On the Relevance of ECG Features for Survival Prediction. Application to Septic Shock

Raphaël Chalard[1], Amar Kachenoura[1], Guy Carrault[1], Di Ge[1],
Antoine Kimmoun[2], Alexandre Mebazaa[3], Ahmad Karfoul[1]

[1] Univ Rennes, Inserm, LTSI - UMR 1099, Rennes, F-35000, France
[2] Faculté de Médecine, INSERM U1116 DCAC, 54511 Vandoeuvre-les-Nancy, France
[3] Inserm UMR-S 942 MASCOT, University of Paris Cité, Lariboisière Hospital, Paris, France

Abstract

Early risk stratification in intensive care units remains particularly challenging for conditions like septic shock, which affects $8-10\%$ *of patients at admission and has a hospital mortality rate close to* 40%*. Although clinical and biological variables are widely used for mortality risk assessments, ECG data, despite systematically collected, are never used in this setting. The aim of this study is to assess the association between ECG-derived features and the one-year mortality risk following hospital admission using unsupervised clustering and compares risk groups based on ECG-related and clinical variables individually, as well as through an aggregated group strategy, using Kaplan-Meier survival analysis. Results show that ECG features effectively distinguish between high- and low-risk patients of one year mortality highlighting their potential in future survival prediction models.*

1. Introduction

Effective early mortality risk stratification in Intensive Care Units (ICUs) poses a significant challenge, as prompt decision-making can profoundly affect patient prognosis. While several studies have examined early mortality among patients admitted to ICUs concentrating on short termed outcome [1], far less is understood about patient trajectories following ICU and hospital discharge, typically one-year post-discharge. To address this gap, the French and European Outcome Registry in Intensive Care Units (FROG-ICU) study was initiated. This prospective, observational, multicenter cohort study seeks to determine the incidence of, and identify risk factors for, mortality during the year following ICU discharge (more details about the study are provided in Section 2). Several research studies have leveraged the FROG-ICU cohort to investigate patient outcomes following ICU and hospital discharge [2–6], to cite a few. Most of these works have focused on biological and clinical variables (e.g., demographics, comorbidities, severity scores, platelet count, glucose, and lactate levels), either to identify patient groups with differing one-year survival rates [4], or to evaluate the impact of specific diseases like diabetes [5], as well as certain invasive procedures such as tracheostomy [6]. Only a limited number of studies have examined ElectroCardioGramme (ECG) features, focusing on specific markers such as QT interval prolongation [2] and atrial fibrillation [3]. Furthermore, similar patterns are observed in other French multicenter cohorts [7], which focuses specifically on patients with septic shock and also rely on clinical and demographic variables for prognostic evaluation, while ECG-related features remain never used. Therefore, motivated by (i) the limited exploitation of ECG features as structured and complementary inputs for long-term follow-up and (ii) the availability of ECG recordings as part of routine monitoring in ICUs, which makes such data readily accessible for analysis, this study aims to investigate the added value of ECG features for improving long-term survival prediction. We focus on patients with septic shock, a frequent and serious condition in critical care, defined by a sepsis plus either hypotension (refractory to intravenous fluids) or hyperlactatemia [8] and affecting around $8-10\%$ of ICU patients and associated with high mortality rates (up to 40%) [9]. Specifically, this study investigates the prognostic value of ECG-derived features by applying unsupervised clustering techniques alongside with survival analysis, to patients admitted with septic shock.

2. Database

The FROG-ICU dataset consists of $2,087$ ICU patients admitted for a range of critical conditions including acute respiratory failure, neurological conditions, septic shock, cardiac arrest, and others. For each patient in this dataset, an electronic case report form was completed to document key information related to their ICU stay and one-year

follow-up. At the time of inclusion, data collected include demographics, past medical history, ICU admission diagnosis, hemodynamic and respiratory parameters (invasive and non-invasive) as well as severity scores such as SAPS-II [10] and Charlson Comorbidity Index (CCI). Among those ICU patients, the current study concerns 468 patients who were diagnosed with septic shock and for whom ECG recordings via the CarTouch device (Cardionics S.A., Brussels, Belgium) are acquired. On average, these 468 patients underwent their first ECG four days after ICU admission, while 75% of them had received their first ECG recording by day five. ECG recordings are then used to compute a set of ECG features such as cardiac conduction phases (atrial/ventricular depolarization, atrioventricular conduction, etc.). Septic shock carries an exceptionally high mortality burden. In our cohort (468 patients), overall mortality for septic shock patients reached 44%, as depicted in Figure 1. Within the ICU itself, 25% of the septic shock patients died, second only to the 30% ICU mortality observed in cardiac arrest cases. Besides, 19% of the latter patients died during the year after ICU discharge, placing it among the highest post-ICU death rates recorded.

The variables considered in the studied cohort fall into two main categories: clinical and ECG, that are summarized below:

• **Clinical variables** encompass patient demographics, admission details, comorbidities, and chronic treatments. These include age, sex, initial admission unit, and inclusion criteria (mechanical ventilation for more than 24 hours or the use of inotropes/vasopressors), as well as severity scores such as SAPS II and CCI. The dataset includes a mix of variable types: continuous variables (e.g., age, SAPS II), taking values in $\mathbb{R}^+$, and binary variables (e.g., comorbidities such as hypertension, diabetes, or HIV; chronic treatments such as beta-blocker use), encoded as 0 (absence) or 1 (presence). It is important to note that the accessibility of these variables in clinical settings can vary. For instance, the SAPS II score relies on standard blood tests typically available upon admission. In contrast, obtaining accurate data on comorbidities and chronic treatments often depends on a thorough medical history, which may be difficult to obtain promptly in emergency settings.

• **ECG features** comprise a total of 308 continuous variables (each taking values in $\mathbb{R}$), organized as follows: 288 measurements derived from the 12 standard ECG leads, with 24 features per lead. These include wave amplitudes (in microvolts) and durations (in milliseconds) for key ECG waves (P, QRS, and T) as well as durations of specific segments such as QT interval, and ST segment deviation. In addition, 20 global features are included, such as heart rate, RR interval, electrical axes (average direction of the heart's electrical activity during specific phases of the cardiac cycle), QT dispersion, and various corrected QT intervals (e.g., Bazett's and Fridericia's formulas).

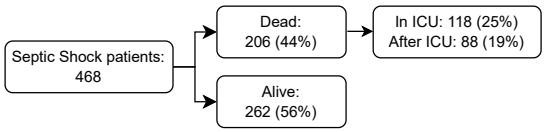

Figure 1. Septic shock cohort (% over the septic cohort)

3. Methodology

As previously mentioned, the aim of this study is to assess the extent to which ECG-derived data can provide insights into patient survival outcomes after ICU or hospital discharge, either by matching the predictive power of commonly used clinical variables or by demonstrating their added value when combined with these clinical variables to enhance survival prediction. To this end, an unsupervised clustering strategy based on survival analysis is proposed and illustrated in Figure 2. Clustering is performed on datasets that are deliberately left unaltered (except for the handling of missing values), ensuring maximal objectivity and maintaining a blind approach throughout the process. As depicted in Figure 2, the proposed survival prediction pipeline comprises the following processing steps:

i. Preprocessing of ECG features: This step primarily involves removing ECG features with missing values, which originate from issues such as acquisition errors, signal artifacts, or computational problems (e.g., division by zero). This step is essential to reduce the risk of introducing bias into the subsequent survival analysis. Missing values are most commonly found in temporal interval variables, such as the corrected QT, ST intervals, and in the P-wave axis. After preprocessing, the number of retained ECG features is reduced from 308 to 165 comprising amplitudes and durations of the P, QRS, and T waves across the 12 leads, as well as global variables such as heart rate, RR interval, and electrical axes (QRS and T).

ii. Dimensionality reduction: Principal Component Analysis (PCA) is applied to enhance clustering performance by minimizing redundancy and highlighting the most significant variables, capturing at least 80% of the cumulative variance in the data.

iii. Clustering: The extracted principal components are used as input to a k-means clustering algorithm to identify distinct patient groups (i.e., clusters). To determine the optimal number of clusters, k (denoted k_1 for ECG-based clusters and k_2 for clinical-based ones), Pairwise log-rank tests [11] are then conducted to assess statistical differences between the computed Kaplan–Meier survival curves, using the associated p-values as the evaluation metric. The optimal number of clusters is selected

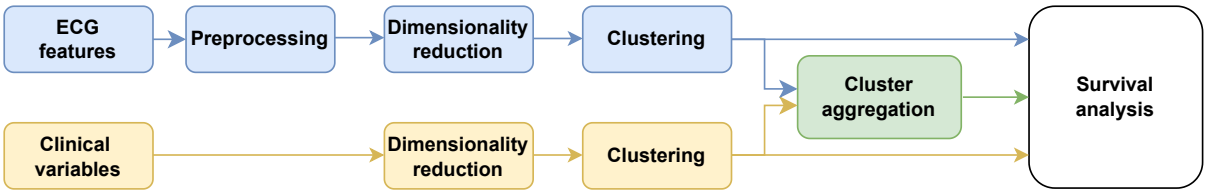

Figure 2. The proposed survival analysis pipeline.

as the value of k for which all pairwise comparisons are statistically significant ($p < 0.05$). If multiple values of k satisfy this condition, the one with the smallest minimum p-value across all comparisons is chosen, indicating the strongest overall separation between survival profiles. Once the optimal number of clusters is determined, a bootstrap resampling strategy is applied to evaluate the stability and robustness of the clustering results. Specifically, for each clustering approach (i.e., ECG-based and clinical-based), 80% of the population is randomly sampled and the clustering procedure is repeated over 100 trials. Thus, the clustering approaches result in two distinct sets of groups, $E = \{E_1, \ldots, E_{k_1}\}$ and $C = \{C_1, \ldots, C_{k_2}\}$, where the m-th element E_m (respectively C_m), with $m \in \{1, \ldots, k\}$ and $k \in \{k_1, k_2\}$, denotes the m-th ECG-based (clinical-based) cluster.

iv. Cluster aggregation: After identifying the two sets E and C, the objective of this step is to evaluate the impact of aggregating the ECG-based and clinical-based groups on survival prediction performance. To this end, we create $L = |E| \times |C|$ groups where $|\cdot|$ denotes the cardinality of the argument set. The $(m + (n-1)k_1)$-th aggregated group (i.e., cluster) with $1 \leq m \leq k_1$ and $1 \leq n \leq k_2$, corresponds to the intersection $E_m \cap C_n$. Subsequently, pairwise log-rank tests are performed over the resulting L groups to assess the survival differences. Any pairs of aggregated clusters that do not exhibit statistically significant separation are then merged to enhance interpretability.

v. Survival Analysis: The goal of this final step is to assess differences in survival between the sets of resulting clusters. These differences are evaluated through a log-rank test on the corresponding Kaplan–Meier curves [11]. The obtained clusters can then be used for survival follow-up.

4. Results and discussion

According to the processing pipeline illustrated in Figure 2, once the dimensionality reduction step is completed, the clustering phase involves selecting the optimal number of clusters. This is achieved using a grid search over candidate values $k \in \{2, 3, 4, 5\}$, with the optimal value determined based on the log-rank test ($p < 0.05$). For both ECG features and clinical variables, $k = 2$ yields

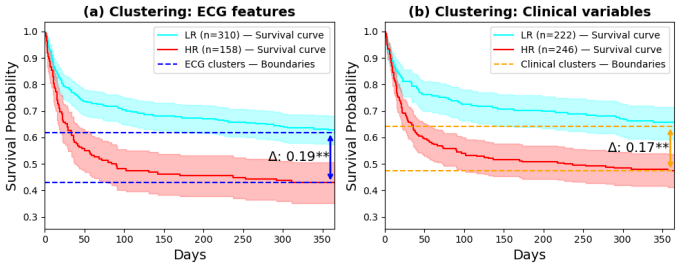

Figure 3. Kaplan-Meier Survival Curves over One-Year Post ICU or Hospital Discharge based on (a) ECG features, (b) clinical variables. HR, and LR represent, High and Low Risk groups, respectively. Δ indicates the survival gap; $^*p < 0.05$, $^{**}p < 0.005$. (n) denotes the number of patients in each group.

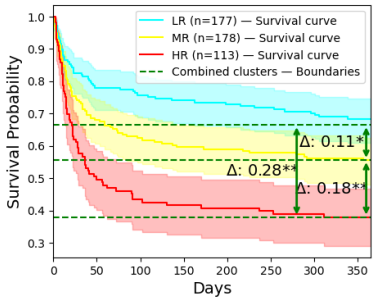

Figure 4. Kaplan-Meier Survival Curves over One-Year Post ICU or Hospital Discharge based on clusters aggregation. HR, MR, and LR represent High, Middle, and Low Risk groups, respectively. Δ indicates the survival gap; $^*p < 0.05$, $^{**}p < 0.005$. (n) denotes the number of patients in each group.

the most distinct cluster separation: E_0 and E_1 clusters using ECG features, and C_0 and C_1 ones using clinical variables. To evaluate clustering stability, 100 bootstrap trials are performed on randomly selected samples each comprises 80% of the original population, with clustering re-applied to each sample. Patient-level consistency in cluster assignments is then assessed across all trials. ECG-based clustering shows relatively high stability, with approximately 4% of patients being misclustered and fewer than 1% consistently assigned to incorrect clusters. In con-

trast, clinical-based clustering exhibits greater variability, with 19% of patients inconsistently assigned and 7% frequently misclustered. The log-rank test is then used to assess the statistical significance of the gap, denoted here by Δ, between the Kaplan–Meier curves associated with each cluster. Cluster E_0(respectively C_0) corresponds to a group with a lower one-year survival probability of 0.43 (0.48), High Risk (HR) groups, while E_1 (respectively C_1) corresponds to a higher probability of 0.62 (0.64), Low Risk (LR) groups, as shown in Figure 3 (a)-(b). Clusters induced from the same variables exhibits statistically significant gap Δ that is equal to 0.19 for the ECG-based clusters and 0.17 for the clinical-based ones. By aggregating the ECG and clinical clusters, in order to investigate the extent to which combined ECG and clinical insights can further improve the separability between HR and LR groups, a set of four aggregated groups are formed: $\{E_m \cap C_n\}_{(m,n)\in\{0,1\}\times\{0,1\}}$. Survival analysis and log-rank testing of these combinations yield three risk categories as shown in Figure 4: a HR group, $E_0 \cap C_0$, a LR group, $E_1 \cap C_1$ with respective one-year survival probability of 0.38 and 0.66; and a Middle-Risk (MR) group exhibiting a one-year survival probability of 0.56. The MR group is formed as $(E_0 \cap C_1) \cap (E_1 \cap C_0)$ since the two groups, $E_0 \cap C_1$ and $E_1 \cap C_0$, display no statistically significant difference in survival ($p \gg 0.05$). Furthermore, Figures 3 and 4 clearly shows, on one hand, that using only ECG features to define High-Risk (HR) patient groups yields survival outcomes comparable to those obtained using only clinical variables (0.43 for E_0 and 0.48 for C_0). This indicates that ECG features contain relevant information for reliably predicting one-year survival probability after ICU or hospital discharge. On the other hand, when both ECG and clinical insights are considered together to define HR patient groups, a lower survival probability is observed for the HR group (0.38 for $E_0 \cap C_0$). This suggests that a multimodal analysis can further enhance the identification of patients at risk, providing a more accurate assessment of survival outcomes.

5. Conclusion

This study explored the potential of admission ECG features, an underutilized yet easily accessible resource, for predicting one-year survival after ICU or hospital discharge in patients with septic shock. Results demonstrated that ECG variables offered predictive performance comparable to that of standard clinical variables. Additionally, a cluster aggregation strategy revealed that combining ECG- and clinical-based insights enhanced risk stratification, particularly for identifying high-risk patients. A dedicated processing pipeline was developed to support this analysis using the FROG-ICU database. Future work will focus on integrating advanced machine learning methods, such as Cox proportional hazards models and survival deep learning approaches, to further improve predictive accuracy.

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Address for correspondence:
Ahmad Karfoul
LTSI-Inserm UMR 1099, Bâtiment 22, Campus de Beaulieu, Université de Rennes, 35042 Rennes, France
ahmad.karfoul@univ-rennes.fr