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# A QUICK LOW COST METHOD FOR SYNCOPE PREDICTION

*Mathieu Feuilloy*[1,2]*, Daniel Schang*[1] *and Pascal Nicolas*[2]

[1]ESEO,
4, rue Merlet de la Boulaye, BP 926,
49009 ANGERS Cedex 01, France
phone: (33)241 86 67 67, fax: (33)241 87 99 27,
email: {mathieu.feuilloy, daniel.schang}@eseo.fr

[2]LERIA, University of Angers,
2, bd Lavoisier,
49045 ANGERS Cedex 01, France
phone: (33)241 73 54 20, fax: (33)241 73 50 73,
email: pascal.nicolas@univ-angers.fr

## ABSTRACT

*The aim of this study is to present a method that predicts unexplained syncope or presyncope occurrences induced by a head-upright tilt-test (HUTT). The HUTT is based on the reproduction of symptoms in combination with hypotension and bradycardia induced by a tilt at 70° during 45 minutes. The main drawback is the duration of this test because, by adding the supine position of 10 minutes, the test could reach 55 minutes. Therefore, this paper proposes a new method for syncope prediction by using only the supine position. We describe the signals used to extract the features employed for the prediction and we develop the preprocessing techniques of these signals in order to increase the quality interpretation of these features. We conclude by presenting the results obtained by the use of an artificial neural network.*

## 1. INTRODUCTION

Syncope is currently defined as a sudden and temporary loss of consciousness and a postural tone. Furthermore, 3% of emergency room visits and 6% admissions hospital are directly related to symptoms of syncope. Its diagnosis is currently based on the reproduction of symptoms in combination with hypotension and bradycardia induced by a 45 min of 60-80° head-up tilt test [2]. This test is very used; after 10 minutes in a supine position, the patient is upright tilted during 45 minutes. If any symptom of syncope or presyncope occurs, the patient is returned to the supine position. The major problem is the examination duration and the challenge consists in reducing it while keeping a right prediction. To evaluate the quality of the prediction, we use two parameters, the *specificity* (the percentage of patients among the non-fainters who are accurately classified as non-fainters) and the *sensitivity* (the percentage of patients among the fainters who are accurately classified as fainters). Both characterize the percentage of correct patients classification.

Many studies worked on the first minutes of tilting: Pitzalis *et al.* [12] have studied the 15 first minutes where the patients are in the tilted position. They predict syncope occurrence with a specificity of 93% and a sensitivity of 58% on a retrospective study of 238 patients. They reach 85% of specificity and 80% of sensitivity in a prospective group of 80 patients. This prediction has been done by the analyze of the systolic arterial pressure. An other study of Mallat *et al.* [10] has reduced the duration of examination to 6 minutes by the determination of a predictive criterion, based on heart rate variation. They have obtained for a retrospective group of 110 patients, a specificity of 100% and a sensitivity of 88.6%. With a group of unknown patients they found a specificity of 96.4% and a sensitivity of 87.3%. The period of examination has been reduced but these studies imply a tilting and can cause very unpleasant symptoms (pallor, nausea). Recent studies [1],[13] tried to achieve the prediction by using only the supine position. An other similar characteristic of the latter studies was the use of transthoracic impedance signal which allows the computation of ventricular ejection variations. The first work of Bellard *et al.* [1] has been done only on a retrospective group of 71 patients, they found a specificity of 63% and a sensitivity of 68%. Contrary to this study which used thresholds to predict the syncope, Schang *et al.* [13] worked with neural networks (multi-layer perceptrons); they obtained a specificity and a sensitivity of 100% for a retrospective group of patients and 73% of specificity and 69% of sensitivity in a prospective group of patients. An other study of Feuilloy *et al.* [5] obtained a good prediction for the same period of rest. They obtained a specificity of 87% and a sensitivity of 86% in a prospective group of 29 patients, but they used several variables which are costly and not easily recordable (plasma volume, hematocrit, hemoglobin).

The study presented in this paper tries to obtain a good prediction by using variables which can be recorded and processed quickly by using only the supine position. This diagnosis method is based on artificial neural networks. Thus, the electrocardiogram (*ECG*) and the transthoracic impedance signal (*Z*) are used to extract the features allowing the syncope prediction. After a description of data acquisition, we give an overview of the feature extraction process, then the prediction process will be detailed. Furthermore, the results show the interest and the performances of this method. The performance of the measures will be evaluate in terms of Receiver Operating Characteristics (ROCs) curves, and particularly the area under the ROC curves (AUCs) [9]. The results will be compared statistically by cross-validations.

## 2. DATA ACQUISITION

### 2.1 Subjects

In the experiments, 129 patients (mean age: 43$\pm$ 15 years, range 18-73 years, 63 males, 66 females) with history of unexplained recurrent upright syncope or presyncope at least twice within the last 3 months were included in the study. For all patients, evidence of neurological, structural heart disease, metabolic and psychiatric illness was eliminated on the basis of physical examination and additional investigations (blood tests, ambulatory 12-lead ECG, transthoracic echocardiography, endocavitary investigations and carotid sonography). The patients were included in the study only when these data remained negative. Medications which could in-

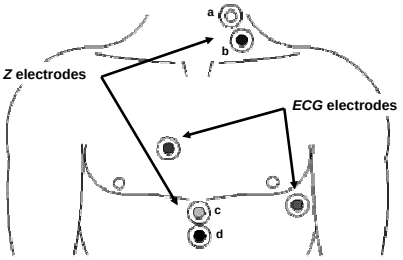


Figure 1: Electrodes positions to observe the *ECG* and *Z*

terfere with the test (i.e: diuretics, vasodilatators, betablockers) were interrupted at least 2 days before the study. All the patients gave their written informed consent and the study was approved by our local ethic committee.

### 2.2 Protocol

The experiment was performed between 2:00 and 5:00 PM in a quiet and temperature controlled room (24-25°C) with light dimmed. The patients were installed in supine position on a motorized tilt table (FGCK, Couverchel, Draveil, France) with footboard and equipped for instrumentation, knee and abdominal straps prevented fall. As explained earlier, after the supine position, the patients were upright tilted at an angle of 70° for 45 min [6]. If symptoms occurred, the subjects were returned supine and the test ended. The upright tilt test was considered positive on the reproduction of syncopal (loss of consciousness and postural tone) or near-syncopal (pallor, nausea, dizziness, lightheadedness, sensation of imminent syncope). If no symptoms occurred after 45 minutes the patients were returned supine. According to the outcome of the 45-min head-upright tilt test, the patients were divided in two groups: non-fainters (66) with negative response to 70°-HUTT, and fainters (63), with a positive response.

### 2.3 Recorded variables

Changes in the transthoracic impedance signal were recorded using an electrical impedance device (Physioflow, Manatec Biomedical, France, [4]). The transthoracic impedance signal *Z* was obtained by injecting (figure 1) a high-frequency (75 kHz) and low-amperage (1.8 mA) alternating electric current through 4 spot electrodes (Ag/AgCl, 40493E). Two electrodes were positioned over the neck and two over the xyphoid process. The impedance signal was gated to Lead II ECG collected from 2 electrodes (*b* and *d*). It is based on the variations of transthoracic impedance caused by the blood volume variation obtained by the application of electric current. Thus, the current was injected by the electrodes *a* and *c*. The transthoracic impedance waveform *Z* and *ECG* were sampled at 240 Hz. The data were stored during all the HUTT phase.

## 3. METHOD

The measure during the supine position allows to obtain temporal signals of 10 minutes: *ECG* and *Z*. During this period, the signals can undergo perturbations. Indeed, with the electrodes positioned on the neck and the thorax, several perturbations can occur on *ECG* and *Z*, caused by strong respirations, muscular contraction or patient movements. Therefore, we choose to select a part of signal with the weakest

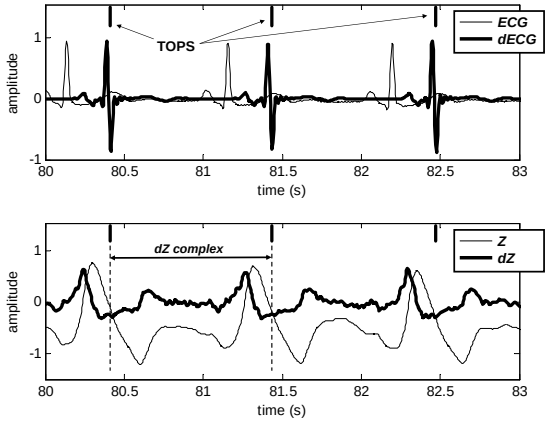


Figure 2: Representation of *ECG* and *Z* signals and their derivatives

signal perturbations on the *ECG* and *Z* curves. The extracted part is of one minute among the 10 first minutes of the resting period. The pertinent selection of a subpart of the signals *ECG* and *Z* is very important because it impacts strongly the computation of the further extracted features.

### 3.1 Preprocessing

The analysis is based on the *ECG* and *Z* signals obtained in the first step of TILT-test, during the supine position. These two signals are filtered by using a 128-th order lowpass Finite Impulse Response digital filter [11] based on a Hamming window. The cut-off frequency is of 30 Hz for the *ECG* and 40 Hz for the *Z*. The first derivative of the *ECG* and *Z* signals are computed by central derivation [7]. So, the *dECG* and *dZ* signals are computed with the following expressions:

$$\begin{aligned} dECG(n) &= ECG(n+1) - ECG(n-1) \\ dZ(n) &= Z(n+1) - Z(n-1) \end{aligned}$$

with $1 < \mathrm{n} < \mathrm{N}$.

### 3.2 Complexes extraction

The features used for the syncope prediction are extracted on the *dZ* signal. So, for our analysis, we need to extract each complex of *dZ*. We define a *"dZ complex"* of *dZ* signal as a period or heartbeat of this signal (figure 2). As mentioned, during the 10 first minutes, a continuous duration of 60 seconds is extracted. The employed method extracts the heartbeats between two *TOPS*, obtained by an amplitude threshold computed on the *dECG* signal and equal to $0.3 \cdot \mathtt{max}(dECG)$ [7].

### 3.3 Selection of a part of the *dZ* signal

The method is developed around three parameters: *P*, *T* and *L*. The sampled signal of *P* points must be periodic with an approximate duration of *T* points, where each period is defined as a "*complex*" from the *dZ* signal. The method extracts a part of *L* samples from the signal. Therefore, the total number of periods is equal to $P/T$, and the number of periods of the extracted part is of $K = L/T$. Naturally, these parameters must follow the condition: $P - T > L > 2T$.

In our experimentation, *P* and *T* vary in function of the recorded measures on the patients and the length of *L* reaches 14400 points (60 seconds). The procedure which evaluates

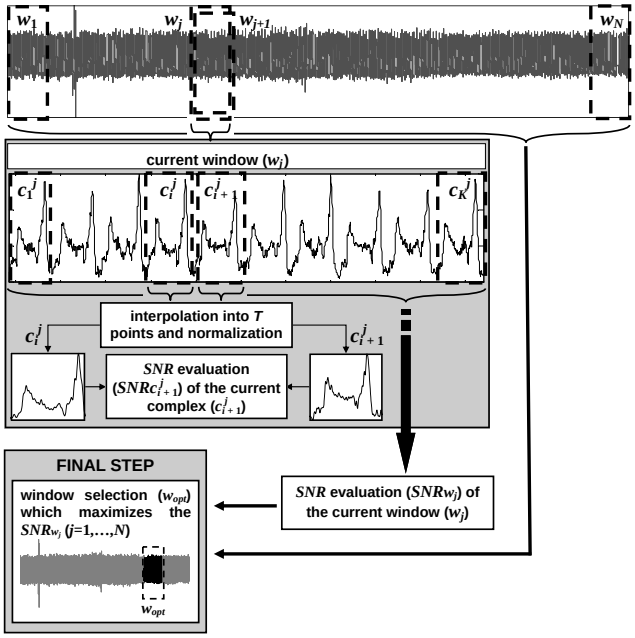


Figure 3: Block diagram for the selection of the best part of the signal

and extracts the best part is shown in the figure 5. This procedure prevents an important variation on the $K$ successive periods. The extracted part is called "*window*" ($w$).

The signal variability in the window $w_j$ is obtained by taking the signal as a periodic noised signal. Thus, to compute the variability, we use the Signal-to-Noise Ratio (called *SNR*). The window evaluation considers the mean of all the *SNR* complexes of the extracted window. The *SNR* of a complex $c_i$ (equation 1) is computed by using two successive complexes ($c_i$ and $c_{i+1}$), where the complex $c_i$ represents the reference complex. Thus, the noise measured on the complex $c_{i+1}$ of the window $w_j$ is computed by the following expression:

$$SNR_{c_{i+1}^j} = 10 \cdot \log_{10}\left(\frac{P_{c_{i+1}^j}}{P_{c_i^j} - P_{c_{i+1}^j}}\right) \quad (1)$$

where, $P_{c_i^j}$ is the power of the complex $i$ of the window $j$. Therefore, the noise of the window $w_j$ (equation 2) is obtained by the sum of all the *SNR* contained in the window.

$$SNR_{w_j} = \frac{1}{L/T-1} \cdot \sum_{i=2}^{K-1} 10 \cdot \log_{10}\left(\frac{P_{c_{i+1}^j}}{P_{c_i^j} - P_{c_{i+1}^j}}\right) \quad (2)$$

The evaluation of a next window $w_{j+1}$ is determined by the elimination from the first complex ($c_1^j$) of the window $w_j$ and by the addition of the next complex to the last complex ($c_K^j$) of the window $w_j$.

After the *SNR* computations of each extracted window, the method gives the window having the biggest *SNR*, defined by $w_{opt}$ which maximizes the *SNR* of the windows $w_j$, with $j = 1, \cdots, N$.

### 3.4 Input feature selection in the frequency domain

Usually, the features are extracted in the time domain taking into consideration intervals time and some amplitudes of the signal, as [10], [12], [13] and [1]. Our approach seeks new features by working in the frequency domain, thus the power spectral density (PSD) $\hat{S}$ of $dZ$ (equation 3) is estimated by using an improved version of the periodogram which is Welch's method [15]. This method has the advantage to offer a diminution of the variance by a signal segmentation and the overlap between segments. Moreover, the bias is modified by using a Hamming window $w_h$ on each segment, so $\tilde{x}(n) = dZ(n) \cdot w_h(n)$. The PSD is computed on 1 minute of signal, the parameters used are: an overlap of 50%, a segment size $K$ of 2048 points (8.6 seconds) and the number of segments $M$ equal to 13. While the data were sampled at 240 Hz, therefore the frequency resolution is of 0.117 Hz.

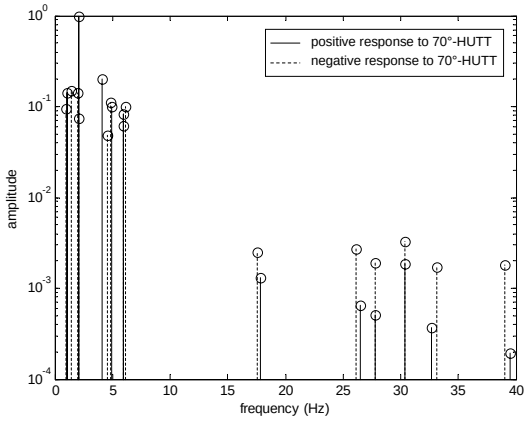


Figure 4: Representation of the 14 preselected frequencies for the one patient of each group (positive/negative response to 70-HUTT: syncopor/non-syncopor)

$$\hat{S}(n) = \frac{1}{M}\sum_{m=0}^{M-1}\left(\frac{1}{K}\left|\sum_{k=0}^{K-1}\tilde{x}(mK/2+k)e^{-2j\pi\frac{kn}{K}}\right|^2\right) \quad (3)$$

The amplitudes of frequencies obtained on the PSD determine the features allowing to establish the syncope prediction. But, all the frequencies cannot contribute to the prediction, therefore a selection is done by taking into consideration a condition. This condition requires the presence of the frequency on all the syncopor or/and non-syncopor patients to be preselected. In our study, 14 relevant frequencies between 0 and 40 Hz emerged. The figure 4 shows a comparison between two patients (syncopor and non-syncopor) which allows to observe some differences between the frequencies of the two classes.

A procedure commonly used to evaluate the quality of the features is the ranking computation [8] and [14]. The ranking criterion is interesting for its simplicity and its rapidity. The Pearson correlation coefficient defined by the equation 4 allows to obtain the correlation coefficient ${R_i}^2$, between the $i^{th}$ feature ($X_i$) with the associated outputs (targets) $Y$.

$$R_i = \frac{cov(X_i, Y)}{\sqrt{var(X_i)var(Y)}} \quad (4)$$

In our case, the output is not continuous and each sample is labeled by $Y \in \{+1, -1\}$, therefore, to determine the correlation (the relevance index) of each feature $i$, the use of

$R_i{}^2$ can be replaced by the Fisher criterion [3], defined by the following expression:

$$F_i = \frac{\left(\mu_i^{+1} - \mu_i^{-1}\right)^2}{\sigma_i^{+1} + \sigma_i^{-1}} \quad (5)$$

where $\mu_i^{+1}$ and $\sigma_i^{+1}$ represent respectively the mean and the variance of the $i^{th}$ feature for the class $\{+1\}$. This score $F$ must be maximized in order to increase the between-classes variance (*numerator* of equation 5) and to reduce the within-classes variance (*denominator* of equation 5) for each feature $i$.

These 14 frequencies are given with their respective criterion values in the table 1.

| **frequency** | 1.17 | 1.05 | 4.69 | 17.58 | 39.26 | 5.85 | 26.25 |
|---|---|---|---|---|---|---|---|
| **criterion** | 0.093 | 0.076 | 0.046 | 0.017 | 0.017 | 0.011 | 0.010 |
| **frequency** | 2.34 | 4.34 | 5.74 | 27.54 | 30.24 | 32.93 | 2.23 |
| **criterion** | 0.010 | 0.007 | 0.006 | 0.006 | 0.002 | 0.001 | 0.000 |

Table 1: Extracted frequencies and their criterions

They are sorted in descending (the maximum value of *criterion* corresponds to the best feature), thus, the amplitudes corresponding to frequencies are used as features and they are proposed to the classification and prediction tool. In our experiments, we add progressively a new feature by following the order induced by the criterion.

### 3.5 Prediction by neural networks

Among Artificial Neural Networks (ANNs), Multi-Layer Perceptrons (MLPs) [3] are often used, particularly in pattern recognition applications. In this study of syncope prediction, an architecture of one-hidden-layer has been chosen, with activation functions of sigmoid type. The inputs of MLP are the amplitudes of the frequencies selected in the previous section. The MLP is trained by the "Levenberg-Marquardt" algorithm [3], during the learning phase. The use of the *softmax* function normalizes the outputs and interprets them as posterior probabilities of class membership. Thus, the decision of the output for a feature input vector is defined by the largest posterior probability.

### 3.6 Performance measure

The performance measure commonly used for a classifier is the classification accuracy. This method must consider two conditions to interpret suitably the results: the distribution of classes must be constant and the misclassification data must be equal. Both conditions are not often satisfied in real problems, thus contrary to the classification accuracy, the ROC curves are often used. The ROC method has the advantage of being independent of class distribution and independent of misclassification data proportion. The curves are constructed by plotting the $sensitivity$ with $1 - specificity$ for different cutoff values of a diagnosis test. The area under the ROC curve [9] can be interpreted as the test accuracy: the highest the area, the highest the accuracy is reached.

To estimate the generalization error, *K-fold cross-validation* is often used [3]. This technique allows to give an estimation with a small bias and a small variance. Thus, the data set is randomly divided into $K$ subsets ($K$-folds) of equal size. The classifier is trained on $K-1$ subsets, then the validation is measured by testing the subset that was not used during the learning phase. This process is repeated $K$ times by using a different subset to estimate the validation.

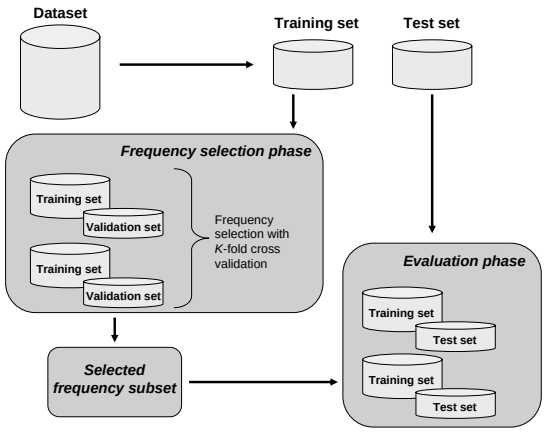


Figure 5: Block diagram for the selection of the best part of the signal

Therefore, the performance of the classifier is obtained by averaging the $K$ AUCs.

## 4. EXPERIMENTATION AND RESULTS

The 129 patients included in this study are divided into two groups. Each group was builded with $50\% \pm 5\%$ of fainters and non-fainters, randomly chosen. The first (70 patients) is used to construct and to determine the best feature subset with the forward selection method based on ranking. The patients in the second group (59 patients) are only used to estimate the performance of selected subsets, thus these test data are not employed in the feature selection phase. This decomposition of the dataset is shown in figure 5.

Cross-validation is a method of estimating generalization performance, and the obtained results are often used to compare models. In our experiments, this method is used to estimate the syncope prediction in order to eliminate a bias, which could be caused by a favorable data distribution in our classification problem. Thus, each group is divided into 7-folds (K=7), by keeping the same proportion between the syncopor and the non-syncopor patients for each subdataset. The performances on the validation and test sets are obtained by averaging the $K$ AUCs, called respectively $\overline{AUC_V}$ and $\overline{AUC_T}$.

In order to increase the statistical estimation, the *K-fold cross-validation* is repeated several times. Thus, the learning has been done hundreds of times for each case, with several number of neurons in the hidden layer (from 2 to 10). In our experiments, each input, composed by the amplitudes of the frequencies, is normalized to obtain a mean value of 0 and a standard deviation of 1. All signals were analyzed off-line using a software that we have developed, in MatLab$_{\copyright}$ (The Mathworks Inc., South Natic, MA, USA).

### 4.1 Evaluation of the relevance of frequencies

The Fisher coefficients are computed on the training set. The figure 6 shows the prediction results $\overline{AUC_V}$, on the $K$ validation sets with the architecture (number of neurons in the hidden layer optimizing the prediction). These results are computed by increasing the size of the input vector (for example, for a size of input vector set to 4, we use the 4 first frequencies appearing in table 1). Thus, with the use of the

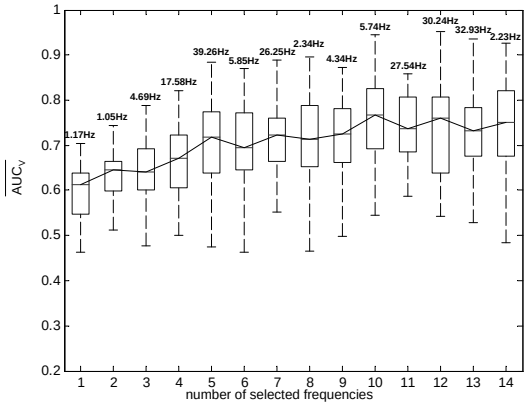


Figure 6: Evolution of the $\overline{AUC_V}$ during the forward input selection, on the validation sets. The line in the middle of the box is the sample median, the lower and upper lines of the box are the 25th and 75th percentile of the sample

10 first frequencies the prediction of syncope is optimal (figure 6).

### 4.2 Evaluation of the syncope prediction

The amplitudes of these 10 frequencies are extracted from PSDs on the second group of patients (noted "Test set" on the figure 5). The average estimation of the generalization reaches similar value to the performances from the previously phase of the frequency selections. The median value of the $\overline{AUC_T}$s is equal to 0.794 (0.728 and 0.856 for the 25th and 75th percentile), thus the generalization performances are confirmed with these descriptive features. With the adapted parameters for the classification model, the best performance among the hundreds of times of learning reaches 0.967. In table 2 we compare our results with the results of the other studies described in the introduction. Thus, we can notice that this study can predict unexplained syncope occurrences by using only the supine position with a better specificity and sensitivity than other studies using the tilted position. So far, we obtain a mean estimation of 86% for the specificity and 79% for the sensitivity. Moreover, it is important to notice that our sensitivity (false negative) is superior or equal to other studies. This fact shows the interest of the diagnosis, indeed, the cost of false negative errors (no detection of the pathology when it exists) is more catastrophic than the cost of false positive errors (detection of the pathology when none pathology exists).

| **State of patient** | **supine position** | | | | **tilted position** | |
|---|---|---|---|---|---|---|
| **Studies** | **this study** mean and SD values | **this study** optimal value | **[5]** | **[13]** | **[10]** | **[12]** |
| **Specificity (%)** | $79 \pm 0.014$ | 97 | 87 | 73 | 96 | 85 |
| **Sensitivity (%)** | $86 \pm 0.007$ | 100 | 86 | 69 | 87 | 80 |

Table 2: Comparison of prediction methods

## 5. CONCLUSIONS

This study is a step in the direction of early syncopes prediction by using only the resting period of the 70°-HUTT. Indeed, we obtain a prediction with an average specificity and sensitivity of 79% and 86% on a prospective group of unknown patients, reaching respectively 97% and 100% for the best initialization parameters of the MLP. These results show the possibility to improve the prediction by a choice of adapted classifiers (parameters or models). The obtained performances contribute to a new approach in the early detection of positive outcome contributing as a first step in the avoidance of the costly and time consuming HUTT in the future.

Moreover, the use of these variables which are easily recordable, offers a considerably advantage, indeed in this case, the processing can be done on-line and the diagnosis can be obtained during the exam.

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