Cardiovascular Risk Stratification in Decision Support Systems: A Probabilistic Approach. Application to pHealth

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Abstract

There is a growing demand for developing personalized and non-hospital based care systems to improve the management of cardiac care. The EPI-MEDICS project has designed a Personal ECG Monitor (PEM) capable of recording a simplified 4-electrode, professional quality 3-lead ECG, detecting arrhythmias and ischemia by means of committees of Artificial Neural Networks (ANN), and alerting the relevant health care professionals. Our objective is to improve the patient risk stratification and to reduce the number of false positive and false negative alarms by taking into account the demographic and clinical data featured by the user's Electronic Health Record (EHR) stored in the PEM device. To design and assess such a new type of system, we adopted a decision making solution based on Bayesian Networks (BN) that we trained to predict the risk of a cardiovascular event (infarction, stroke, or cardiovascular death) based on a set of demographic and clinical data (age, BMI, etc.) as provided by the INDANA database, from which we randomly extracted a training set of 15013 subjects and a testing set of 5004 subjects. The BN is then compared to an ANN committee (N=50) and a Logistic Regression (LR) model in terms of sensitivity, specificity, and area under the ROC curve (AUC). AUC = 0.80 for the BN, 0.75 for the ANN committee and 0.74 for the LR model. Conclusion: the Bayesian Network approach achieved a high overall accuracy over both the neural network and logistic regression models on the testing set, and therefore can be useful in pHealth systems such as the PEM.

1. Introduction

Recent years have witnessed a growing interest in developing personalized and non-hospital based care systems to improve the management of cardiac care. The reason behind such interest is due to the fact that cardiovascular diseases represent nowadays the leading cause of mortality in Europe and reducing the time before treatment is crucial to reduce cardiac morbidity and mortality.

The European EPI-MEDICS project has designed a solution based on the interpretation of the ECGs acquired by means of a friendly and easy-to-use, cost-effective intelligent Personal ECG Monitor (PEM) [1]. The device is capable of recording a simplified 4-electrode, professional quality 3-lead ECG, to detect arrhythmias and ischemia or acute myocardial infarction by means of committees of Artificial Neural Networks (ANN), and to send an alarm message with a copy of the patient's Electronic Health Record (EHR) and the concerned ECG to the relevant health care professionals.

Our objective is to improve the patient risk stratification and to reduce the number of false positive and false negative alarms by designing a multivariate decision making system modulating the results of the embedded ANN-based ECG interpretation model by taking into account the demographic and clinical data featured by the user's EHR stored in the PEM device.

Ideally, to design and assess such a new type of system, we would need large, coherent databases including for each patient, clinical data and serial digital ECGs in a synchronized fashion. However, since such databases do not yet exist, we followed an alternative approach consisting in separately designing the ECG classifiers and the risk predicator, then in merging the ECG interpretation and the risk prediction into one final decision using empirical rules.

To facilitate future ECG measurements integration, we adopted a decision making solution based on Bayesian Networks (BN) that calculate the probability of the event knowing the symptoms or signs. The choice of using BN is justified by their capacity to model the uncertainty inherent in medical reasoning and to make decisions based on incomplete data [2].

2. Material and methods

2.1. Study population

The INDANA database consists in a collection of individual clinical data of 10 randomized controlled trials designed to evaluate the preventive effects of antihypertensive drugs with at least six-year followup for cardiovascular events and deaths [3]. In this study, we only used data from the control groups from which we randomly extracted a training set of 15013 subjects and a testing set of 5004 subjects. Observations with missing data were kept in the study population. The outcome considered in this paper is defined as the occurrence during the six-year followup of any of the following cardiovascular events: myocardial infarction, stroke or cardiovascular death.

Table 1. Variables used to train the bayesian network, the neural network and the logistic regression model.

Variable	Variable type
Age	continuous
Systolic BP	continuous
Diasystolic BP	continuous
Body Mass Index (BMI)	continuous
Cholesterol	continuous
Blood Glucose	continuous
Sex	discrete
Old Left Ventricular Hypertrophy	discrete
Old Myocardial Infarction	discrete
Old Stroke	discrete
Diabetes	discrete
History of Hypertension Treatment	discrete
Smoking	discrete
Cardiovascular Outcome	discrete

2.2. Neural network design and training

We built up an ANN ensemble that consists of a committee of 50 ANN of the figure 1 type using the Matlab™ ANN toolbox. Each individual ANN consists in one input layer with m input neurons (one for each predictive variable), an output layer with 1 output neuron (occurrence or no occurrence of the outcome event), and 1 hidden layer of 10 neurons.

The outputs of the ANN committees are obtained by summing (and dividing by 50) the outputs of the 50 individual ANN. This averaging process has proven to provide, as a result of the central limit theorem, higher performances than each individual network sub-solution [1,4].

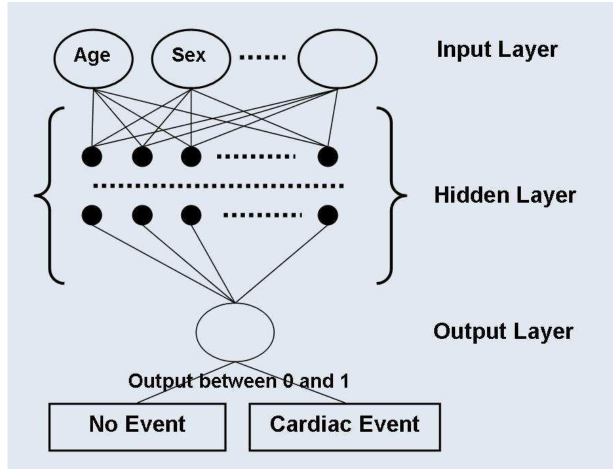

Figure 1. ANN architecture used to predict the possibility of the occurrence of a cardiac event.

2.3. Bayesian network design and training

The bayesian network uses the patient data (age, sex, diabetes, etc.) to predict the risk of cardiovascular event (Fig. 2). The structure of the BN was designed using a heuristic approach based on the authors' expertise in biochemistry and cardiology. The BN was then trained using BAYESIALAB™ software.

2.4. Statistical analysis

We evaluated the ability of the BN, the ANN committee and the LR model to estimate cardiovascular risk in the independent testing set. For each testing case, the BN and the LR model generated a probability, and the ANN generated an activation value. For each model, we calculated the sensitivity and specificity, and determined the area under the ROC curve (AUC) as a measure of accuracy.

3. Results

The assessment over the INDANA database of the bayesian network in comparison to the neural network committee and the logistic regression model showed a clear advantage of the BN compared with the two other methods. The AUC was respectively 0.80 for the bayesian network, 0.75 for the ANN committee and 0.74 for the logistic regression model. The increase of performance of the bayesian network over the ANN committee can be explained by the fact that neural networks are rather inefficient in processing hybrid data (continuous, dichotomous, categorical) without a proper:

- data pre-processing step (1-out-of-n encoding, discretization, etc.),
- or a data post-processing step, as the approach adopted in [5].

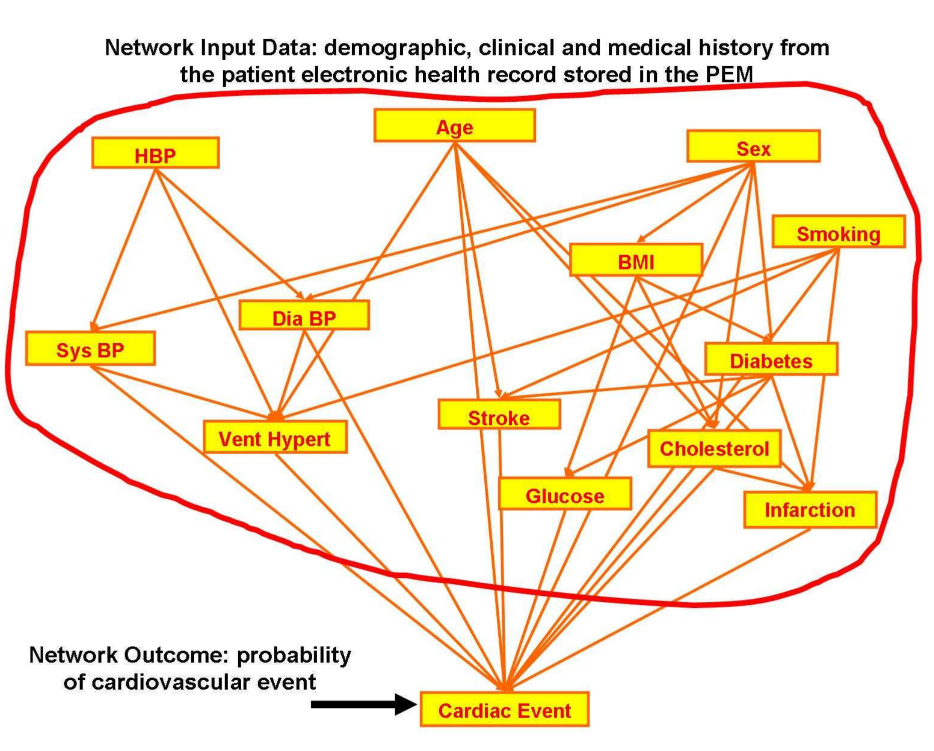

Fig. 2 Architecture of the bayesian network used to estimate the risk of cardiovascular outcome. The architecture design is based on the authors' expertise in the cardiovascular domain.

4. Collaboration scheme

To improve the PEM decision making, we propose to combine the outputs of the ECG interpretation module and the risk factors estimation module by means of a fuzzy logic based layer that shall control the dialogue between both modules. The choice of fuzzy-logic [6] is due to the fact that such a technology allows a smooth collaboration between classifiers and is thus expected to enhance the global decision-making process. Figure 3 illustrates an example of such a collaboration scenario:

- A patient, suffering from fatigue or any other common symptoms indicative of a possible cardiac event, uses the PEM system to acquire an ECG.
- Once successfully recorded and stored in the system, the ECG is interpreted by the neural-network module and a first risk score is calculated. Diagnosis of ischemia is performed by a committee of 100 ANN for unary decision making and 75 ANN for serial analysis [1]. Unary analysis is triggered only if no reference ECG is available:
  - If the risk score calculated by the ANN passes the high risk threshold, the ECG is considered as *abnormal*, the system will trigger an alarm.
  - If the risk score falls within the medium or minor risk interval, the ECG is considered as "borderline", and the risk score calculated by the ECG classifier is combined with an additional risk score issued by the bayesian module and the global risk score allows to trigger the appropriate alarm level: major, medium, minor.

The development of the fuzzy-logic interaction layer and the validation of the global decision making process need to have a database that contains not only serial 12-lead and PEM 3-leads ECGs but also an exhaustive electronic health record for all patients of the database. Such a PEM-specific database is currently under construction.

5. Conclusion

In this paper, we described some of the latest ambient intelligence and pervasive solutions that are being designed and are deployed in the PEM device, and more specifically the BN risk factor stratification module and its integration into the overall PEM telemedical platform.

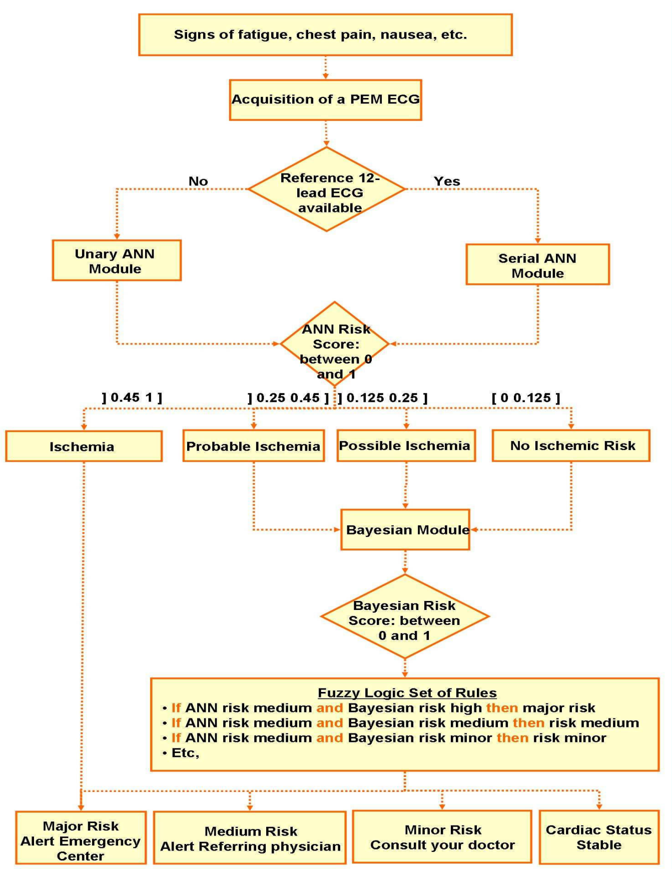

Fig. 3 Illustration of the decision making model for detecting ischemia to be embedded in the PEM system after adding the bayesian and fuzzy modules in the decision-making process.

At this stage of development, and after conducting several clinical trials involving both patients and health professionals [1], the PEM and the associated software tools were judged very easy-to-use and user-friendly and already allowed the detection of several arrhythmia events that would have remained unwitnessed if not recorded in self care situations (intermittent WPW, intermittent atrial fibrillation, etc.). The capability of the PEM to detect acute infarction in self-care situations remains, however, to be demonstrated because no such event occurred during the clinical trials.

Ongoing works are intended to create and deploy a palette of predictors for a variety of profiles representative of the PEM potential user (male $\geq$ 45 years, female $\geq$ 55 years…). The next step is to deploy and validate the global decision platform and investigate ways to make the system self-improving on both the embedded intelligence and communication levels.

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