

Classification Tree for Risk Assessment in Patients Suffering From Congestive Heart Failure via Long-Term Heart Rate Variability

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Abstract—This study aims to develop an automatic classifier for risk assessment in patients suffering from congestive heart failure (CHF). The proposed classifier separates lower risk patients from higher risk ones, using standard long-term heart rate variability (HRV) measures. Patients are labeled as lower or higher risk according to the New York Heart Association classification (NYHA). A retrospective analysis on two public Holter databases was performed, analyzing the data of 12 patients suffering from mild CHF (NYHA I and II), labeled as lower risk, and 32 suffering from severe CHF (NYHA III and IV), labeled as higher risk. Only patients with a fraction of total heartbeats intervals (RR) classified as normal-to-normal (NN) intervals (NN/RR) higher than 80% were selected as eligible in order to have a satisfactory signal quality. Classification and regression tree (CART) was employed to develop the classifiers. A total of 30 higher risk and 11 lower risk patients were included in the analysis. The proposed classification trees achieved a sensitivity and a specificity rate of 93.3% and 63.6%, respectively, in identifying higher risk patients. Finally, the rules obtained by CART are comprehensible and consistent with the consensus showed by previous studies that depressed HRV is a useful tool for risk assessment in patients suffering from CHF.

Index Terms—Congestive heart failure (CHF), data mining, decision tree, heart rate variability (HRV).

I. INTRODUCTION

CONGESTIVE heart failure (CHF) is a pathophysiological condition due to an abnormal cardiac function, which is responsible for the failure of the heart to pump blood as re-

quired by the body. CHF severity can be measured with the symptomatic classification scale of the New York Heart Association (NYHA) [1]. Classification via NYHA scale has been proved to be a risk factor for mortality [2], [3].

Heart rate variability (HRV) is the variation over time of the period between consecutive heartbeats (RR intervals) [4] and is usually extracted from electrocardiographic signal (ECG) recorded through a noninvasive technique. HRV is commonly used to assess the influence of the autonomic nervous system (ANS) on the heart [5]. HRV has been widely studied in patients suffering from CHF [6]–[19]. Many studies demonstrated that HRV is an effective means for the risk assessment of mortality [8], [10], [13]–[15], [17].

A number of studies [6], [7], [11], [12], [18] demonstrated the relationship of HRV measures and the NYHA classification scale. In our previous papers, we demonstrated that HRV might be used to detect CHF using short-term [20] or long-term measures [21]. Moreover, we proposed a classifier based on short-term HRV measures to individuate severity of CHF [22].

Over the past years, automatic classifiers, based on several clinical and instrumental parameters, have been proposed to support CHF assessment [23]. However, to the best of the authors' knowledge, these classifiers are not based on HRV features, except for those proposed by Yang *et al.* [24] who included HRV features but did not provide details about the related processing.

In this study, we present a classifier, based on long-term HRV measures, for the individuation of high-risk conditions in CHF patients, estimated via NYHA scale. Patients were considered at higher risk if suffering from severe CHF (NYHA III or IV) and at lower risk if suffering from mild CHF (NYHA I or II).

The method we used to develop the classifier is classification and regression tree (CART). CART, developed by Breiman [25], has been used in several applications of pattern recognition especially for medical diagnosis [26]. The CART algorithm iteratively splits the dataset, according to a criterion that maximizes the separation of the data, producing a tree-like decision structure [25]. CART was applied to HRV measures for other investigations [27]. We adopted CART in previous studies [20], [28], in which a larger dataset was available to train the CART and/or the final classification of the patients was based on a combination of trees. On the contrary, in this study, the selected dataset is small and unbalanced. A number of solutions to the class-imbalance problem were previously proposed at data, feature selection, and algorithmic levels [29]. At the data level, these solutions include many different forms of resampling. At the algorithmic level, solutions include adjusting the costs of the

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various classes so as to counter the class imbalance, adjusting the probabilistic estimate at the tree leaf (when working with decision trees) and adjusting the decision threshold. As regards feature selection, Zheng *et al.* [30] proposed a framework to deal with imbalanced dataset, showing the importance of feature selection methodology and performance measurement.

In this study, we adopted CART algorithms with a feature selection algorithm in order to handle a small and unbalanced dataset. We compared the performance of the proposed method with a standard data-level-based method to deal with imbalance that is the oversampling technique. We preferred a data-level solution as the benchmark since the algorithmic level solutions require the probability and the misclassification cost of the class that are difficult to estimate particularly in this case, as the rare class is also the milder one. Moreover, we compared the results of the proposed method with other classifiers based on decision trees, i.e., C4.5 [31] and random forest (RF) [32].

We implemented decision trees as they provide a classification model, i.e., “if . . . then” rules, which can be easy to read and interpret. This is crucial in medical applications [33] in which the physician is personally responsible of the diagnosis.

The HRV measures were extracted from two Holter monitor public databases [34] by using only open source and validated HRV toolkit software in order to allow other scientists to reproduce our results.

II. METHODS

A. Data

We analyzed 44 nominal 24-h recordings from 12 lower risk patients (LRPs) suffering from mild CHF (NYHA Classes I and II) and 34 higher risk patients (HRPs) suffering from severe CHF (NYHA Classes III and IV). Only patients with a satisfactory signal quality, as described in the Section II-B, were selected as eligible. The data were retrieved from the Congestive Heart Failure RR Interval Database [34] and from the BIDMC Congestive Heart Failure Database [34]. The former database includes RR intervals extracted from 24-h ECG-Holter recordings of 8 men, 2 women, and 19 unknown-gender subjects, aged 34–79 years (55 ± 11 years). The original ECG recordings were digitized at 128 samples per second, and the beat annotations were obtained by automated analysis with manual review and correction. The latter database includes long-term ECG recordings from 11 men and 4 women, aged 22–71 years (56 ± 11 years). The recordings were sampled at 250 samples per second and were automatically annotated. There were no significant differences between the two database in terms of age (*t*-test *p*-value: 0.85) and gender (exact Fisher’s test *p*-value: 0.83) profiles.

B. Long-Term HRV Measures

We performed standard long-term HRV analysis on nominal 24-h recordings according to International Guidelines [5]. The series of normal-to-normal (NN) beat intervals were obtained from the beat annotation files of the selected databases and the NN/RR ratio was computed as the fraction of total RR intervals classified as NN. This ratio has been used as a measure

of data reliability, excluding recordings with a ratio less than a threshold. We chose the threshold of 80% [34] as it was a satisfactory tradeoff between numbers of included subjects and quality of NN signals. Using this technique, 3 recordings were excluded (1 LRPs and 2 HRPs) and the final dataset consisted of 41 subjects: 11 LRP and 30 HRPs. There were no significant differences between the two subsamples (LRPs versus HRPs) in terms of age profile (*t*-test *p*-value: 0.11). Comparison of gender is not possible as this information is not available in the LRPs.

All the computed basic time- and frequency-domain HRV measures were widely used in literature as reported in International Guidelines [4] and in a recent review on HRV [5]. A number of standard statistical time-domain HRV measures were calculated: AVerage of all NN intervals (AVNN); standard deviation of all NN intervals (SDNN); standard deviation of the averages of NN intervals in all 5-minute segments of a 24-h recording (SDANN); mean of the standard deviations of NN intervals in all 5-minute segments of a 24-h recording (SDNN IDX); square root of the mean of the sum of the squares of differences between adjacent NN intervals (RMSSD); and percentage of differences between adjacent NN intervals that are longer than 50 ms (pNN50). Moreover, pNN10 (that is, percentage of differences between adjacent NN intervals that are longer than 10 ms) was computed because Mietus *et al.* [7] showed that among the family of pNNx measures, pNN10 can provide the maximum separation.

The frequency-domain HRV measures rely on the estimation of power spectral density (PSD) computed in this work by Lomb–Scargle (LS) periodogram [35]. Fast implementation and further detail of LS periodogram can be found elsewhere [35]–[37]. After PSD estimation, six standard frequency-domain HRV measures were calculated: total spectral power of all NN intervals up to 0.4 Hz (TOTPWR); between 0 and 0.003 Hz (ULF); between 0.003 and 0.04 Hz (VLF); between 0.04 and 0.15 Hz (LF); between 0.15 and 0.4 Hz (HF); and ratio of low- to high-frequency power (LF/HF).

C. Statistics

Since not all the HRV measures were normally distributed [38], the data were reported in terms of median, 25th and 75th percentiles, in order to describe distribution of measures in the two groups (LRPs versus HRPs) and univariate differences were assessed by Wilcoxon test.

D. Feature Selection

Even if CART implements a stepwise feature selection, it may happen that one feature is excluded because other variables masked its effect. This could be particularly critical in small and unbalanced dataset. In order to deal with masking and to be sure that the tree included the best subset of features, we adopted the so-called exhaustive search method [39], investigating all the possible combinations of k out of N features (with k from 1 to N). Since the number of features N is 13, we investigated $2^{13} = 8092$ subsets of features, training and testing the same number of classifier, as further discussed. Among the 8092 classifiers, we choose the one with the lowest value of

the misclassification error estimated by tenfold cross-validation approach, as described in the following paragraph. Even if the cross-validated estimate could provide limited information in small and imbalanced dataset, the feature selection improves the classification since it enables to consider combination of n feature with n smaller than the size of available samples.

E. CART Method

The CART algorithm consists of two stages: tree growing and tree pruning [25]. In the former stage, the tree grows by selecting among all the possible splits, which generate the “purer” child nodes where the purest node is the one containing elements of only one class. The outcome of this step is further referred to as the large tree (LT). Among different functions that have been proposed for the measure of the impurity of each node “ t ” [25], we adopted the Gini index criterion [25], which for binary classification can be computed as follows:

$$\text{Gini index}(t) = 1 - \left(\frac{n_i}{n}\right)^2 - \left(\frac{n_j}{n}\right)^2 \quad (1)$$

where “ t ” is the considered node, “ i ” and “ j ” are the two class labels, “ n_i ” and “ n_j ” are the number of subject present at the node belonging to the class “ i ” or “ j ,” respectively, and “ n ” is the number of subject present at the node.

In the latter stage, the LT is pruned according to a minimal cost-complexity function, which relies on the tree size and the misclassification error. The misclassification error is estimated by the inner tenfold cross-validation of the CART. The dataset is randomly divided into ten subsets. One of the subsets is used as independent testing dataset while the other nine subsets are used as training dataset. The tree-growing and pruning procedure is repeated ten times, each time with one of the ten different subsets used as a testing set. The misclassification error is calculated as the percentage of misclassified cases averaged over all the ten subsets.

This procedure is repeated pruning the tree, and for each subtree, the cost complexity function is computed as a linear combination of the number of nodes and of the cross-validated estimated of the misclassification error. The outcome of this stage is referred further to as the best subtree (BST), which is the subtree achieving the lowest value of the cost-complexity function. Further details about minimal cost-complexity pruning can be found in Breiman [25].

The most common measures for binary classification were estimated by tenfold cross-validation, using the formulas reported in Table I, in particular F_1 is one of the most suitable metric for imbalanced class problem, as it is the harmonic mean of precision and sensitivity (recall).

F. Benchmarks

We compared the method proposed in this paper with a standard approach for class-imbalance problem based on over-sampling that is the synthetic minority oversampling technique (SMOTE). The rare class (mild CHF) was oversampled by creating new synthetic rare class samples according to each rare class sample and its k nearest neighbors. Different values of the

TABLE I
BINARY CLASSIFICATION PERFORMANCE MEASURES

Measure	Abbr.	Formula
F_1	F_1	$\frac{2TP}{2TP + FP + FN}$
Accuracy	ACC	$\frac{TP + TN}{TP + TN + FP + FN}$
Precision	PRE	$\frac{TP}{TP + FP}$
Sensitivity	SEN	$\frac{TP}{TP + FN}$
Specificity	SPE	$\frac{TN}{TN + FP}$
Area Under the Curve	AUC	$\frac{1}{2} \left(\frac{TP}{TP + FN} + \frac{TN}{TN + FP} \right)$

TP: the number of HRPs correctly classified.

TN: the number of LRPs correctly classified.

FP: the number of LRPs incorrectly classified as HRPs.

FN: the number of HRPs incorrectly classified as LRPs.

parameter k (from 2 to 8) were tested and the value with the higher F_1 measure was selected. As classifiers, we also adopted two other decision-tree-based methods: C4.5 [31] and RF [32].

G. Implementation Details

The HRV extraction and analysis was performed using PhysioNet’s HRV Toolkit [34]. We chose this toolkit as it is an open source and a rigorously validated package. In particular, the implementation of the LS periodogram adopted in this paper is the *lomb.c* program available from Physionet [36].

The feature selection and classification were performed by in-house software developed in MATLAB version R2009b (The MathWorks, Inc., Natick, MA, USA). In particular, CART was implemented by utilizing the methods and construction of the MATLAB class *classregtree*. The benchmark methods were implemented in Weka.

III. RESULTS

Table II shows the descriptive statistics of HRV measures in LRPs and HRPs. Among time-domain measures, SDNN, SDANN, SDNN IDX, and RMSSD were significantly reduced in HRPs. All the frequency-domain measures were significantly depressed in HRPs with the only exception of LF/HF.

The performance of the proposed method and benchmarks are reported in Table III. The proposed method achieved higher values of F_1 measure and accuracy than the benchmarks. The higher performances were obtained by two different combinations of features: “TOTPWR, pNN10, pNN50, SDNNIDX” and “ULF, TOTPWR, pNN50.”

The selected BSTs are represented in Figs. 1 and 2. Each terminal node is the graphical representation of a set of “if . . . then” rules. For instance, the terminal node 2 in the Fig. 1 can be read as: “if TOTPWR is lower than 11080.25 ms², the subject is classified as a higher risk patient.”

In the model shown in Fig. 1, the initial variable selected by CART (at node 1 split) was TOTPWR. The subjects whose

TABLE II
COMPARISON OF HRV BETWEEN THE TWO GROUPS

Measure	Units	LRPs			HRPs			Wilcoxon test p-value
		25 th	50 th	75 th	25 th	50 th	75 th	
AVNN	ms	631	674	785	620	697	778	0.803
SDNN	ms	184	399	525	67	90	180	0.003
SDANN	ms	63	87	206	47	60	76	0.026
SDNNIDX	ms	79	177	295	25	50	87	0.005
RMSDD	ms	242	515	675	18	110	234	0.003
pNN10		26.78	39.66	55.33	27.50	33.48	43.76	0.385
pNN50		0.52	3.02	7.25	0.40	1.70	2.94	0.257
TOTPW	ms ²	20145	132516	184566	3660	6718	27751	0.005
ULF	ms ²	3991	8914	28656	1852	3575	6430	0.013
VLF	ms ²	1874	12553	16577	202	622	2604	0.005
LF	ms ²	4328	28813	45652	133	595	5234	0.003
HF	ms ²	9013	60783	102470	101	1691	11678	0.003
LF/HF		0.44	0.45	0.47	0.44	0.46	0.64	0.222

25th: 1st quartile / 25th percentile; 50th: median / 2nd quartile / 50th percentile; 75th: 3rd quartile / 75th percentile.

TABLE III
CLASSIFICATION PERFORMANCE MEASUREMENTS OF THE SELECTED CLASSIFIER ESTIMATED BY TENFOLD CROSS-VALIDATION

Classifier	Methods to handle class-imbalance	TP #	FN #	TN #	FP #	F1 %	ACC %	PRE %	SEN %	SPE %	AUC %
CART	Proposed in the current study	28	2	7	4	90.3	85.4	87.5	93.3	63.6	78.5
RF	SMOTE (k=5)	25	5	18	4	84.7	82.7	86.2	83.3	81.8	82.6
C4.5	SMOTE (k=5)	25	5	19	3	86.2	84.6	89.3	83.3	86.4	84.8
CART	SMOTE (k=5)	22	8	17	5	77.2	75.0	81.5	73.3	77.3	75.3
RF	None	26	4	4	7	82.5	73.2	78.8	86.7	36.4	61.5
C4.5	None	22	8	5	6	75.9	65.9	78.6	73.3	45.5	59.4
CART	None	29	0	0	11	84.5	73.2	73.2	100.0	0.0	50.0

TOTPW is lower than 11080.25 ms² were all correctly classified as HRPs. CART selected pNN50 for the second node split. In this node split, the subjects whose pNN50 were lower than 1.22% were classified as LRPs. Otherwise, the following classification split was based on pNN10, that is, if it is lower than 36.093%, the subject was classified as HRP; otherwise, a final classification split is based on SDNNIDX with a threshold of 100.910 ms².

In the model shown in Fig. 2, the initial variable selected by CART (at node 1 split) was ULF. The subjects whose ULF is higher than 21026.850 ms² were correctly classified as LRPs. CART selected TOTPW for the second node split. In this node split, the subjects whose TOTPW were lower than 11080.250 ms² were classified as HRPs. A final classification split is based on pNN50, that is, if it is lower than 1.22%, the subject was classified as LRP, otherwise as HRP.

IV. DISCUSSION

In this study, we developed a classification tree based on standard long-term HRV for risk assessment in patients suffering from CHF.

The classifiers based on the combinations of standard long-term HRV measures “TOTPW, pNN10, pNN50, SDNNIDX”

and “ULF, TOTPW, PNN50” enable distinguishing HRPs from LRPs with an accuracy rate of 85.4%, a sensitivity rate of 93.3%, and a specificity rate of 63.6% (tenfold cross-validation estimates). The existence of these two best combinations can be explained by the high correlation between HRV measures [5], [38].

The selection of pNN10 in the best combination would confirm its discrimination power proved by Mietus *et al.* [7], even if the differences in pNN10 values between the two groups were lower than those of other measures, as shown by the statistical analysis performed in the current study. As concerns pNN50, Mietus *et al.* [7] showed that pNN50 failed to distinguish the LRPs and HRPs, while pNN50 is used in the BSTs (see Fig. 1 node 2 and Fig. 2 node 4). This apparent inconsistency may be explained by considering that pNN50 could have a discriminative power only for the subgroups of patients which had high value of TOTPW (TOTPW > 11080.25 ms²), consistent with the absence of statically significant differences between the two patient groups.

The sets of rules of both the models are clinically consistent, even if CART does not use any medical priori knowledge. In fact, the main clinical result of this research is that terminal node classifying as HRPs are on the left, thereby revealing

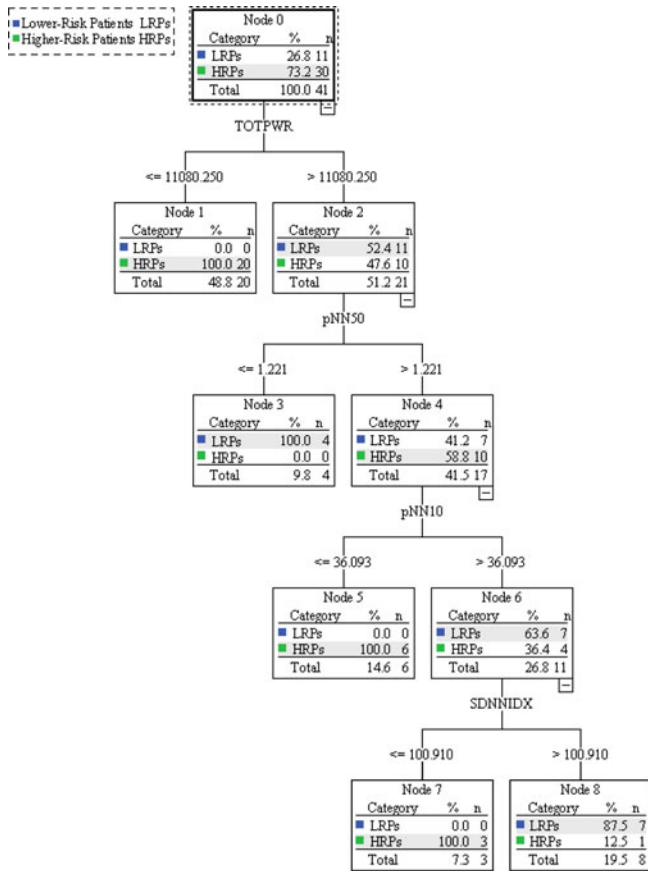


Fig. 1. Final model tree for the combination of HRV features: TOTPWR, pNN50, pNN10, and SDNNIDX.

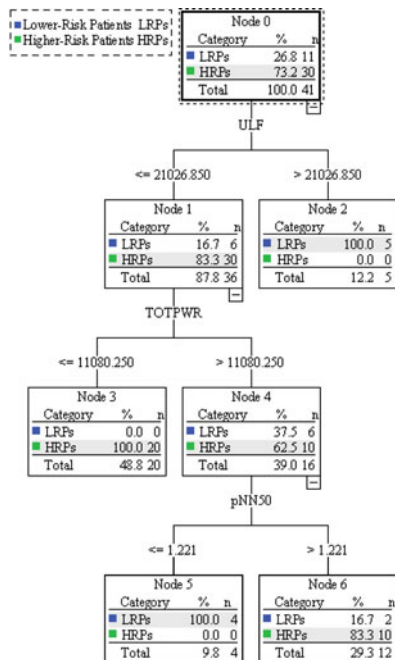


Fig. 2. Final model tree for the combination of HRV features: ULF, TOTPWR, and pNN50.

lower values of the splitting features for severe CHF patients (with the only exception of pNN50). This is coherent with the statistical analysis performed in the current study and with the results showed by Casolo *et al.* [18], Panina [6] and Arbolishvili [12]. It should be emphasized that the findings of Casolo *et al.* [18], Panina *et al.* [6], and Arbolishvili *et al.* [12] were obtained adopting different methods for PSD estimation. Several methods were proposed in literature in order to estimate PSD of RR intervals [4], [5]. Particularly, many PSD estimators are based on the hypothesis that the signal under examination is uniformly sampled [36]. In contrast, the RR series is unevenly sampled and requires resampling before PSD estimation. In this paper, LS periodogram [35] was chosen as it estimates PSD of unevenly sampled signals without the requisite of resampling and its estimation has been proven to be more accurate than fast Fourier transform (FFT)-based method for RR data [40].

In relation to the methodology, the exhaustive research for feature selection improved the classification performance compared to CART model obtained using all the features. Moreover, as the study dataset is imbalanced, we compared the performance of the proposed method with SMOTE, an approach based on oversampling to handle the class-imbalance problem and with other two widely used decision-tree methods. The proposed method achieved the highest performance in terms of accuracy rate and F_1 , which is one of the most suitable metrics for rare class problems [41]. Compared to our previous studies, based on short-term measures [22], the classifier proposed in the current studies achieved an higher accuracy and sensitivity (85.4% versus 79.3% and 93.3% versus 82.4%, respectively), even if with a lower specificity (75.0% versus 63.6%). This result led us to consider long-term HRV measures more effective for the individuation of higher risk patients than short-term ones.

As regards the other classifier proposed in literature for CHF assessment, Guidi [23] compared different algorithms to automatically classify CHF patients in three groups (mild, moderate, and severe) and achieved an accuracy of 86% (independent set estimate; sensitivity and sensibility are not reported) by using neural network. Yang *et al.* [24] proposed a classifier based on support-vector machine, which achieved an accuracy of 74% (tenfold cross-validation estimate) in discriminating between mild CHF (NYHA I) and moderate/severe CHF patients (NYHA II and III). We underline that the classifier proposed by Guidi [23] was based on anamnestic and instrumental data (not including HRV measures), and the one by Yang *et al.* [24] was based on 12 parameters, including LF/HF and other parameters from clinical tests (blood test, echocardiography test, electrocardiography test, chest radiography test, and 6-min walk distance test). For that reason, some parameters needed by the automatic classifier proposed by Guidi [23] or Yang *et al.* [24] should be entered by physicians, while the adoption of only HRV measures, as in the current study, enables a completely automatic assessment.

Our study had the following limitations related to the employed Holter databases: 1) a small and unbalanced dataset; 2) the differences in the sampling frequency of ECG recordings; and 3) the different extraction procedures of NN intervals

(for instance, some recordings were not manually reviewed and incorrect RR detections due to artifact may occur).

The small sample size could result in biased cross-validated performance estimates, even if we adopted strategies (feature selection and tree pruning) to avoid overfitting and to increase the generalization ability. A study with a larger dataset would be useful to confirm the generalization of our findings. Unfortunately, to the best of the authors' knowledge, a larger public dataset is not available and the choice of only public databases (and freely available HRV software) enables other researchers to reproduce our results and compare different classification methods.

As regards the imbalanced dataset problem, we adopted a standard approach (oversampling) as a benchmark to compare the proposed method, as previously described.

As regards the sampling frequency of ECG, it should be remembered that finite sampling frequency introduces an error in the RR interval measurement, as previously shown by Merri *et al.* [42]. However, a sampling rate of 128 Hz, which is the lowest sampling rate of the recordings used in this paper, has been found to be accurate enough to locate the R-peaks and, hence, compute HRV [5]. Finally, in order to handle unreliable RR interval measurements due to artifacts, following previous studies, the automated outlier removal provided by the adopted software was performed and a measure of data reliability (NN/RR) was adopted to discard unreliable results, as described in Section II. In the future research, we are planning to develop a similar study on a larger (although nonpublic) dataset of ECG recordings digitalized at the same sampling frequency and annotated with a stated procedure, i.e., the database of Regione Campania Network [43]. Moreover, nonlinear [44], [45] and/or point process time-frequency [46] analysis could provide additional useful measures for automatic classification. Finally, the classification algorithms could be integrated in portable sensing devices [47]–[49].

We conclude that the long-term HRV measures enable higher risk patients to be distinguished from lower risk ones. The classification trees developed achieved an accuracy rate of 85.4%, a sensitivity rate of 93.3% and a specificity rate of 63.6% (tenfold cross-validation estimates) using the combination of features "TOTPWR, pNN10, pNN50, SDNNIDX" and "ULF, TOTPWR, PNN50." Finally, our results are consistent with the consensus that depressed HRV values are associated with higher cardiovascular risk.

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