# Predicting Readmission of Heart Failure Patients

Zuzana Koscova[1], Eniko Vargova[1], Jan Pavlus[1], Radovan Smisek[1, 3], Ivo Viscor[1], Veronika Bulkova[2], Filip Plesinger[1]

[1]Institute of Scientific Instruments of the Czech Academy of Sciences, Brno, Czechia
[2]Medical Data Transfer, s.r.o. Brno, Czechia
[3]Brno University of Technology, Fac Elect Engn and Commun, Dept Biomed Engn, Brno, Czechia

**Abstract**

*Heart failure (HF) is the main reason for readmission in hospitals, especially for elderly patients. To prevent HF recurrence, we propose a method to predict HF probability for patients leaving intensive care units.*

*We use structural data from the freely available MIMIC-III database. We retrieved 2 demographic attributes, 5 physiological measurements from electronic charts, and 10 laboratory features for 7,697 patients.*

*We predict HF with 4 random forest (RF) models at time intervals up to a week, a month, 6 months, and a year. Optimal hyperparameters are calculated for each of the individual models using a grid search on the training set. Next, an ensemble model was constructed from these 4 submodels. The test part of the data (N=1,234) was dichotomized by the ensemble model and survival analysis was performed over a time period of 5.6 years.*

*Results of the log-rank test for dichotomized cohort show a significant difference (p<0.0001) and a Hazard ratio of 3.68 (2.68-5.05). The 4 most important features of the RF model according to the Gini importance namely systolic blood pressure, blood oxygen saturation, blood urea nitrogen, and heart rate are consistent with the parameters observed during discharge of patients from the ICU. Our model also suggests that age and blood glucose play a significant role in predicting HF recurrence.*

## 1. Introduction

Heart failure (HF) is a chronic and progressive syndrome that results from a functional or anatomical cardiac disorder that impairs the filling of ventricles or blood supply to the circulatory system. It is a highly prevalent disorder worldwide related to an increase in mortality and rehospitalization. Heart failure is the main reason for readmissions in individuals over the age of 65 and is associated with significant financial expenses [1]. Identifying those at the highest risk of HF recurrence and ensuring they receive appropriate treatment can not only prevent premature deaths but also can reduce the burden on the healthcare system and thus decrease healthcare costs. Physiological factors, including high blood pressure, high blood cholesterol, and high blood sugar etc. can be easily measured even in primary care facilities and indicate an increased risk of HF.

In this paper, our aim is to predict the readmission or death of patients hospitalized with HF who are expected to be discharged from the intensive care unit (ICU) in the near future and thus simplify physician decision-making and help to identify preventable HF recurrence.

## 2. Data

In this study, we used the MIMIC-III critical care clinical database [2,3] available on PhysioNet [4]. It contains health-related information about more than 40,000 patients who were admitted to the critical care units from 2001 to 2012. Our focus was primarily directed at patients who were diagnosed and hospitalized with heart failure in the ICU. We retrieved patients diagnosed with HF based on the ICD-9 diagnosis code [5]. The number of unique patients and admissions with heart failure was 9,697 and 14,040, respectively. For these patients, demographic data namely age (73.09 ± 13.13) and sex (4,005 male and 3,692 female) were extracted from the database. In MIMIC-III, subjects over age 89 at any time in the study have their date of birth artificially shifted to 300 years before their first admission to make their age obscure. To ensure that the final model for HF prediction work with real data, we assigned age 90 to all these patients, and we also created an ordinal variable age_ordinal to add patients to groups based on decades.

Further, patient information from electronic charts was obtained. An electronic chart stores patients' routine vital signs and any additional data related to their care. In total, the following information was extracted from the electronic chart: heart rate [bpm], respiratory rate [breaths/min], systolic and diastolic blood pressure [mmHg], and blood oxygen saturation [%]. These measurements are nurse-verified and documented hourly. For each patient, a daily average was taken from the last calendar day in the ICU.

Next, laboratory-based measurements were extracted: serum creatinine [mg/dl], sodium [mEq/l], blood urea nitrogen (BUN) [mg/dl], chloride [mEq/l], glucose [mg/dl], hematocrit [%], magnesium [mmol/l], phosphate [mg/dl] and potassium [mEq/l]. These measurements were taken as the last measurements for the patient before discharge. The average time when the measurements were taken is 10.82 ± 10.74 days from hospital admission, while the average length of hospital stay is 11.68 ± 10.08 days.

Because we want to predict a patient's readmission, we use only data from the first admissions for a given HF patient. Thus, the dataset size is initially 9,697 patients x 18 features.

We also identified follow-up times based on the date of HF readmission or date of death for patients with HF recurrence, and the time of the last hospital visit outside the cause of HF for patients without a record of HF recurrence.

## 3. Preprocessing

In the beginning, the records (first HF admissions) with at least one missing feature are removed, leaving us with 8,791 records. Then the outliers are deleted based on the interquartile range for a specific feature. If a particular patient has more than 1 outlier in its features, it is removed from the dataset. Thus, the final number of outliers is 432, i.e., we are left with 7,697 patients. The final number of patients without HF recurrence is 2,952, with HF readmission is 1,494, and with all-cause death is 3,251.

## 4. Method

In this study, we want to develop a model which outputs the probability of heart failure recurrence in patients hospitalized with HF in the ICU. To prevent our model from overfitting and to evaluate our model effectively, we randomly split our input data into training, validation, and testing subsets in a ratio 2:1:1 in the manner of equal distribution of an event (HF recurrence or all-cause death) within the splits.

To predict the HF recurrence, 4 random forest models were created from which an ensemble was subsequently constructed. Each of these models predicts HF for different time periods: week, month, half a year and a year. The number of patients with HF recurrence or all-cause death (event) vs patients without recurrent HF (event-free) for each follow-up time is shown in Table 1.

Table 1. Number of patients with (Event) or without (Event-free) HF recurrence for a specific follow-up time.

| Model | Week | Month | 6 months | Year |
|---|---|---|---|---|
| Event | 343 | 1,102 | 2,378 | 2,912 |
| Event-free | 7,354 | 6,595 | 5,319 | 4, 785 |

For each model with specific follow up-times, optimal hyperparameters (Table 2.) were calculated based on the grid search method using 5-fold cross-validation on the training data. Subsequently, 4 models were trained and validated using the optimal hyperparameters.

Table 2. Optimal hyperparameters of 4 random forest models created for a specific follow-up time calculated using the grid search method.

| Model | Week | Month | 6 months | Year |
|---|---|---|---|---|
| Max depth | 8 | 14 | 12 | 14 |
| Min s. leaves | 3 | 3 | 2 | 2 |
| Min s. splits | 3 | 3 | 5 | 6 |
| No of estimators | 150 | 200 | 200 | 190 |

To select the optimal threshold for binary classification, we employ the receiver operating characteristic curve (ROC) which illustrates model performance at various discrimination thresholds. The optimal threshold was selected as the position of a maximal geometric mean of sensitivity and specificity. Figure 1 shows 4 ROC curves generated using data from the validation set. Individual curves correspond to 4 RF classifiers trained for different follow-up times. The overall workflow to predict the recurrence of HF is shown in Figure 2.

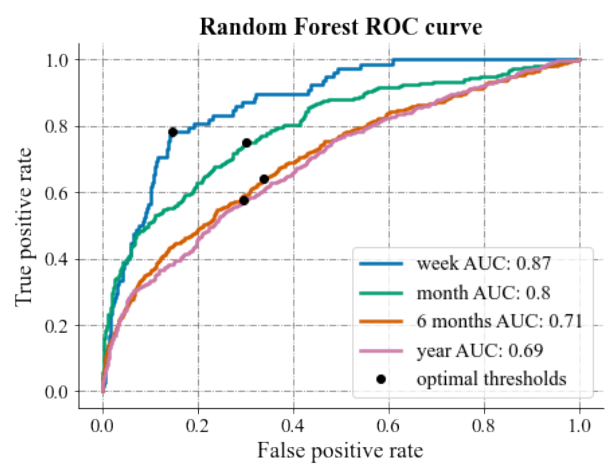


Figure 1. ROC curves for models trained on week, month, 6 months, and 1 year follow-up illustrating performance on validation dataset for various thresholds. Black points represent the optimal threshold selected for a specific model. AUC stands for Area under the ROC curve.

To verify the ability of our model to predict the HF in time we performed a survival analysis. This analysis was performed at a follow-up time equal to half the duration of the study (5.6 years). Patients who did not have an event during this time and had no further information about them in the study were censored. The number of uncensored patients in the dataset is shown in Table 3.

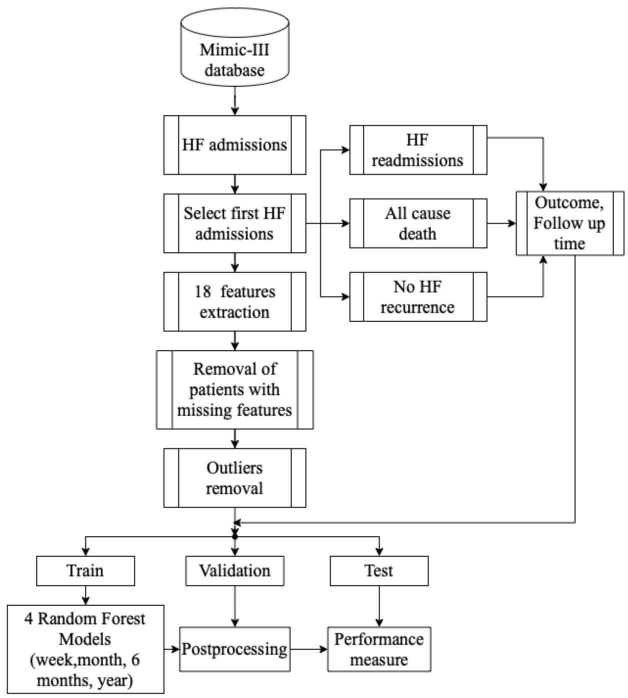


Figure 2. The overall workflow to predict HF recurrence from MIMIC-III database.

Table 3. Number of uncensored patients in training, validation and test sets with and without event for follow-up of 5.6 years (half of the study duration).

| | Training | Validation | Test |
|---|---|---|---|
| Event-free | 251 | 108 | 111 |
| Event | 2,217 | 1,119 | 1,123 |

Patients were divided into two groups by each model; the separation threshold (0.54) was based on the event and event-free proportion (0.89).

To make our method more robust, we created an ensemble model from all four RFs by taking the average of their probabilities. The ensemble model's ability to dichotomize patients to those with better or worse prognosis was evaluated using survival analysis (software GraphPad Prism 9.5.1).

## 5. Results

Thresholds for four RF classifiers calculated using ROC curves are applied to evaluate the performance of the models using recall, precision, F1 score and specificity. We use weighted metrics because of the imbalanced dataset. The final performance scores are reported on the test set (Table 4.).

Table 4. Performance reported on the test dataset.

| Model | Week | Month | 6 months | Year |
|---|---|---|---|---|
| Recall | 0.84 | 0.70 | 0.67 | 0.69 |
| Precision | 0.95 | 0.84 | 0.71 | 0.70 |
| F1-score | 0.88 | 0.74 | 0.68 | 0.70 |
| Specificity | 0.73 | 0.70 | 0.68 | 0.66 |

Results of the log-rank test for comparison of survival curves created using the test set are shown in Table 5.

Table 5. Results of the log-rank test for comparison of survival curves created from test data using 4 classification models. HR stands for Hazard ratio and CI for confidence interval.

| Model | Week | Month | 6 months | Year |
|---|---|---|---|---|
| Chi square | 231.8 | 230.5 | 143.7 | 75.6 |
| HR | 2.9 | 4.0 | 3.9 | 3.3 |
| 95% CI | 2.4-3.7 | 2.8-5.7 | 2.5-6.1 | 2.0-5.6 |

In terms of the F1-score, the best prediction model is for a follow-up of one week. In terms of survival analysis, models predicting an event in one month or later shows a higher hazard ratio (HR).

The final ensemble model (Figure 3.) shows an HR of 3.68 (95% CI from 2.68 to 5.05) using the test dataset.

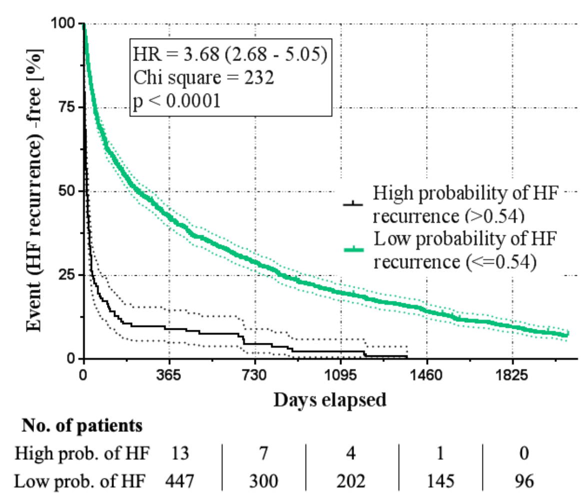


Figure 3. Kaplan-Meier plot was created using an ensemble of RF models. The black-bordered rectangle shows the results of the log-rank test for the comparison of

the 2 groups. HR stands for Hazard ratio with 95% confidence intervals (CI) in the brackets.

## 6. Discussion and conclusion

The results of the log-rank test indicate that the final model could assist in decisions whether release a patient from hospitalization or not. A study [6] shows that 30% of HF readmissions occur in the first week after hospital discharge and since one of the partial models is focused on the one-week time frame, it is likely that the presented solution could also assist in this scenario.

We also compared feature importance in the presented solution to current guidelines for patient discharge. By current guidelines, patients eligible for discharge must maintain systolic blood pressure ≥ 90 mmHg, heart rate < 80 or <100 bpm (subjects with atrial fibrillation), blood oxygen saturation of ≥95%, and stable renal function [6,7]. Figure 4 shows the importance of the presented RF model features. The first three most important features and the fifth feature (SBP, SaO2, BUN and HR) correspond to the attributes that should be checked during discharge.

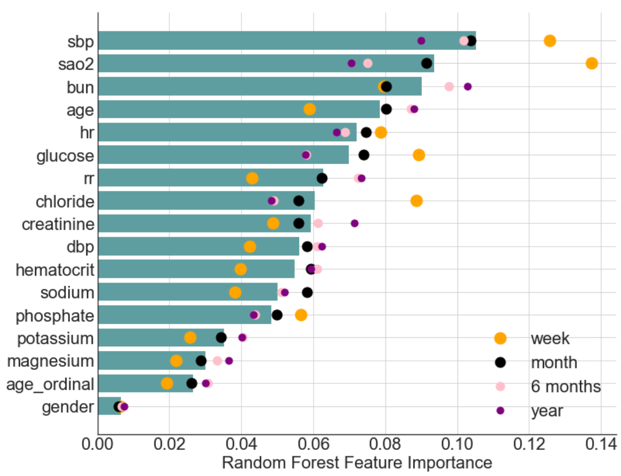


Figure 4. Random Forest features importance for the ensemble model and 4 submodels. Sbp and dbp stand for systolic and diastolic blood pressure, SaO2 for blood oxygen saturation, bun is blood urea nitrogen, hr stands for heart rate and rr is respiratory rate.

In addition to current guidelines, our results indicate that age plays an important role in predicting readmission in HF patients. Our results also suggest that glucose in the blood is a strong predictor for HF recurrence, especially for the recurrence of HF within the first week after hospitalization.

What could further improve the abilities of the presented solution is the addition of laboratory measurement of natriuretic peptide (NP) from plasma and ejection fraction (EF) to our dataset. Patients whose NP concentrations decrease during hospital admission have lower cardiovascular mortality and incidence of readmission within six months [8]. Studies show that patients with EF<45% during discharge have a poor prognosis [7].

To enhance the performance of the model, in the future, in addition to adding new features, we plan to also add time series of the features and process them with deep-learning methods.

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Address for correspondence:

Zuzana Koscova.
Kralovopolska 147 Brno, Czech republic.
zkoscova@isibrno.cz