When Extra Is Not Extra: Heartbeat Irregularities and All-Cause Mortality in Heart Failure Patients

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Abstract

Heart Failure (HF) is a condition where the heart cannot pump enough blood to meet the body's needs. When symptoms worsen, patients require urgent care to avoid fatal outcomes. This study examined rhythm and ventricular activation stability features and their link to HF patient mortality.

We analyzed data from 10,800 hospitalized HF patients using MIMIC-IV ECG and clinical datasets. Automated processing extracted QRS complex and heart rhythm features. Seventeen features were assessed for their ability to predict 3-year mortality using survival analysis. Lasso regression selected key predictors and built a multivariate model. Hazard ratios (HR) were calculated using the log-rank method.

Mortality was strongly associated with QRS morphology and RR-interval instability (e.g., RR-interval variation range, $\chi^2 = 68.1$, $p < 0.0001$), though age remained the most powerful predictor ($\chi^2 = 476.7$, $p < 0.0001$). The model built from 13 selected features yielded an HR of 2.26 (95% CI 2.03–2.52), compared to 2.09 (95% CI 1.88–2.33) for age alone.

This study highlights the significant role of rhythm and conduction instability in HF mortality, though age remains the dominant predictor.

1. Introduction

Heart failure (HF) is a leading cause of hospitalization and mortality worldwide. Accurate risk stratification is crucial for improving outcomes, yet current models rely heavily on demographic and clinical variables.

Electrocardiographic (ECG) features, particularly those reflecting rhythm and conduction stability, may offer additional prognostic value but are underexplored in large HF populations. This study investigates the predictive power of ECG-derived features - such as QRS morphology, ectopic beats presence as premature ventricular contractions (PVC), atrial premature contractions (PAC), and RR-interval variability - for long-term mortality in hospitalized HF patients.

Using automated analysis of MIMIC-IV data and survival modeling, we assess whether these features improve risk prediction beyond age and other clinical factors. Our findings suggest that rhythm and conduction instability are significant mortality predictors, with potential to enhance HF management strategies.

2. Method

For this study, we utilized the MIMIC-IV ECG dataset [1], the MIMIC-IV Clinical Database [2], and the MIMIC-IV-ECG-Ext-ICD dataset, which provides links between the ECG and Clinical parts, all of which are available from PhysioNet [3].

2.1. Dataset

From the MIMIC-IV dataset, we extracted all patients with a heart failure diagnosis, as classified by the International Classification of Diseases (ICD-9/10), who were discharged from the Intensive Care Unit (ICU) or the emergency department. The resulting cohort description is shown in Table 1.

Table 1. Patient cohort summary table.

Variable	Value
Count	10,800
Age (years)	72.3 ± 13.5
Gender - female	5,006 (46%)
Died 3 years after discharge	3,405 (32%)
Avg. time to death (days)	867

We acquired each patient's ECG signal (12-lead, 10 seconds, 500 Hz sampling, WFDB format) from the MIMIC-IV-ECG, together with QRS duration, QT interval, QRS axis, and T-axis. Furthermore, we acquired the age, gender, death status, and time to death from the MIMIC-IV Clinical database.

2.2. Data processing

Since MIMIC-ECG data (Fig.1-A) are in WFDB format, we loaded signals and converted them to EDF using the "pyedflib" Python package (Fig.1B). Then, EDF files (lead "I" only) were fed into J.O.S.E.P.H. solver version 0.4.2 [4], producing XML files describing heart activity (Fig.1C). From J.O.S.E.P.H. we derived detailed descriptors as ratio of PVCs, PACs, number of QRS morphological groups, RR statistical description, and BPM statistical description.

QT intervals, obtained from the MIMIC-IV dataset, were corrected using Bazett's formula into QTc (Fig.1D). The combination of these features formed a complete feature dataset (Fig.1E), further used for univariate (Fig.1F) and multivariate analysis (Fig.1G)

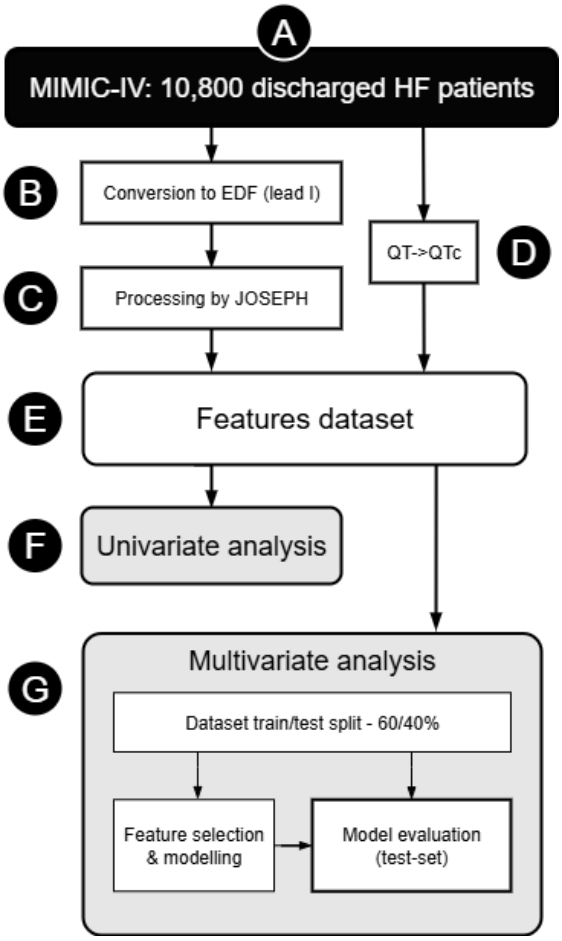

Figure 1. Method workflow: MIMIC-IV data (A) ECGs are converted into EDF files (B) and processed with J.O.S.E.P.H. solver (C). Other features are acquired from the database (D). Complete feature dataset (E) is used for univariate analysis (F) and multivariate analysis (G).

From the feature dataset, we removed features with less than 2% of positive cases (detected PVCs/PACs in couplets, triplets, quadruplets, bigeminies, and trigeminies).

2.3. Univariate analysis

For each feature, we evaluated its association with all-cause mortality: we dichotomized the population by feature median and quantified its ability to separate the population into groups with better and worse prognosis. Separation ability in the 1-year follow-up was measured by the log-rank test and chi-square using the lifelines Python package [5].

2.4. Multivariate analysis

In multivariate analysis (Fig.1G), we split the dataset into a training and testing part (60-40% ratio). Non-categorical variables were standardized. Then, we employed LASSO regression from the scikit-learn package for feature selection (in 5-fold cross-validation) and building the model. The target for the modelling was 3-year mortality.

Finally, we processed test data with the produced model. The population was split using the model output median, and model performance was evaluated using the chi-square (χ^2), log-rank test, and hazard ratio (HR) with 95% confidence intervals (CI) using the GraphPad Prism software (version 9.5.1). Dichotomization was visualized using Kaplan-Meier plots.

When multivariate analysis was done, we returned to univariate analysis and examined changes in selected features in terms of prediction performance in 0-1 month, 2-6 months, 7-12 months, and 13-36 months time frames. Using the Mann-Whitney U-test, we compared changes in consecutive time frames as well as differences in the population surviving at least 3 years.

3. Results and discussion

3.1. Univariate analysis

Univariate analysis (Tab.2) has shown the expected strong effect of age (χ^2 476.7), but also revealed other associations, such as the standard deviation of heart rate (χ^2 76.5), the variation range of beat-to-beat RR intervals (χ^2 68.1), or the minimal RR interval (χ^2 44.9).

We also tested the association with the presence of other QRS morphological groups in several ways. The ratio of abnormal QRS complexes (PVCs, PACs, aberated beats, fusion beats…) showed χ^2 of 42.8; the total count of QRS morphological groups showed χ^2 of 17.8. The PVC ratio showed χ^2 43.8, while the count of isolated

PVCs led to χ^2 of 36.9. However, the association with PACs was much weaker, shown only χ^2 of 4.8 and 4.6 for the PAC ratio and count of isolated PACs, respectively.

Table 2. Univariate and multivariate results. Feature medians were used to split the population; p-value and χ^2 refer to the results of the log-rank test. Coefficient refers to LASSO regression coefficients. If it is missing, the feature was not selected.

Feature	p-value	χ^2	Coefficient
Age	0.000	476.7	+ 0.114
Gender (F)	0.974	0.0	- 0.003
QRS Morphs.	0.000	17.8	+ 0.008
Ab. QRS rat.	0.000	42.8	
PVC ratio	0.000	43.0	
PVC isolated	0.000	36.9	+ 0.013
PAC ratio	0.029	4.8	- 0.000
PAC isolated	0.031	4.6	- 0.016
H. rate min	0.178	1.8	+ 0.036
H. rate max	0.000	44.9	
H. rate std	0.000	76.5	
H. rate avg	0.000	13.4	
RR avg	0.012	6.3	
RR std	0.000	57.8	
RR min	0.000	44.8	- 0.010
RR max	0.171	1.9	
RR range	0.000	68.1	+ 0.010
QRS-axis	0.000	18.9	+ 0.007
T-axis	0.015	5.9	- 0.006
QRS duration	0.000	29.3	+ 0.016
QTc	0.000	22.9	+ 0.004

These results suggest that a fast and varying (in terms of morphology and timing) heart rhythm is associated with higher mortality.

We also tested markers describing ventricular depolarization and repolarization in terms of durations and directions. From this domain, QRS duration showed the strongest association, with a χ^2 of 29.3, followed by the corrected QT interval (χ^2 = 22.9). Direction descriptors showed weaker associations with χ^2 of 18.9 and 5.9 for the QRS axis and T axis, respectively.

3.2. Multivariate analysis

The model was trained on 60% of the dataset, resulting in the selection of 13 features. The feature coefficients are shown in Tab.2, the last column. Feature importance is the absolute value of each coefficient. While age remains the strongest coefficient (0.114), the LASSO selection process changed the order of other features, automatically finding the optimal combination to predict the outcome.

In terms of rhythm pace, the strongest feature was minimal heart rate (+0.036) together with maximal RR interval (-0.010), both showing that elevated heart rhythm is associated with a worse outcome. The variation range of RR intervals, the number of isolated PVCs, and the number of QRS morphological groups also suggest that strong rhythm variations and their connection to PVCs are associated with a worse prognosis. However, the PAC ratio (describing the presence of all kinds of PACs) and the count of isolated PACs showed a negative association with the outcome. Contrary to this finding, univariate analysis showed a positive association with the outcome, meaning that the model might use this feature to reduce the effect of irregular rhythm when it is caused by PACs.

Finally, we dichotomized the test set data by (training) median output and evaluated model performance using survival analysis. Tab.3 shows the model's results (χ^2 209.6, HR 2.26 with 95% CI between 2.03-2.52) and, for comparison purposes, the dichotomization based on age alone (χ^2 169.3, HR 2.09 with 95% CI between 1.88-2.33).

Table 3. Survival analysis using test set; population was dichotomized using the median output of the proposed model (2nd row) and the median age (1st row).

	χ^2	p-value	HR (95%CI)
Age	169.3	<0.0001	2.09 (1.88-2.33)
Model	209.6	<0.0001	2.26 (2.03-2.52)

The survival analysis in Fig.3 shows strong separation of patients above and below the model median output in the 3-year follow-up.

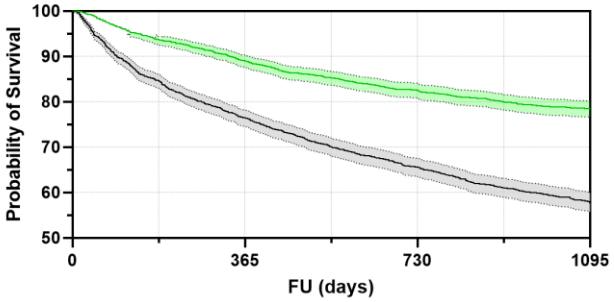

Figure 2. Kaplan-Meier curve for population (N=4,195) separated by model median shows significant separation. Green – patients above model median; gray – patients below model median. Transparent zone: 95% confidence intervals.

Findings related to heart rate and QRS duration point to the same association as shown in the independent VICTORIA study[6]. That study also showed a similar, but non-significant, effect of QTc.

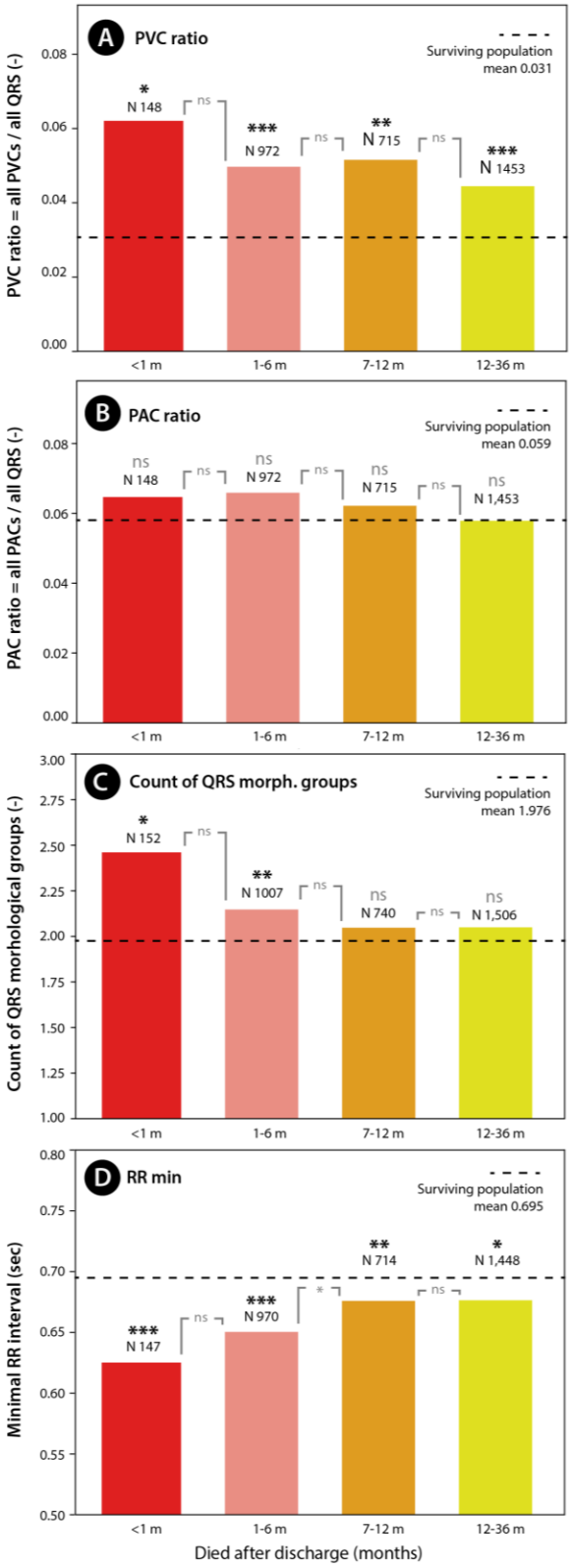

Figure 3. Selected features for the population deceased in specific timeframes. Dashed line - surviving population (≥ 3-years). P-values: * <0.05,0.01), ** <0.01,0.001), *** <0.00, ns – non-significant.

Finally, we examined selected features univariately within specific timeframes to investigate how their associations evolve over time. Fig. 3 shows changes in consecutive timeframes. It also shows associations with the surviving population (Fig.3, dashed line). These results suggest that modeling across different timeframes will likely yield different feature sets.

4. Conclusions

In this study, we explored the association of ECG-derived markers with the survival of HF patients discharged from the ICU/emergency departments. Results showed that features describing the heart rhythm play a statistically significant role in cases of elevated resting heart rate, the presence of PVCs, and the presence of multiple QRS morphological groups.

Acknowledgments

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