ECG-Derived Biomarkers for Early Detection of Hemodynamic Instability in Critical Care

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Abstract

Cardiogenic shock (CS) is a critical condition resulting from severe cardiac dysfunction, often following myocardial infarction, advanced heart failure, or major surgeries. Hemodynamic instability (HI)—marked by hypotension and compensatory tachycardia—is a key precursor that can rapidly progress to multi-organ failure if not detected early. Traditional HI monitoring relies on intermittent blood pressure (BP) measurements, causing detection delays of 15–35 minutes, while continuously available ICU ECG signals remain underused due to difficulty in predicting BP directly from ECG. This study proposes identifying ECG-derived biomarkers that signal impending HI by linking subtle ECG variations to BP fluctuations for earlier intervention. Using the MIMIC-III Clinical and Waveform Databases, we identified ICU patients over 45 who developed CS during hospitalization and did not survive; among 100+ discharge summaries, 15 cases had confirmed in-hospital CS onset, and 6 (4 males, 2 females) showed concurrent hypotension and tachycardia suitable for HI analysis. From their ECG segments, we extracted linear and nonlinear time- and frequency- domain features from 10-, 5-, 3-, and 2-minute windows. A 5-fold cross-validated Random Forest classifier trained on the most relevant (primarily nonlinear) features detected HI onset with 95% accuracy using an optimal 3-minute ECG window.

1. Introduction

Cardiogenic shock (CS) is a life-threatening condition caused by the heart's inability to maintain adequate tissue perfusion, commonly following myocardial infarction (MI), advanced heart failure, or major surgery. Hemodynamic instability (HI)—marked by sustained hypotension (SBP < 90 mmHg) and tachycardia (HR > 100 bpm)—is a key early indicator of CS. In intensive care unit (ICU) settings, early identification of HI is critical, as the transition to full-blown CS can occur within hours [1]. Conventional HI detection typically relies on intermittent monitoring of vital signs (e.g., blood pressure, heart rate) and periodic lab tests [2]. While HR is continuously monitored via noninvasive ECG, continuous blood pressure (BP) measurement requires invasive arterial catheterization, which are reserved for the most critically ill due to procedural risks [3]. Most ICU patients are instead monitored with noninvasive BP devices, recording readings every 10–30 minutes depending on clinical status [4]. This intermittent sampling limits timely detection of HI and is further confounded by vascular memory—delayed vasoregulatory responses that introduce a minimum 5-minute lag in measurable BP changes [5]. These temporal gaps can obscure rapid physiological deterioration, delaying intervention during the early, potentially reversible phase of HI. In contrast, ECG provides a continuous, noninvasive data stream that reflects cardiac electrophysiology and is indirectly linked to hemodynamic function [6]. However, directly estimating BP from ECG has proven difficult due to the complex, nonlinear relationship between the two [7], limiting its clinical applicability. This study proposes a novel strategy: rather than attempting direct BP prediction, it aims to identify ECG-derived biomarkers that precede and signal impending HI. By correlating these ECG features with subsequent BP changes, the goal is to develop an early warning system for HI. This approach shifts the focus from direct BP estimation to uncovering subtle electrophysiological indicators of hemodynamic compromise, offering a new direction for continuous, noninvasive HI monitoring and timely clinical response.

2. Data and Methods

This study utilized the MIMIC-III Clinical Database for Electronic Health Records (EHR) and the MIMIC-III Waveform Database for ECG signals. MIMIC-III comprises de-identified data from over 40,000 ICU pa-

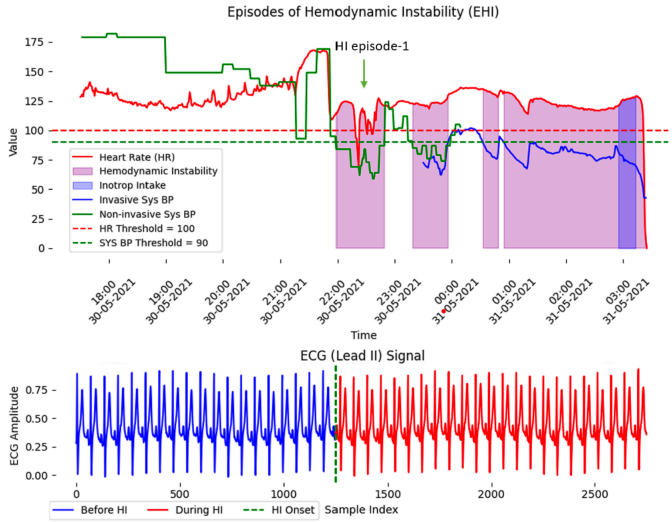


Figure 1. Top: CS progression timeline—HI onset at 22:00 hrs, BP measurement switches to invasive at 23:00 hrs, and inotropes are administered at 3:00 hrs, highlighting delayed intervention due to late HI detection. Bottom: ECG Lead-II signals corresponding to the timeline, segmented into pre- and post-HI onset.

tients admitted to Beth Israel Deaconess Medical Center (2001–2012), including vitals, labs, medications, imaging, and discharge summaries [8, 9]. To investigate hemodynamic instability (HI) and cardiogenic shock (CS), we identified ICU patients who developed CS and did not survive. Cases were initially screened using ICD-9 codes, followed by manual review of over 100 discharge summaries to confirm 15 patients with in-hospital CS onset. From the MIMIC-III Waveform Matched Subset, we extracted ECG and corresponding numeric data (e.g., blood pressure, heart rate) to identify episodes of hemodynamic instability (EHI), defined as systolic BP < 90 mmHg with heart rate > 100 BPM sustained for ≥ 10 minutes. Six of the 15 CS cases met this criterion. The final cohort included four males and two females, aged 46-82 years (mean 66.17). As shown in Figure 1, we aligned ECG segments to EHI onset, using one hour of ECG data before EHI as the stable state and ECG during EHI as the unstable state. Figure 1 also highlights the delay in HI detection under intermittent monitoring: the first EHI episode occurred at 22:00 hrs, followed by 10-minute interval monitoring. Invasive BP recording (blue line) began only at 23:00 hrs, and therapeutic intervention for stage C CS was initiated at 03:00 hrs. ECG Lead II signals (125 Hz sampling rate) were denoised using wavelet filtering and a bidirectional bandstop filter to suppress powerline interference [7]. Preprocessed signals were segmented into non-overlapping windows of 10, 5, 3, and 2 minutes to identify the optimal duration for analysis. A total of 35 features were extracted per window, covering time and frequency domains (Table 1). To optimize feature selection, Recursive Feature Elimination with Cross-Validation (RFECV) was applied using a Random Forest (RF) classifier. Features were iteratively removed based on importance scores, with 5-fold cross-validation ensuring robustness and preventing overfitting [10]. To ensure a robust and comprehensive evaluation, we utilized four machine learning classifiers for binary classification: two linear models—Logistic Regression and Linear Discriminant Analysis (LDA)—and two non-linear models—Random Forest and Support Vector Machine (SVM). Model performance was assessed using stratified 5-fold cross-validation (CV) to mitigate bias and ensure generalizability. Additionally, we computed the receiver operating characteristic (ROC) curve and evaluated key performance metrics, including accuracy, sensitivity, specificity, and F1 score, to provide a well-rounded assessment of each classifier's effectiveness.

3. Results and Discussion

Using RFECV, a refined subset of features was selected from the initial set of 35 for each time window. For the 10-minute windows, 18 features were identified, with a relatively uniform contribution across all feature families (Figure 2). In the 5-minute windows, 34 features were retained, with the nonlinear time-domain features contributing the most at 39%. The 3-minute windows resulted in the selection of 22 features, predominantly from the linear and nonlinear time-domain families, while the frequency-domain features showed reduced relevance. For the 2-minute windows, 30 features were selected, with the nonlinear time-domain features again dominating at 40%. Overall, the nonlinear time-domain feature family consistently demon-

Table 1. Significant Linear and Non-Linear Features in Time and Frequency Domains

Domain	Category	Feature	Count
Time	Linear	Maximum, Minimum, Mean, Median, Standard Deviation, Variance, Kurtosis, Skewness, Number of Zero-Crossing, Positive to Negative Ratio, Mean Absolute Value	11
	Nonlinear	Lempel-Ziv Complexity, Hjorth Mobility, Hjorth Complexity, Fisher Information, Petrosian Fractal Dimension, Katz Fractal Dimension, Higuchi Fractal Dimension, Detrended Fluctuation, Approximate Entropy, Sample Entropy, Permutation Entropy, SVD Entropy, Shannon Entropy, Renyi Entropy	14
Frequency	Linear/Nonlinear	Maximum, Minimum, Mean, Median, Standard Deviation, Variance, Kurtosis, Skewness, Spectral Entropy, Band Power	10
Total Features			**35**

strated high relevance across all window lengths, whereas the frequency-domain features diminished in importance as the window duration decreased. The consistent dominance of nonlinear time-domain features across all window lengths suggests their strong discriminative power in characterizing the underlying physiological signals, regardless of temporal resolution. As the window length decreases, the declining relevance of frequency-domain features indicates that shorter time segments may not capture sufficient spectral information, thereby reducing their utility. This emphasizes the robustness of nonlinear time-domain features for feature selection in dynamic, time-constrained monitoring scenarios. Among the nonlinear time-domain features, Approximate Entropy, Sample Entropy, Permutation Entropy, and Rényi Entropy consistently emerged as the most significant across all time windows. In the frequency domain, Spectral Entropy stood out as a key nonlinear contributor. The consistent dominance of nonlinear features—particularly from the time domain—across all window lengths underscores their critical role in capturing the complex, irregular dynamics of ECG signals. This highlights their importance in the accurate detection of hemodynamic instability (HI), especially in scenarios requiring quick and early diagnosis. Among the linear statistical features in the time domain, median, standard deviation, variance, kurtosis, skewness, and the positive-to-negative sample ratio (PNR) consistently exhibited high importance scores during RFECV-based feature selection. Notably, PNR emerged as one of the top-ranked features, highlighting its effectiveness in quantifying asymmetry and polarity shifts in the ECG waveform. This suggests that PNR is particularly sensitive to morphological variations associated with hemodynamic instability (HI), reinforcing its value as a robust linear descriptor in the context of early HI detection. Table 2 presents a comparative analysis of model performance for hemodynamic instability (HI) detection across varying ECG segment lengths, using the selected feature subsets. The evaluation includes both linear models—Linear Discriminant Analysis (LDA) and Logistic Regression (LR)—and nonlinear models—Random Forest (RF) and Support Vector Machine (SVM). Among all classifiers, the RF model consistently outperformed the others across all time windows, as highlighted in Table 2. The 3-minute window yielded the highest classification performance, achieving an accuracy of 95% and an F1 score of 94%. The 2-minute window followed closely, with both metrics at 94%. Notably, these were also the time windows in which nonlinear entropy-based features demonstrated the highest relevance (Figure 2). While previous studies have shown that well-engineered, interpretable models using nonlinear features can achieve strong performance [11]-[13], in this case, the complexity of the HI detection task favored nonlinear classifiers—particularly the RF model—despite the dominant contribution of nonlinear features. To further substantiate these results, the Area Under the Curve (AUC) of the RF model was computed for the 3-minute and 2-minute windows using 5-fold cross-validation. The model achieved a mean AUC of 0.97 and 0.99, respectively, for these durations. These findings underscore the potential for rapid and reliable HI detection using as little as 2–3 minutes of ECG data, offering a significant advantage over traditional monitoring approaches.

4. Conclusions

This study highlights the efficacy of ECG-derived biomarkers for early detection of hemodynamic instability (HI), addressing the limitations of intermittent blood pressure (BP) monitoring in intensive care settings. By applying machine learning to time- and frequency-domain features extracted from ECG signals, we achieved a detection accuracy of 95% using a 3-minute data window with a random forest classifier. This method provides a timely

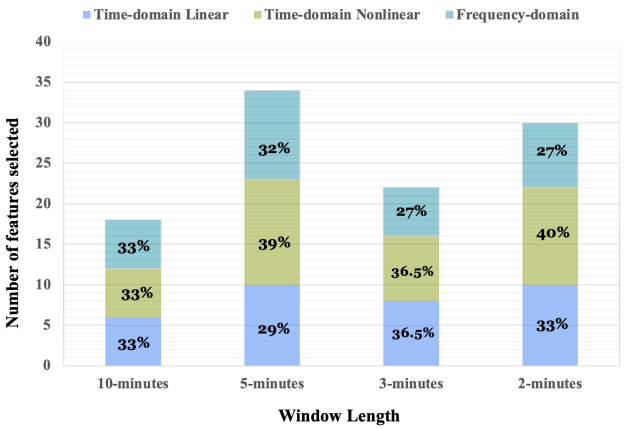


Figure 2. Features selected using the RFECV method, with the number of features and their percentage contribution to HI detection shown for different time windows.

Table 2. ML model performance metrics for HI detection across various time windows.

Window Length	Model	Accuracy	F1-Score
10 minutes	**RF**	**0.86**	**0.86**
	SVM	0.63	0.63
	LR	0.64	0.64
	LDA	0.66	0.66
5 minutes	**RF**	**0.89**	**0.89**
	SVM	0.68	0.64
	LR	0.75	0.73
	LDA	0.81	0.81
3 minutes	**RF**	**0.95**	**0.94**
	SVM	0.76	0.73
	LR	0.77	0.76
	LDA	0.82	0.82
2 minutes	**RF**	**0.94**	**0.94**
	SVM	0.77	0.75
	LR	0.81	0.81
	LDA	0.85	0.85

and continuous alternative to traditional BP-based monitoring, enabling earlier identification of HI and reducing the risk of progression to cardiogenic shock (CS). Integrating such a predictive system into critical care workflows has the potential to enhance patient outcomes through earlier intervention and proactive hemodynamic management.

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