A Computational Model for Heart Failure Stratification

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Abstract

Heart failure (HF) is a kind of serious cardiovascular diseases, leading to an increasing burden imposed on public healthcare. Early diagnosis and proper treatment of HF are essential to reducing its morbidity and mortality. In spite of the implementation of clinical guidelines for HF, early recognition and stratification of HF risk remain unsolved. In this work, we supposed a computational model to classify HF stages. With aid of Monte Carlo simulation, Naïve Bayesian Classifier (NBC), Support Vector Machine (SVM) and Radial Basis Function Network (RBF) etc. models were investigated.

On the basis of the model assessment, an optimum classification model constitutive of SVM was derived. The model was tested on 389 subjects. The results show that 81.06% cases in total are consistent with the outcomes by AHA/ACC staging system. This work may offer a quantitative tool for HF stratification and facilitate early diagnosis for HF.

1. Introduction

Heart failure (HF) is one of the major causes of death and hospitalization, and worldwidely it is rapidly becoming the most expensive disease to manage [1,2]. Early diagnosis and treatment of HF are essential to reducing its morbidity and mortality. HF severity is usually evaluated according to the American Heart Association (AHA) /American College of Cardiology (ACC) staging system, which focuses on the progression and worsening of the condition over time [3].

For proper treatment of HF, it is vital to stratify risk in HF patients, especially for those in early stages. However, due to reasons like uncertainty in clinical practice and influences of clinicians' personal preference and qualitative evaluation, diagnosis by clinical assessment through current guidelines is difficult and is only correct in less than half of the cases confirmed by echocardiography [4]. For solving the problem, objective and quantitative models for identifying patients' HF risk stages need to be explored. Therefore, in this study, we present a novel intelligent model for HF risk stratification. The selection of classification algorithm is a core step in model construction, thus Monte Carlo simulation (MCS) is employed to ascertain optimal algorithms from multifarious choices.

2. Materials and methods

The modeling process is divided into three steps: First, MCS is applied to determine the optimal classification algorithms for the datasets. Then, the statistical characteristics of clinical data are analyzed. Finally, the proper model for HF risk stratification is designed based on the MCS results and the features of clinical data.

2.1. Monte Carlo simulation

Monte Carlo simulation (MCS) is a technique measuring the impact of uncertainty in forecasting models [5]. In this study, MCS is used to determine proper model methods for datasets with different characteristics. The procedure is as follows:

Step 1. Generate a set of random inputs. In this study, we input three features into a dichotomous simulation model. The features are in the form of continuous, categorical, or binary. The description of the model is shown in Figure 1. The classifier is used to assign class labels (A or B) to the testing instances whose features are X_1, X_2 and X_3.

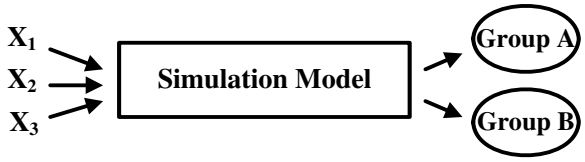

Figure 1. Schema of the simulation model.

Regarding the factors that may affect the classification results, we take account of five aspects that vary generally in different tasks [6]: the distribution types of variables, the sample size, the proportion of two groups' sample size, the proportion of the groups' covariance and effect size. A detailed description of these five parameters used in this study is provided in Table 1.

Step 2. Create a parametric model with RBF, NBC, or SVM, and then put the random samples into it.

Step 3. Evaluate the model and store the results as Y_i, including overall recognition accuracy, sensitivity, and specificity for each method.

Step 4. Repeat steps 2 and 3 for $i = 1$ to n. We set $n = 1000$ in our project to draw a realistic estimation.

Step 5. The simulation results are the average of overall accuracy rates, sensitivities, and specificities of the 1000 Monte Carlo simulation runs. The results are analyzed by summary statistics, and optimal classification algorithms under various conditions are obtained.

2.2. Clinical data analysis

2.2.1. Study population

The study was conducted in patients in Zhejiang Hospital, China, from June 2007 to February 2010. Since the study focuses on improving early recognition of HF, patients in ACC stage D, whose symptoms are easy to recognize, were excluded, so the inclusion criteria for all subjects were physician-diagnosis of AHA/ACC stages from A to C. Totally 389 patients were involved in the study, and the numbers of patients in stages A, B, C are 114, 130 and 145, respectively.

2.2.2. Feature selection

The purpose of feature selection is to find out the HF risk stage-specific parameters from medical test result, i.e. blood test, heart rate variability test, echocardiography test, electrocardiography test, chest radiography test, six minutes' walk distance test, and physical test. At first, original clinical parameters of HF were obtained from the hospital. Earned on ANOVA, a parameter set specific for HF risk stratification model ($P<0.05$) is constructed. Moreover, some parameters are added or removed according to the opinions of clinicians.

2.2.3. Statistical analysis

RBF, NBC, and SVM, incorporated with a two-layer decision tree are used to develop the model for HF risk stratification. Figure 2 shows the schema of the classification model. Model 1 divides subjects into two groups: one is HF-prone group (stage A and B); the other is Symptomatic HF group (stage C), and model 2 then identifies subjects as HF high risk group (stage A) or asymptomatic HF group (stage B).

Using Box's M test, we tested the equality of covariance matrices (Stage A+B vs. C, Stage A vs. B). P level of 0.001 is set as significance. Kolmogorov-Smirnov test is applied to examine whether the selected features distributions conform to hypothesized types. The types supported in this study are normal, skew normal, binomial (0-1), and mix distributions.

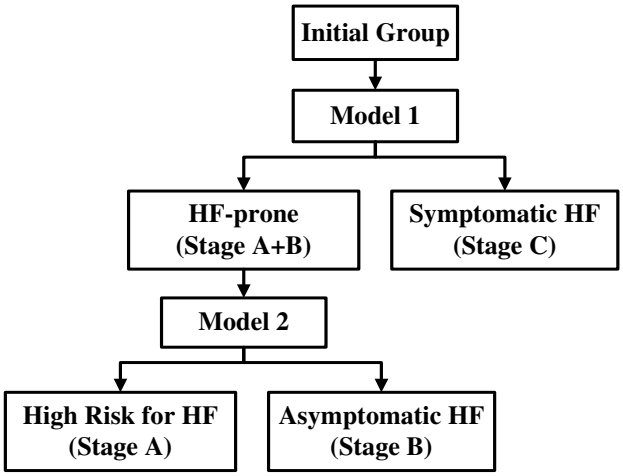

Figure 2. Schema of the HF risk stratification model.

2.3. Selection and verification

On the basis of MCS results and the statistical characteristics of clinical data, optimal HF classification methods are determined. The validity of the models is investigated by analysis of recognition accuracy of all possible model structures.

Table 1. Detailed description of the five parameters used in this study.

Parameter	Description
Distribution type of variables	Normal, skew normal, binomial (0-1) distributions or mix distribution
Sample size (N)	60, 100, or 400 for both groups
Proportion of two groups' sample size (n_1:n_2)	1:1, 1:3 or 1:9
Proportion of two groups' covariance (cov_1:cov_2)	1:1, 1:4 or 1:8
Effect size (d)	0.2, 0.5 or 0.8

3. Results

3.1. Analysis of HF clinical data

Among all 161 clinical testing parameters, we selected 14 and 13 parameters for model 1 and model 2, respectively. Table 2 and table 3 involved parameters and their statistical characters for each model. Among the parameters, PR interval, E/A, IVS, and LVIDs are in skewed distribution, NO, edema, DJV, HR, CF, MI, myocardiopathy and NV are in binomial distribution, while the others are distributed normally ($P<0.05$).

Table 2. Parameters in each model.

Model	Parameters
Model 1	NO, edema, DJV, HR, 6WTD, $VmaxO_2$, SV, BNP, LA, LVIDd, LVIDs, LVPW, LVEF, and Tei-index.
Model 2	CF, PR interval, E/A, IVS, MI, NV, LA, myocardiopathy, LVIDd, LVIDs, LVPW, LVEF, and Tei-index.

NO, nocturnal orthopnea; DJV, distension of jugular vein; HR, hepatojugular reflux; 6WTD, six minutes walk distance; $VmaxO_2$, standard maximum oxygen consumption; SV, strok volume ; BNP, B-type natriuretic peptide; LA, left atrium maximal volume; LVIDd, left ventricle end-diastolic diameter; LVIDs, left ventricle end-systolic diameter, LVPW, left ventricular posterior wall; LVEF, left ventricular ejection fraction; CF, cardiac function; E/A, early (E)/ late (atrial-A) ventricular filling velocity; IVS, interventricular septal thickness; MI, myocardial infarction; NV, nonrheumatic valvular heart disease.

Table 3. Statistical characters of clinical subjects.

Model	Box's M test Sig.	N	$n_1:n_2$	d
Model 1	0.000	389	1.7:1	1.25
Model 2	0.000	245	0.87:1	0.55

3.2. Optimal model determination and verification

Corresponding MCS results were analyzed (Table 4). Through the comparison of sensitivities, specificities, and accuracies of those three methods, SVM turned out to be the most proper method for both models.

Furthermore, in order to verify the validity of the proposed model, all possible model structures constructed by those four algorithms were implemented on HF clinical data. Table 5 reveals that the most satisfactory categorization effectiveness is achieved by the combination of a decision tree and SVM definitely.

4. Discussion and conclusions

A novel computational model constitutive of SVM and decision tree is derived and validated for improving early diagnosis of HF.

It has been reported that ensemble methods often perform extremely well among the great variety of machine learning (ML) algorithmic approaches [7]. In this study, we incorporated NBC, SVM, and RBF into two-level decision trees to create diagnostic prediction rules for HF risk stratification. The choice of stratification algorithm is critical. A common method for assessing ML algorithms is to compare the accuracies of trained classifiers on specific datasets [8]. However, it is onerous and time-consuming to assess the accuracy of all candidates on multi-dimensional problems and select the most accurate one.

Our resultant findings support a strategy for treating proper classification method determination as a statistical estimation by MCS. The results indicate that MCS would conveniently and efficiently dictate the preferred approach based on the data characteristics of instances.

A recent study has shown that only 25% to 50% of the HF cases can be correctly labeled in clinical practice when patients are assessed against current diagnostic criteria [9]. A considerable improvement has been achieved by the selected optimum methods. The results show that 81.06% cases in total are consistent with the outcomes by AHA/ACC staging system. In addition, model 1 was able to predict the outcome with a sensitivity of 77.67 % and a specificity of 99.38%, and model 2 had specificity and sensitivity of 83.70% and 83.82%, respectively.

The present model was selected on the basis of the combination of four ML methods and tested in limited size of patients. For further improving, other intelligent algorithms need to be prospectively analyzed as well and more subjects should be investigated to keep upgrading the classifier.

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Table 4. Relevant MCS results.

cov_1:cov_2		1:4			1:8		
		Sen.	Spe.	Acc.	Sen.	Spe.	Acc.
Model 1	NBC	0.92	0.67	0.86	0.91	0.86	0.90
	SVM	0.97	0.69	0.90*	0.97	0.75	0.92*
	RBF	0.65	0.75	0.68	0.84	0.75	0.82
Model 2	NBC	0.66	0.84	0.75	0.73	0.83	0.78
	SVM	0.73	0.85	0.79*	0.77	0.85	0.81*
	RBF	0.58	0.64	0.61	0.60	0.84	0.72

Model 1: Mix distribution; n_1:n_2=1:3; N=400; d=0.8.
Model 2: Mix distribution; n_1:n_2=1:1; N=100; d=0.5.
Sen.: Sensitivity; Spe.: Specificity; Acc.: Accuracy.
*: Methods with the highest accuracy for each model.

Table 5. Comparison of the performance of models.

Methods	Model 1			Model 2			Acc.
	Sen.	Spe.	Acc.	Sen.	Spe.	Acc.	
R+S	72.82	100	89.39	82.80	83.82	70.90	79.17*
R+B	72.82	100	89.39	84.95	55.88	61.90	72.73
R+R	72.82	100	89.39	80.65	77.94	67.72	76.89
S+R	77.67	99.38	90.91*	80.43	77.94	69.40	78.41
S+B	77.67	99.38	90.91*	84.78	55.88	63.39	74.24
S+S	77.67	99.38	90.91*	83.70	83.82	73.22*	81.06**
B+R	83.50	91.93	88.64	80.00	79.37	71.52*	77.27
B+S	83.50	91.93	88.64	82.35	82.35	74.55**	79.17*
B+B	83.50	91.93	88.64	83.53	60.32	64.85	72.76

R: RBF; S: SVM; B: NBC; R+S: Model 1 is constructed by R and model 2 by S, and so forth.
Sen.: Sensitivity; Spe.: Specificity; Acc.: Accuracy.
**: Models with significantly higher accuracy; *: Higher accuracy.

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