacity caused by discharge delay can result in the delayed admission of emergency patients requiring ICU care[2,3]. Furthermore, patients remaining in the ICU after they are medically fit to leave experience detrimental effects on physical rehabilitation and psychosocial well-being[4].

The identification of individuals that are ready to leave ICU is a key component of patient flow through the hospital. At present this identification is a manual process, relying on physicians reviewing patients on a ward round at a standard point in time. There is a lack of formal guidance to inform discharge readiness and as such the process is sensitive to both the decision making heuristics of individual clinicians and structural factors within the hospital[5]. These issues may introduce undesirable variability in the timeliness of the discharge decision. A number of studies have looked to address this problem by attempting to standardise the discharge process[6]. One such study by Knight[7] proposed a set of physiological criteria to enable nurses to identify patients that are fit for discharge from a high dependency unit (HDU), thereby expediting the discharge process.

Increasingly ICUs are using clinical information systems (CIS) to collect, store and display physiological data. The availability of such routinely collected patient data presents the opportunity to apply methods from data science, with the potential to transform healthcare in a number of ways[8,9]. Two particular avenues for development are the automation of simple tasks[10] and the implementation of decision support systems[11], both of which would reduce the cognitive load of clinicians and free up scarce resource for tasks that require human expertise. We believe that the ICU discharge process is one area of healthcare practice that could be significantly improved by such data driven approaches.

In this study we investigated the possibility of using routinely collected data to identify patients that are ready for discharge. We studied two historical cohorts. One cohort consisted of patients treated on the general intensive care unit at the Bristol Royal Infirmary, while the second consisted of patients selected from the MIMIC-III database[12] (see Materials and Methods for details). Since there is no generally accepted definition of readiness-for-discharge, we adopted the criteria published by Knight[7] as a baseline for automation. Given the rationale behind these criteria they represent a general and highly conservative set of constraints on physiology that characterise a patient as suitable for care on an acute ward (level 1 care). We initially posed the question: how many patients met the proposed criteria at the time they were declared ready for discharge? We then attempted to improve upon the performance of the original criteria by using machine learning techniques to identify patients that were ready for discharge. This work represents the first steps towards a decision support tool that will run in real time alongside our CIS and help clinicians identify dischargeable patients.

Methods

Discharge criteria

The nurse-led discharge (NLD) criteria proposed by Knight[7] consist of a set of constraints on various routinely collected vital signs and laboratory results. If a patient meets all the constraints for a period of at least four hours, Knight states that they may be safely discharged by a nurse. In order to test the NLD criteria on historical patient data we codified the constraints (see SI, section C) into 15 binary tests, which are defined in table 1.

TestID	Test name	Variable	Test conditions
R0	Respiratory: Airway	airway	airway patent
R1	Respiratory: FiO2	fio2	fio2 \leq 0.6
R2	Respiratory: Blood oxygen	spo2	spo2 \geq 95 (%)
R3	Respiratory: bicarbonate	hco3	hco3 \geq 19 (mmol/L)
R4	Respiratory: rate	resp (rate)	10 \leq resp \leq 20 (bpm)
C0	Cardiovascular: blood pressure	bp (systolic)	bp \geq 100 mmHg
C1	Cardiovascular: heart rate	hr (rate)	60 \leq hr \leq 100 (bpm)
P	Pain	pain	0 \leq pain \leq 1
CNS	Central nervous system	gcs	gcs \geq 14
T	Temperature	temp	36 \leq temp \leq 37.5 (C)
B0	Bloods: haemoglobin	haemoglobin	haemoglobin \geq 9 g/dL
B1	Bloods: potassium	k	3.5 \leq k \leq 6 (mmol/L)
B2	Bloods: sodium	na	130 \leq na \leq 150 (mmol/L)
B3	Bloods: creatinine	creatinine	59 \leq creatinine \leq 104 (umol/L)
B4	Bloods: urea	bun (urea)	2.5 \leq bun \leq 7.8 (mmol/L)

Table 1: Codified version of the discharge criteria for application to electronic health record data. Here the fifteen criteria have been grouped into intuitive subsets and each assigned a test ID ('R0' to 'B4'). If all 15 criteria are met for a period of at least four hours the patient can be safely discharged.

Cohort selection

Subjects for this study were selected from two distinct historical data sources to form two patient cohorts. The inclusion criteria are detailed in SI section A.2. The first data source consists of the routinely collected data from 1933 patients treated on the general intensive care unit at the Bristol Royal Infirmary between 01/02/2015 and 01/02/2017. We refer to the cohort selected from this dataset as GICU. The second data source is derived from the MIMIC-III database[12], from which 10658 patients were selected to form the cohort referred to as MIMIC.

The use of two cohorts was motivated by two concerns. Firstly, the volume of data was significantly increased by the inclusion of the MIMIC cohort, increasing the volume of data available for training classifier algorithms. Secondly, the use of two cohorts allowed us to study the generalisation of our results between different patient populations under different healthcare systems.

Readiness-for-discharge

The key to testing and improving on discharge criteria was to be able to identify, from the historical data, patients that were ready-for-discharge (RFD) and not-ready-for-discharge (NRFD). These two subsets of patients, RFD and NRFD, define the positive and negative classes respectively. The datasets contain a callout for each patient, which marks the time at which a patient was declared clinically ready to leave the intensive care unit. For the positive class we selected patients at their

time of callout who went on to have a positive outcome on leaving the unit. Conversely, patients who were declared clinically ready to leave the unit, but subsequently had a negative outcome, were included in the negative class. A positive outcome was defined as the patient leaving the hospital alive without readmission to ICU. A negative outcome was defined as either readmission to ICU during the same hospital admission, or in-hospital mortality after discharge from ICU. Given the low rates of negative outcome following callout in both MIMIC and GICU (see table 2), we generated further instances of the negative class, in order to balance the class sizes. To do this we sampled patients at between three and eight days prior to their callout, under the assumption that patients were not-ready-for-discharge at this point in time, regardless of their eventual outcome state (positive or negative). Full details of this procedure are given in appendix A.2.

	patients	mortality	readmission	negative outcomes	mean(LOS)
MIMIC	10658	0.048	0.063	0.095	3.02
GICU	1933	0.038	0.031	0.062	4.92

Table 2: Summary of the two study cohorts: MIMIC and GICU. Negative outcome after discharge is defined as either readmission to ICU or patient mortality during the same hospital admission (not mutually exclusive). Length of stay(LOS) given in days.

Feature extraction

We used the same feature set to evaluate the NLD criteria and to train machine learning classifiers. We constructed either one or two features corresponding to each of the NLD criteria, depending on the criteria in question and on data availability. For example, the features ‘resp min’ and ‘resp max’ were used to test the criterion R4, whereas the single feature ‘bun’ was used to test B4. Where possible the feature values were calculated from a four hour sample window, as specified by the original NLD criteria. In the cases where no data was available during the four hour window, an extended 36 hour window was used. This extended window was mainly relevant for infrequently measured laboratory test results (see table 1 in appendix B). Full details and justification of the feature extraction procedure are provided in appendix B, and the resulting 18 features are listed in the first column of table 3.

The results presented in the main text represent a complete case analysis, with all instances containing missing data entries removed. This removal reduced the sizes of the MIMIC and GICU feature matrices to 5033 and 1858 instances respectively (see appendix B). The validity of the complete case analysis was investigated with a sensitivity analysis that used k-nearest neighbour imputation[13] to fill missing data (see appendix F). When training and testing the machine learning classifiers, features were standardised by subtracting the column mean and dividing by the standard deviation. The feature matrices are visualised in figure 1 using the t-SNE algorithm[14].

Analysis of NLD criteria

Knight originally specified that all 15 criteria must be met in order to allow safe discharge by a nurse[7]. Following this specification we evaluated the criteria for both MIMIC and GICU, determining which instances were classified as RFD and NRFD, and comparing these results to ground-truth. We then further investigated the performance of the NLD criteria as a classification system, by relaxing the constraint that all 15 tests must be passed in order to make an RFD classification. Instead we used the NLD criteria to produce probability estimates of being RFD, by summing the number of tests passed and dividing by 15 to produce a normalised output between 0

and 1. In this formulation each of the 15 criteria contribute equally to the RFD probability. Using the probability outputs it was possible to evaluate the performance of the NLD criteria in the same way as the machine learning classifiers described below.

Machine learning classifiers

To improve upon the performance of the NLD criteria, we trained and tested two machine learning classifiers: a random forest (RF)[15], and a logistic classifier (LC)[16]. These two algorithms were chosen for their simplicity in implementation and ease of interpretation in their predictive output. Both classifiers were optimised over a range of hyper-parameter values using cross-validation (see appendix E). To do so, we produced an ensemble of 100 randomised train:test data splits for both MIMIC and GICU (70 : 30 and 67 : 33 respectively). We then optimised each classifier using cross-validation, with the larger subset of MIMIC as training data and the larger subset of GICU as validation data. Having obtained the optimised classifier for the given data split, the classifier was then refitted to the full training set (MIMIC + GICU). The remaining data (i.e. the smaller subsets of MIMIC and GICU) were then used to test the performance of the optimised classifier. This optimisation/testing procedure was repeated for all 100 data splits in the ensemble to produce estimates of the mean and standard deviation of the classifier performance. The methodology described was intended to produce classifiers that generalised well from MIMIC to GICU, and by extension to other patient populations.

Both the RF and LR classifiers contained mechanisms to promote model sparsity. For the RF this mechanism was a restriction in the hyper-parameters *tree_depth* and *max_features* (appendix E), while for the LC this was ‘l1’-regularisation. In both cases the intention was to learn which features were most and least predictive of readiness-for-discharge. For the RF, feature importance was given by the total reduction in Gini impurity provided by each feature. Intuitively this metric captures the reduction in uncertainty brought about a given feature, therefore giving a measure of how important that feature is, on average, in classification decisions. For the LC, the importance was given by the absolute value of the coefficient for each feature in the trained model, capturing the effect of a small change in a given feature value on the prediction probability with all other feature values held constant.

Classifier performance was evaluated across a range of prediction thresholds by producing receiver-operator-characteristic (ROC) and precision-recall (PRC) curves[17]. Given the need to minimise the false positive rate, while retaining high recall, we chose to use the partial area under the ROC curve (pAUC) as the overall performance metric[18]. The pAUC was evaluated up to a false positive rate of 0.3, using linear interpolation to approximate the true positive rate at this point on the ROC curve. Performance was evaluated in this way for the RF and LR classifiers, and for the original NLD criteria.

Results.

The original specification of the NLD criteria proved to be highly conservative as expected, producing low false positive and true positive rates for both cohorts (see confusion matrices in table 1 of appendix A). The true positive rates for MIMIC and GICU were 0.4% and 6.4% respectively. As such the NLD criteria were sufficiently insensitive as to call into question their usefulness in their current form.

By relaxing the constraint that all 15 tests must be passed, the NLD criteria were able to successfully identify more patients as RFD. This is illustrated in figure 2 for a single train:test data split, alongside the performance of the corresponding optimal random forest classifier. On this data split the NLD criteria obtained precisions of ~ 0.8 at a recall of 0.4 for both cohorts. The performance gain obtained by using a random forest was significant, with precisions of >0.8 at a recall of 0.7 for both cohorts.

Feature	Importance (RF)	Importance (LC)	Rank (RF)	Rank (LC)
gcs_min	0.352 (± 0.054)	1.127 (± 0.050)	0	0
airway	0.302 (± 0.048)	0.870 (± 0.038)	1	1
bun	0.034 (± 0.007)	0.437 (± 0.047)	4	2
fio2	0.048 (± 0.007)	0.317 (± 0.024)	2	3
temp_max	0.024 (± 0.008)	0.263 (± 0.126)	7	4
haemoglobin	0.029 (± 0.006)	0.256 (± 0.029)	5	5
resp_max	0.017 (± 0.004)	0.236 (± 0.038)	10	6
resp_min	0.045 (± 0.015)	0.233 (± 0.053)	3	7
temp_min	0.014 (± 0.004)	0.213 (± 0.126)	12	8
hr_min	0.022 (± 0.005)	0.181 (± 0.044)	8	9
hr_max	0.025 (± 0.005)	0.168 (± 0.044)	6	10
spo2_min	0.012 (± 0.004)	0.158 (± 0.027)	14	11
na	0.009 (± 0.003)	0.110 (± 0.032)	16	12
bp_min	0.012 (± 0.004)	0.059 (± 0.027)	13	13
hco3	0.010 (± 0.004)	0.051 (± 0.028)	15	14
k	0.008 (± 0.003)	0.041 (± 0.022)	17	15
creatinine	0.021 (± 0.005)	0.031 (± 0.027)	9	16
pain	0.016 (± 0.008)	0.021 (± 0.018)	11	17

Table 3: Feature importances given by the random forest (RF) and logistic classifier (LC), evaluated over 100 train:test data splits. Importance values are given as: mean(\pm standard deviation). Features are ranked according to mean importance value, and the table is ordered according to the ranking given by the logistic classifier.

Broadly the two classifiers agreed as to which features were most predictive of readiness-for-discharge (see table 3). Eight of the logistic classifier’s top ten important features were also ranked in the top ten by the random forest, when averaged over the ensemble of 100 data splits. The

Spearman's rank correlation coefficient between the feature rankings was 0.800 ($p=0.00006$), and both classifiers ranked *gcs_min* and *airway* as the two most important features by a significant margin. The inclusion of instances with missing data did little to change these feature rankings (appendix F).

Figure 3 summarises classifier performance, quantified using the partial area under the ROC curve (pAUC), over the ensemble of data splits. On average the original NLD criteria performed slightly better for GICU than MIMIC. The two machine learning classifiers performed similarly well, producing large gains in pAUC over the NLD for both cohorts, and higher pAUC values for MIMIC than GICU. There was little to distinguish between the random forest and logistic classifiers based on pAUC. In the sensitivity analysis (see figure 2 and table 1 in appendix F) both machine learning classifiers still performed better than the NLD criteria, but all classifiers showed a performance drop for MIMIC and one classifier tended to perform better for each cohort (the random forest and logistic classifiers for MIMIC and GICU respectively).

Given the similarity in classifier performances we chose to use the average feature importances of the simpler model – the logistic classifier - to weight the NLD criteria. The weighted version of the NLD criteria (referred to as NLD_{opt}) performed better than the original criteria when tested on both MIMIC and GICU. On MIMIC the performance gain was larger, with pAUC scores approaching those of the machine learning classifiers. Qualitatively the same effect was observed under the sensitivity analysis.

Examples in practice

To illustrate the results in a more human-interpretable fashion we have selected five informative examples from the GICU cohort. Table 4 summarises the performance of the different classification systems for these five examples, which are labelled as true or false positive/negative (TP,FP,TN,FN) according to how they would be classified under the original nurse-led discharge criteria. One patient (ID 4065) is included twice: once at 72 hours before callout, and again at the time of callout. All four classification systems show an increased RFD probability for this patient between the two time points, as would be expected. Patient 868 is a false negative under the original criteria - despite failing two criteria (C0 and T) their callout was successful. The three alternative classification systems (NLD_{opt}, RF and LC) correctly assign a high RFD probability for this patient, therefore improving upon the original criteria.

For these select examples the logistic classifier is the only system to assign lower RFD probabilities to the two false positive instances (1034 and 10783) than to the true positive instance (4065). Despite this correct ordering by the logistic classifier its RFD probabilities for the false positives are relatively high. Given the conservative nature of the NLD criteria it is expected that correct classification of the false positive instances is a hard problem.

Patient	NLD	NLD _{opt}	RF	LC	NLD fails	Notes
1034 (FP)	0.010 (1.0)	0.010 (1.0)	0.071 (0.784)	0.096 (0.765)	-	Patient admitted to ICU post surgery (primary lung tumour). Discharge to ward. Readmitted within 24 hours with bacterial pneumonia.
10783 (FP)	0.010 (1.0)	0.010 (1.0)	0.035 (0.819)	0.163 (0.716)	-	Patient admitted to ICU with secondary hepatic tumour. Appears to be RFD at 96 hours prior to callout.
4065 (TN)	1.0 (0.467)	0.464 (0.702)	0.368 (0.494)	0.395 (0.450)	R2, R4, C0, P, B1, B3, B4	Patient admitted to ICU with intracranial abscess. Not ready for discharge at 72 hours prior to callout.
4065 (TP)	0.010 (1.0)	0.010 (1.0)	0.077 (0.780)	0.047 (0.812)	-	Same patient as above. RFD at time of callout.
868 (FN)	0.113 (0.867)	0.046 (0.939)	0.080 (0.777)	0.054 (0.806)	C0, T	Patient admitted with malignant large bowel tumour. Appears NRFD at time of callout. Positive outcome.

Table 4: Example patients and their scores given by the four classification systems: the original nurse led discharge criteria (NLD); the weighted criteria(NLD_{opt}); the random forest (RF); and the logistic classifier (LC). The reporting score given is the false positive rate at the point where the patient falls on the ROC curve, such that a lower score indicates a higher probability of being RFD according to the given classifier (explicitly, the reporting metric gives the number of false positives that must be accepted before this patient can be classified RFD). These scores can be compared across classifiers. The raw (non-calibrated) classifier scores are given in brackets and cannot be compared across classifiers. The results FP,TN,TP, and FN indicated in the first column correspond to the outcomes of the original NLD criteria. The column ‘NLD fails’ specifies, where relevant, which of the NLD criteria were not met (criteria IDs correspond to those in table 1).

Discussion

Identifying which patients are suitable for ICU discharge is complex[1]. Delayed and out of hours discharges are associated with an increased mortality[19], and patients in ICU who could be managed on the ward put an increasing strain on resources. The determination of the ready-for-discharge status is influenced by many unmeasured factors such as ICU census[20] and this leads to unwarranted variation in clinical decision making. The decision to declare someone fit for discharge is based on the judgement of individual clinicians and is likely to be given a lower priority than decisions around treatment options for patients that are more unwell in the ICU.

In this study we have used routinely collected data to test a set of discharge criteria[7] against two machine learning classifiers. The discharge criteria were found to be highly conservative, with very few successfully discharged patients meeting all the required criteria. This low sensitivity was expected since the original criteria were designed to be implemented independently of usual ward rounds, and false positives in this scenario could have serious consequences. A random forest and a logistic classifier both performed better than the clinically derived discharge criteria when trained on the same feature set. The two classifiers broadly agreed on which features were most predictive of readiness-for-discharge. Weighting the original discharge criteria with the features importances of the logistic classifier improved their classification performance.

An important novel aspect of this work is the use of MIMIC-III to increase the volume of training data available locally. Such applications of machine learning techniques to datasets that span institutions and healthcare settings will be of increasing value as more intensive care datasets become available for research[21]. Our results demonstrate the feasibility of using combined datasets in this way to derive clinical insight, and could be developed by the application of transfer learning approaches[22] to characterise systematic differences between data distributions.

The features identified as important by the classifiers were clinically meaningful. Clinicians will recognise that coma score, respiratory function and renal function are strongly related to successful ICU discharge. It is perhaps surprising that cardiovascular parameters were not ranked higher. We propose two possible mechanisms to account for this apparent discrepancy. Firstly, it may be a consequence of patient heterogeneity on the general intensive care unit[23]. For example, cardiovascular parameters may be highly predictive for cardiac patients yet much of this predictive power is lost in our attempt to fit a general model for the whole ICU population. Secondly, it may be due to our simplistic choice of features, which use the absolute values of physiological parameters. For some parameters we suggest that other features such as the trend, variance, or change since time of admission may be more predictive. For example, improvement in blood pressure may be more informative than absolute blood pressure.

Our feature set was chosen to be directly analogous with those used by Knight's criteria, to allow a direct comparison in performance. This feature set is somewhat restrictive, having been originally designed to be manually recorded by nurses using paper charts. The rich wealth of data held in electronic charting systems could be better exploited by including more physiological parameters, and engineering more predictive features. In particular our modelling did not make use of demographic information, diagnoses, comorbidities or interventions. The latter is of particular importance since many of patient's physiological parameters are controlled by clinical intervention during their stay in ICU. For example, a patient on vasopressors may have close to normal blood pressure despite suffering from severe cardiovascular complications. Therefore, conditioning features on medical interventions represents one avenue to significantly boost performance. Methods to account for patient heterogeneity and individual disease trajectories would also be worth investigating[23,24]. Although the inclusion of entries with missing data did not qualitatively alter the results of our complete case analysis, the development of a robust imputation strategy

would improve performance by making best use of the available training data and exploiting the value in missingness[25].

The machine learning approach produced small absolute performance gains over the original discharge criteria. However, the aggregate effect of such small improvements could be beneficial to many[26]. Therefore we suggest that a future decision support tool embedded within a CIS should use machine learning techniques to alert clinicians when patients appear fit for discharge. The increasing worldwide adoption of information systems in intensive care would make such a system widely applicable in years to come[27]. We have shown in previous work that subtle changes to the presentation of information can have significant impact on clinical decision making[28]. Therefore we anticipate such a tool has the potential to significantly streamline the discharge process. Two issues would need to be addressed prior to implementation on the ICU. The first is the human-interpretability of the classifier output. Depending on the machine learning approach a number of solutions exist[29], including the approximation of random forests with simple decision trees[30], that would allow clinicians to engage with the reasons behind a given classification. The second is the ambiguity behind the ground-truth used to train the classifiers. For example, some patients in the datasets used did not have a recorded callout status and some patients may have been ready for discharge prior to callout. A live implementation with a human-in-the-loop[31] could use clinician input to update ground-truth in such situations and improve learning.

Conclusion

We have shown that it is possible to apply machine learning techniques to routinely collected ICU data in order to solve a significant clinical and operational problem. This approach offers promise in a number of areas. We plan to focus on the development and deployment of a decision support tool in order to inform clinicians of patients that could potentially be discharged from ICU, in order to streamline the process and reduce unnecessary ICU stay. As more patient data becomes available in the wider hospital setting, there is extensive scope to use these methods to solve the problem of poor patient flow through hospitals.

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