An Explainability Study Associated with Fluid Creep Administration During the First 24 Hours of ICU Admission

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Abstract

Intravenous fluid therapy is one of the most common interventions for hospitalised patients admitted to intensive care. In particular, patients may be subject to a progressive and dangerous accumulation of fluids. In this context, we can define Fluid Creep (FC) as those fluids used to dilute drugs and nutritions and to maintain catheter patency. This single-center, retrospective study was carried out on the MargheritaTre database and included 4786 patients with an average of 1606 ml (1 quartile 849-3 quartile 2000) of FC in the first 24 hours of intensive care unit admission. The objective of this analysis is to identify variables significantly associated with FC, initially by means of a linear model and subsequently by means of a classification model aimed at identifying patients at risk of receiving high FC using explainable artificial intelligence (AI) techniques. After comparing the performance of seven machine learning models, logistic regression was found to be the model with the best accuracy on the test set of 0.76. Therefore, the SHAP (SHapley Additive exPlanations) algorithm was applied to conduct an explainable AI analysis, with the aim of interpreting the behaviour of the model and determining the most relevant variables in classifying the risk of high FC.

1. Introduction

Fluid accumulation in critically ill patients tends to progress over time. As the acute illness advances, the fluid needs of patients fluctuate, increasing their susceptibility to fluid overload at different stages of acute illness [1]. The phenomenon known as Fluid Creep (FC) refers to the hidden administration of fluids used as a carrier for intravenous, oral or enteral drug infusion. Recently, this aspect has attracted increasing interest, as has attention due to the side effects associated with intravenous fluid therapy.[2] In this study, the term FC is used to define the amount of fluid used both for drug dilution, nutritions and to ensure catheter patency. This phenomenon refers to the administration of fluids that often occurs secondarily, but that can have a significant impact on the management of treatment and its side effects. This study builds on and further expands a preliminary study [3] that investigated the effects and impacts of FC on patients admitted to the Intensive Care Unit (ICU), focusing on the seventh day post admission. Differently than in [3], in this study we focus on which variables are most signficant to FC administration in the first 24 hours, a crucial interval in terms of clinical outcome of patients admitted to the ICU. Moreover, thanks to the Explainable AI study, it was possible to investigate which variables are most relevant for classifying patients at risk of receiving high FC.

2. Materials and methods

This monocentric study was performed on data from an Italian hospital from the MargheritaTre (M3) database. The M3 project was approved by the Ethics Committee of the Coordinating Centre, the Independent Ethics Committee of Area Vasta Emilia Centro and by each local Ethics Committee of the hospitals using the MargheritaTre software.

2.1. Cohort and variables selection

The inclusion criteria for the patient population are based on the availability of information on the reason for admission, the presence of comorbidities and the type of surgery received. Patients who were still hospitalised in the ICU after July 2023 were excluded from the study. Anthropometric data were collected for each patient, including weight and height, as well as the degree of hypoxia. Subsequently, the volume of FC administered was quantified, including both fluids from drug therapy and those from nutrition. Specifically, the following routes were considered for drug administration: intravenous (IV) bolus, IV elastomer and continuous infusion. For nutrition, on the other hand, central, peripheral and auxiliary peripheral administration were included. Finally, net fluid intake in the first 24 hours of ICU admission was calculated. In addition, data were collected for the assessment of acute kidney injury (AKI), using the Kidney Disease Improving Global Outcomes (KDIGO) score, in view of the established association between fluid management and renal function. Finally, were included also variables for the calculation of the Simplified Acute Physiology Score (SAPS II) i.e sodium, potassium, heart rate, and mean arterial pressure. For each of them was selected the most clinically significant measurement recorded within the first 24 hours in the ICU . Comorbidities and reasons for admission were recorded at the time of admission. For other parameters, such as weight, height, and the PaO2/FiO2 ratio, the first available value within the first 6 hours after admission was considered. The AKI score, according to the KDIGO definition, was calculated using creatinine levels, urine output, and the initiation or discontinuation of renal replacement therapy within the first 24 hours. For the SAPS II score, the included variables were sodium, potassium, heart rate, and mean arterial pressure, selecting the most critical value within the first 24 hours in the ICU.

2.2. Statisitical analysis

LM was used to identify clinically relevant variables associated with FC evaluating two differents cases: the first one conisiders only a small subset of variables that are clinically related to the FC then a second model was developed through recursive feature selection form the entire dataset to determine the most significant predictors of the target outcome.

2.3. Classification and explainable AI analysis

Patients were classified based on their risk of FC during the first 24 hours, as defined using a cut-off value equal to 2000 ml determined on the analized distribution of FC as shown in Figure 1, The threshold was chosen corresponding to the third quartile because target shows a clear change at that point1.

After identifying the threshold, the target variable was transformed into a binary, assigning the value 0 to all patients receiving less than 2 L of FC and the value 1 to all others. For the construction of the classification model, all variables of the dataset were considered, i.e. all previously selected parameters, reasons for admission and comorbidities, followed by a selection of the most relevant variables. For feature selection, numerical features were selected using the SelectKBest method with the ANOVA F-Score test, which identifies the most relevant features based on their relationship with the target variable. For categorical characteristics, the Chi-square independence test was applied to select characteristics that were significantly associated with the target variable. The selected numerical and categorical features were then combined into a final set for model training. In order to reduce the risk of multicollinearity, the correlation matrix was calculated. When the correlation between two variables exceeded 0.58, one of them was removed—namely, the one least correlated with the target. Given the impact of the imbalance in the data (with 25 per cent of cases at high risk), the SMOTE algorithm was used to balance the dataset. To evaluate performance, a five-fold cross-validation was adopted, combined with a grid search for hyperparameter optimization. Seven classification algorithms were tested: K-Nearest Neighbors (KNN), Decision Tree Classifier (DTC),Quadratic Discriminant Analysis (QDA), Logistic Regression (LR), Linear Discriminant Analysis (LDA) , AdaBoost (AB) and Random Forest (RFC). The main objective was to maximize the average classification accuracy on the five subsets by selecting the best hyperparameters.

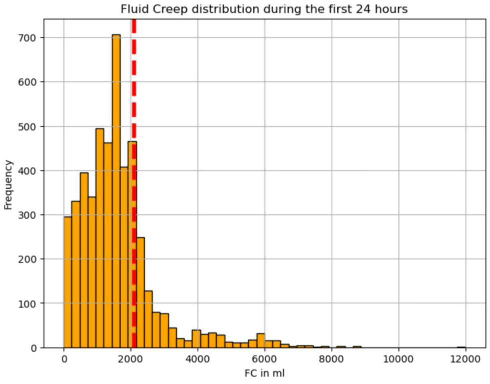

Figure 1: FC distribution during the for 24 hours for the final population(the red line is the threshold for the classification model at 2000 ml).

3. Results

3.1. Population description

The initial population of this study, as described in the previous study[3] consisted of 7.594 individuals with a median age of 65 years, 36% of whom were women, a median stay length equal to 2.8 days, and an ICU mortality rate of 18.8%. After applying restrictions based on the availability of comorbidities, reasons for admission, and the parameters used, the final population consists of 4.786 patients with complete data. The characteristics of this cohort included a median age of 66 years (range: 54-74 years), 37% of whom were female, the median hospital stay is 3.1 days and with an average FC per patient in the first 24 hours after admission is 1606 ml (849-2000).

3.2. Fluid creep linear regression model

The baseline model highlights that mild renal insufficiency, intensive treatment, sodium, and AKI exhibit a significant correlation with the target ($p < 0.05$), and the first three variables are positively correlated with net FC on the first day, while AKI is negatively correlated, as reported in Table 1. From the model using forward feature selection always having as a target the net FC in the first 24 hours we note that sodium ($p < 0.029$), respiratory failure ($p < 0.001$), absence of comorbidities ($p < 0.001$), tumor withouht metastasis (p=0.02), vasculopaty (p=0.03), and surgery (p= 0.04) all emerged as significant and positively correlated with the target, implying an increase in FC. In contrast, the presence of AKI (p= 0.015), metabolic disorder (p= 0.002), trauma (p= 0.01), antiplatelet therapy (p= 0.02), exhibited statistically significant negative associations with the predicted outcome, as we can see in Table 1.

Table 1: Statistical analysis with a recursive algorithm using LM model with the target of the amount of FC within the first 24 hours.

Variables	**Baseline**		**Recursive**	
	Coeff.	**P-val.**	**Coeff.**	**P-val.**
Age	-2.280	0.132	0.885	0.582
Gender	-4.302	0.923	-2.8	0.946
Weight	0.346	0.777	1.58	0.180
Septic shock	-74.927	0.379	16	0.846
Mild renal	590.409	**0.009**	-226	0.313
pfratio	0.137	0.647	-0.022	0.940
Intensive treatment	287.407	$<$**0.001**	89	0.061
Hypoxia level	-20.377	0.712	4.5	0.932
AKI	-91.470	**0.001**	-66	**0.015**
MAP	-1.251	0.389	-1.96	0.160
HR	0.728	0.366	0.23	0.770
Sodium	12.754	**0.001**	8	**0.029**
Potassium	-1.496	0.926	-4.66	0.763
Bicarbonate	-3.932	0.435	-10	0.036
Respiratory failure	-	-	1649	$<$ **0.001**
No comorbidities	-	-	256	$<$ **0.001**
Metabolic disorder	-	-	-554	**0.002**
Tumor without metastasis	-	-	166	**0.017**
Organic brain coma	-	-	164	**0.02**
Trauma	-	-	-171	**0.01**
Antiplatelet therapy	-	-	-342	**0.02**
Vasculopathy	-	-	178	**0.03**
Surgery	-	-	48	**0.04**

3.3. Classification and explainable AI

Table 2 shows the results of the classification. in particular, the accuracy has a value of 0.768 on train set and 0.770 on test set for the LR model but in Table 2 we can see that other models such as AB or DTC also achieve very similar accuracy results.

Figure 2: 20 most important features using the SHAP method for the Logistic Regression classifier model.

In Figure 2, we present the 20 most important features identified via the SHAP method for the Logistic Regression classifier model, as well as their directionality with respect to the target variable; the order of features is from most important to least important. In order to investigate the heart-related variables, which are among the 20 most important for the LR model, the HR, PAM, and myocardial infarction varibles were selected and driven in relation to the binary target. The 3D Boxes visualization represents clinical parameters across patient groups, with each box constructed differently based on variable type. For continuous variables, box centers mark the mean values, while box dimensions extend from mean-SE to mean+SE (where SE is standard error). For binary variables, box centers indicate the proportion of positive cases within each clinical group, with dimensions similarly extending ±SE of proportion. As shown in Figure 3, these three variables distinguish the two target classes, i.e. patients at risk and those not at risk of receiving high FC. In order to generate this image, the dataset was extracted before standardisation and, in addition, to prevent these results from being compromised by data imbalance, a downsample of the majority class was applied, resulting in 1192 samples per class.

4. Discussions, limitations and future developments

In this study, the most useful features are analysed in order to understand which characteristics of patients admitted to the ICU lead to more or less FC administration. In

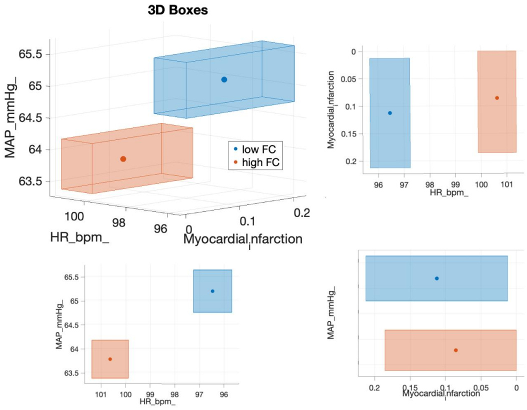

Figure 3: 3D Boxes visualization of the most caridiac relevan variables.

Table 2: Model performance metrics across different classifiers for the preficton of patients at risk of high FC.

Metrics	**KNN**	**DTC**	**QDA**	**LR**	**LDA**	**AB**	**RFC**
Accuracy Train	0.765	0.781	0.765	0.768	0.769	0.766	0.802
Val Acc (Best Mean)	0.750	0.761	0.762	0.765	0.765	0.766	0.768
Accuracy Test	0.753	0.752	0.765	**0.770**	0.763	0.765	0.773
F1-score	0.163	0.243	0.349	0.261	0.280	0.287	0.269
AUROC	0.581	0.577	0.620	0.632	0.630	0.573	0.637
PPV	0.535	0.514	0.571	0.588	0.587	0.600	0.690
NPV	0.763	0.772	0.789	0.775	0.778	0.779	0.778
PRC AUC	0.354	0.325	0.415	0.421	0.422	0.496	0.443

Figure 2 we can see the top 20 most relevant variables for the LR model, which appears to be the best model for classifying patients with high FC. In particular, we note that among these variables there is more than one related to the cardiovascular system[4]: myocardial infarction, MAP and HR; thus highlighting the close relationship between the restoration of cardiovascular stability and the administration of fluid therapy[4]. When comparing the significant variables of the LM linear regression model with the 20 most significant variables of the LR classification model, both similarities and differences emerge. Age, weight and height are among the most important variables in the LR model, but are not statistically significant in the LM. In contrast, respiratory failure, absence of comorbidities, intensive treatment, organic coma, surgery, sodium, HR and trauma are among the most relevant variables in the LR model and have a $p < 0.05$ in the LM as well, also maintaining consistent directionality in predicting outcome in both models. Moreover, The classification algorithm uses data collected mainly on admission but some parameters are collected during the first 24 hours in the ICU so this model does not have the main aim of predicting in advance which patients are at risk of receiving high FC but to explain through the SHAP model which are the most significant variables in the classification of the target and their directionality as we see in Figure 2. In conclusion, our findings highlight the clinical variables that most strongly impact FC administration and support early identification of patients at risk of elevated FC during the first 24 hours. The study has some limitations: being monocentric, the results could be affected by the specific clinical practices of the analysed centre. A multicentre extension would be a useful development to increase the generalisability of the conclusions. Furthermore, the data used were not collected prospectively, but derived from a pre-existing database, which implies a selection constrained by the available variables. Nevertheless, initial cohort characteristics such as age, gender distribution and average length of stay were stable, suggesting no evident bias in patient selection.

5. Conclusions

In conclusion, this study allows us to investigate which variables are statistically significant for the study of FC in the first 24 hours of ICU admissions. Furthermore, the classification model and its related explainable AI analysis done with the SHAP model allows us to understand which are the most important features to classify patients at risk of receiving high FC.

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