Interpretable machine learning models to support differential diagnosis between Ischemic Heart Disease and Dilated Cardiomyopathy

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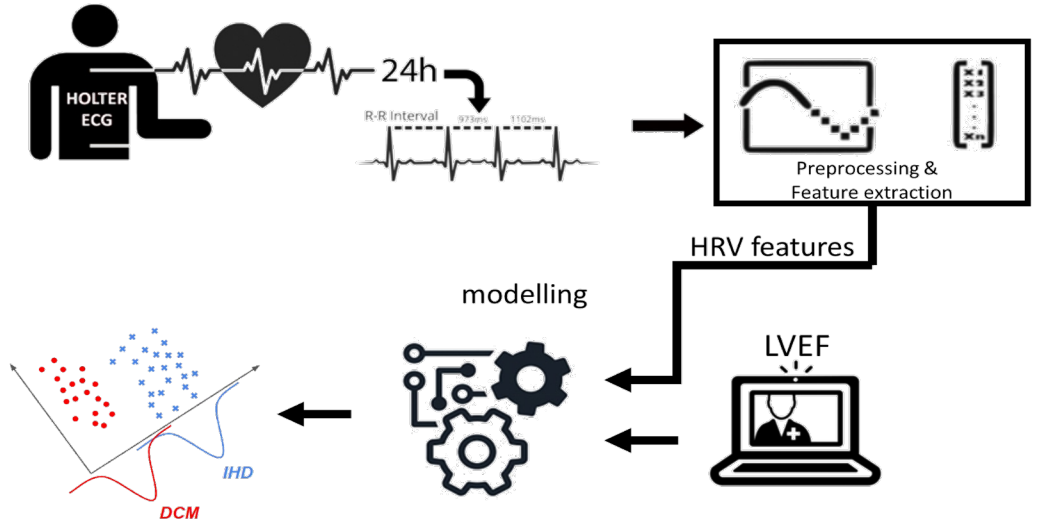
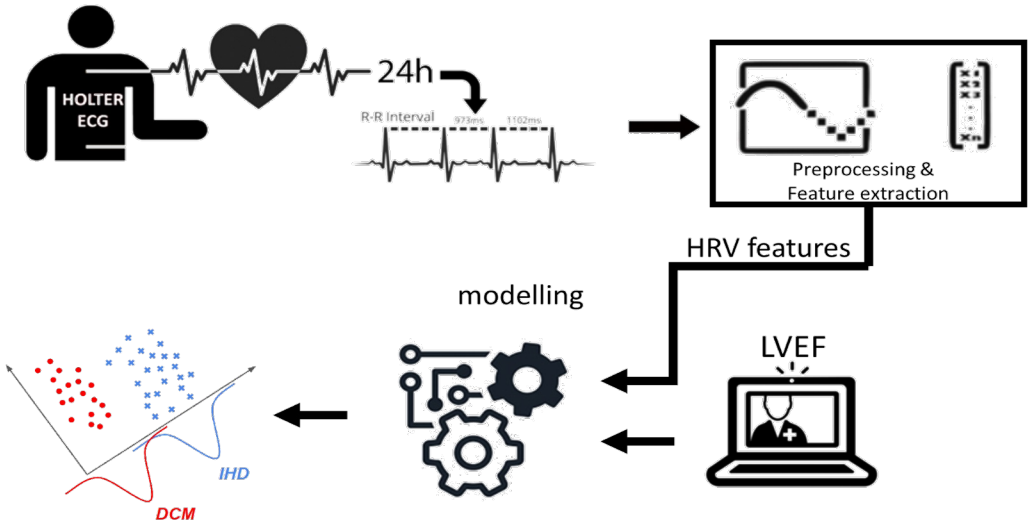


Research project

- Main aim: development of predictive models for classification of different cardiovascular pathologies
- Those models are based on features extracted by processing the data obtained by using non-invasive and highly available diagnostic techniques



Ischemic Heart Disease (IHD) and Dilated Cardiomyopathy (DCM)

- IHD and DCM are two of the most important cardiovascular diseases and the leading cause of mortality worldwide

- The differential diagnosis:
  - can often be difficult
  - only invasive, or often not readily available exams can provide a definite diagnosis

Heart Rate Variability (HRV) and Left Ventricular Ejection Fraction (LVEF)

- LVEF is one of the most often used variable for measuring heart function and predicting outcomes
- Drawbacks:
  - late reduction only in patients with advanced cardiac disease
  - low reliability in patients with left ventricular hypertrophy and volume reduction
  - very poor inter- and intra-observer variability
- The HRV measurement is used to quantify cardiac autonomic activity as a result of sympathetic and parasympathetic activity interaction and is shown to be a helpful tool for diagnosis
- Changes in HRV might give crucial prognostic information

Machine learning models for computer-aided diagnosis

- The limited interpretability of produced black-box models still creates dissatisfaction among the clinicians

- Interpretable models (e.g. classification trees, naive Bayes, and linear/logistic regression algorithms):
  - provide output information about a certain disease
  - help to intrinsically evaluate the plausibility of the model by examining the selected thresholds and branches
  - end-users and healthcare workers can examine the logic behind prediction models

HRV acquisiotion and processing

- 24-hour ECG Holter monitoring session with a three-channel tracking record
- The data was analyzed using a MATLAB (MathWorks) program
- Segments were interpolated with cubic spline and resampled at 2 Hz
- Linear and non-linear HRV parameters were obtained for each segment
- The median of all features from valid 5 min segments during 24h were calculated

HRV parameter	Definition
MeanRR (ms)	mean of RR intervals
SDNN (ms)	standard deviation of RR intervals
RMSSD (ms)	root mean square of the squared differences of successive RR intervals
NN50	number of differences of successive RR intervals greater than 50ms
pNN50	proportion of NN50 divided by the total number of RR intervals
LF (ms^2)	Low Frequency Power (from 0.04 to 0.15Hz)
HF (ms^2)	High Frequency Power (from 0.15 to 0.40Hz)
LF/HF	Low Frequency Power/High Frequency Power
LFn	Low Frequency Power / Total Power
HFn	High Frequency Power /Total Power
betaExp (ms^2/Hz)	Beta exponent
SD1 (ms)	short-term variability of the RR sequence – from Poincaré Plot
SD2 (ms)	long-term variability of the RR sequence – from Poincaré Plot
SD1/SD2	short-term variability / long-term variability of the RR sequence
FD	Fractal dimension

Classification models

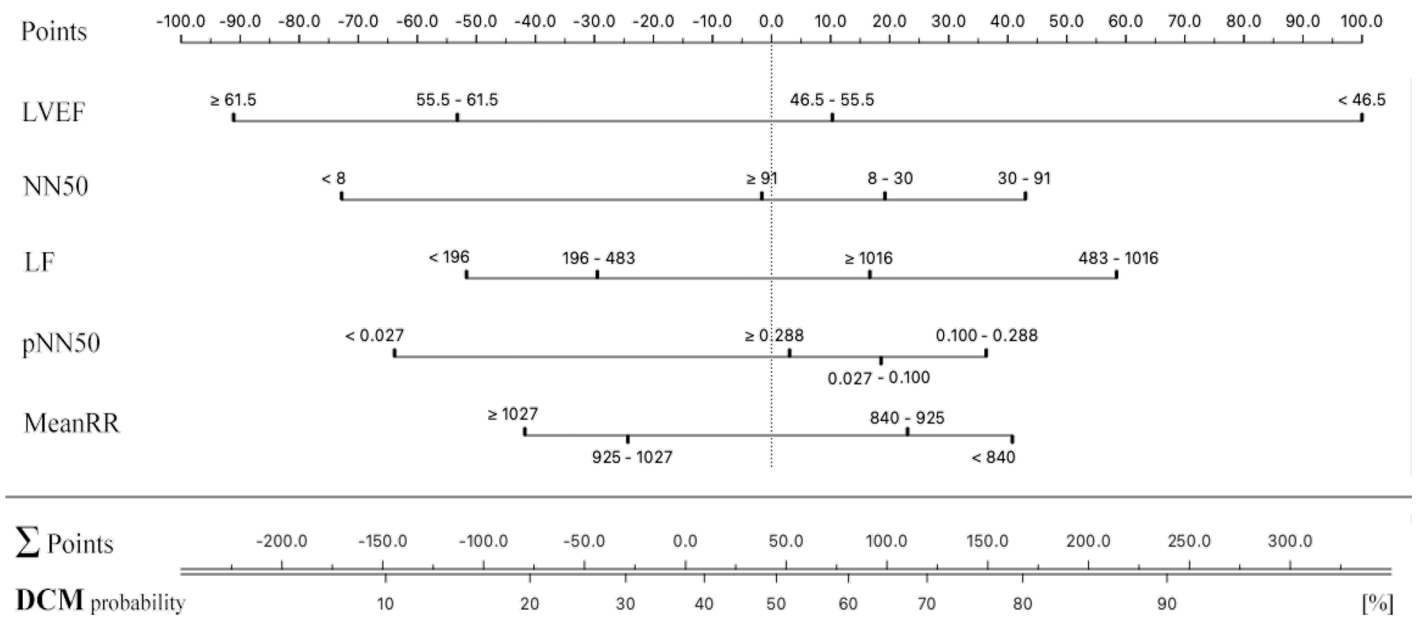
- The models were built considering HRV features together with LVEF
- Classification trees: simple visualization, clinicians can follow a set of rules and thresholds, it is possible to evaluate which are the most important features
- The logistic regression and naive Bayes: nomogram, a basic and self-explanatory visualization, reveal the structure of the model and the relative influences of the features on the class probability

Results

Model	Accuracy	AUC
Classification tree	0.671	0.729
Logistic regression	0.674	0.674
Naive Bayes	0.735	0.740

- Naive Bayes outperformed other interpretable machine learning approaches (logistic regression and classification tree) with a moderately high classification accuracy of 73.5%

- The longest length of the feature LVEF implies that is the most discriminatory feature for the two groups
- The asymmetry around zero implies that the length to the right side is more important for the classification of DCM and vice versa
- The nomograms allow further validation of the produced model by observing the thresholds



Further developments

- In collaboration with Cardiology Department of the Trieste University Hospital (Cattinara) a particular subgroup was selected
  - Subjects in which the diagnosis is even more challenging due to border line LVEF values (LVEF in a range of 40-55%)
- Develope models able to correctly classify DCM and IHD in subjects with LVEF values in the 40-55% range using, in addition to HRV parameters, another non-invasive parameter obtained through echographic imaging, the global longitudinal strain (GLS)

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