Application of the Preoperative ECG to Predict Cox-Maze Surgery Mid-term Outcome

A Hernández[1], R Alcaraz[2], F Hornero[3], JJ Rieta [1]

[1]Biomedical Synergy, Electronic Engineering Dept., Universidad Politécnica de Valencia, Spain
[2]Innovation in Bioengineering Research Group. University of Castilla-La Mancha, Spain
[3]Cardiac Surgery Department, General University Hospital Consortium, Valencia, Spain

Abstract

The Cox-Maze surgery is today the procedure with the highest long-term cure rate for patients in atrial fibrillation (AF). Nonetheless, its mid-term outcome prediction could avoid the application of aggressive pharmacologic treatments in some patients. Previous works have revealed that parameters computed from the preoperative ECG, such as the fibrillatory waves amplitude (fWP), the dominant atrial frequency (DAF) and the sample entropy (SampEn), can identify successfully the Cox-Maze immediate outcome at discharge. This work focuses on analyzing the ability of these parameters to predict the patient's rhythm six months post-surgery. Results showed sensitivity, specificity and accuracy values of 71.43%, 52.94% and 58.33% for fWP, 85.71%, 52.94% and 62.5% for DAF and 85.71%, 58.82% and 66.66% for SampEn, respectively, reporting no statistically significant differences between patients in AF or normal rhythm. Therefore, in contrast to previous results, these metrics did not show to be significant predictors of the Cox-Maze surgery at mid-term. The atrial substrate alteration due to pharmacological and electrical cardioversion in patients relapsing to AF during the follow-up could be the main reason for this result. Further analyses are required to clarify this question.

1. Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia, occurring in 1–2% of the general population [1]. AF is associated with increases rates of death, stroke and other thrombo-embolic events, heart failure and hospitalizations, degraded quality of life, reduced exercise capacity and left ventricular dysfunction [1]. To date, a variety of treatment strategies have been developed to alleviate this disease. Thus, antiarrhythmic drugs, electrical cardioversion (ECV), catheter-based ablation, and surgery have been used with varying efficacies[2]. However, the surgical treatment of AF with the Cox-Maze III procedure is still the most successful way to terminate AF, which long-term cure rates over 90% [3].

After this surgical procedure, patients are routinely evaluated at three, six and twelve months; and then, every year. Moreover, they are habitually treated with oral anticoagulant and antiarrhythmic drugs at the moment of discharge, independently of the presented rhythm, normal sinus rhythm (NSR) or AF [4]. If AF persists after 3 months, ECV is applied to restore NSR. In contrast, antiarrhtymic drugs are withdrawn if a stable NSR is observed. Similarly, anticoagulant treatment is stopped in patients maintaining NSR at six month after surgery [4]. Hence, a preoperative prediction of patient's rhythm at six months post-surgery could avoid the application of an aggressive pharmacologic treatment in patients under low risk of maintaining mid-term AF. Thus, clinical costs could be reduced and the patient's quality of life could be improved.

Although some clinical parameters, such as age, left atrial size and preoperative time in AF, have provided successful predictions of long-term Cox-Maze outcome [3], other indices computed from the surface ECG have shown a notably high effectiveness to predict immediate outcome of the procedure at discharge [5]. Hence, given that the ability of these parameters to predict the patient's rhythm after a six months follow-up has not been assessed yet, the present work focuses on the analysis of this purpose.

2. Methods

2.1. Study population

Twenty-four patients (mean age 68.33 ± 6.36 years) in permanent AF for at least 3 months were enrolled in the study. Cox-Maze procedure was always applied concomitantly to another heart surgery. Six months after the procedure, AF remained in 7 (29%) patients, whereas NSR was restored in the remaining 17 (71%).

A standard 12-lead ECG was acquired for each patient before the Cox-Maze procedure with a sampling rate of

1 kHz and an amplitude resolution of 0.4 μV. From this recording, a 20 second-length interval of lead V1 was selected for the analysis. This lead was chosen because previous works shown that atrial activity (AA) is prevalent in this signal [6]. To improve later analysis, the ECG segment was preprocessed using forward/backward high-pass filtering (0.5 Hz cut-off frequency) to remove baseline wander, low-pass filtering (70 Hz cut-off frequency) to reduce high frequency noise and notch filtering at 50 Hz to remove powerline interference. Additionally, a wavelet denoising was also used to reduce muscle noise [7].

2.2. Preoperative ECG parameters

Before extracting the AA signal, every ECG segment was normalized to its maximum R-peak amplitude in order to get comparable values when relative variations of the proposed parameters were pursued. This operation avoided all the effects than can modify the ECG amplitude as a function of the different gain factors during recording, electrodes impedance, skin conductivity, etc [8]. Next, the AA signal was extracted by means of an adaptive QRST cancelation method [9] and the fibrillatory (f) waves power (fWP) was estimated. This power represents the energy carried by the f waves within the time interval under analysis and, thus, it can be considered as a robust indicator of the signal amplitude [8]. The mean power was calculated by computing the quadratic sum of the signal values at the interval under analysis.

The dominant atrial frequency (DAF) was also computed, because its inverse has been related with atrial refractoriness [10]. To obtain this parameter, the power spectral density of the AA signal was computed making use of the Welch periodogram. A Hamming window of 4096 points in length, 50% overlapping between adjacent windowed sections and a 8192-points fast Fourier transform (FFT) were used as computational parameters. The frequency with the highest amplitude within the 3-9 Hz interval was selected as the DAF, because previous works have reported that this is the typical AF frequency range [10].

Finally, pattern repetitiveness in the AA signal and, thus, its organization, was estimated by means of a nonlinear regularity index, such as sample entropy (SampEn) [11]. This tool quantifies the predictability of fluctuations in the values of a time series and assigns a nonnegative number to the sequence, with larger values corresponding to more irregularity in the data [12]. SampEn is defined as the negative natural logarithm of the conditional probability that two sequences similar for m points remain similar at the next point, where self-matches are not included in calculating the probability [12]. Two input parameters must be specified to compute the SampEn, the length of the sequences to be compared, m, and the pattern similarity tolerance, r. As suggested by previous works dealing with AF signals, values of $m = 2$ and $r = 0.35$ times the standard deviation of the AA were used [13]. Moreover, a remarkable SampEn shortcoming is its sensitiveness to noise and ventricular residua [11]. Hence, to reduce the influence of these nuisance signals, SampEn was computed on the main atrial wave (MAW) of the AA. This signal was obtained by applying a selective filtering to the AA centered around the DAF [11].

2.3. Statistical analysis

The nonlinearity in the AA signal was studied through the surrogate data test to confirm the suitability of using SampEn in the analysis. The test consists of obtaining a surrogate dataset from the original data. Then, a number that quantifies some aspect of the series, called discriminating statistic, has to be computed over the original and surrogate data. When the original series discriminating statistic is significantly different than the surrogate data values, nonlinearity can be assumed [14]. In the present work 40 surrogate data were generated for each AA signal and the analyzed statistic was SampEn. The Wilcoxon T test was used to assess statistical differences between original and surrogate data.

On the other hand, statistical differences between patients in NSR and those in AF at six month post-surgery were evaluated with a Student's t-test for normal parameters and with a U Mann-Whitney test for not normal ones. In both cases, a statistical significance (p) lower than 0.05 was considered as significant. Normality and homoscedasticity in parameters distributions was determined by using Shapiro-Wilk and Levene tests, respectively. Additionally, the value of each parameter that provided maximum discrimination between patient's groups was obtained by means of a receiver operating characteristic (ROC) curve. The ROC curve is a graphical representation of the tradeoffs between sensitivity and specificity. In this work, sensitivity was the proportion of patients in AF at 6 months post-surgery correctly identified, whereas specificity was considered as the proportion of patients in NSR correctly classified. The total number of patients properly discerned was considered as the diagnostic accuracy of the parameter and its highest value was used to determine the optimum classification threshold.

In order to improve the group classification, a binary classification tree was developed to combine the three analyzed parameters. The used stopping criterion for the tree growth was that each node contained only observations of one class or fewer than 3 observations. Moreover, the impurity-based Gini's index was used to look for the best parameter and its threshold for the splitting of each node [15].

Table 1. Classification results for fWP, DAF and SampEn together with the statistical significance obtained for each parameter.

	Sensitivity	Specificity	Accuracy	p
fWP	71.43%	52.94%	58.33%	0.975
DAF	85.71%	52.94%	62.50%	0.395
SampEn	85.71%	58.82%	66.66%	0.254

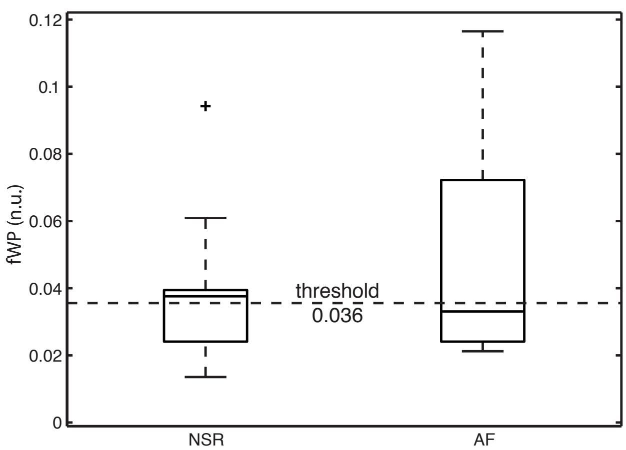

Figure 1. Box-and-whisker diagram for fWP considering the patient's rhythm at six months after Cox-Maze surgery.

3. Results

Statistically significant differences between original and surrogate data were noticed with the Wilcoxon T test, thus assuming nonlinearity in the AA signal. In this way, the suitability of applying SampEn in the AA organization estimation is proved.

Sensitivity, specificity and accuracy values for the analyzed indices are shown in Table 1. As can be seen, accuracy values were lower than 70% for all the metrics, the specificity values being especially reduced. Although, sensitivity values higher than 85% were noticed for DAF and SampEn, their influence in the final diagnostic accuracy was limited given the reduced number of patients in AF at the follow-up end. In agreement with this classification result, no statistically significant differences between patient groups were observed for the indices, as Table 1 also shows. Indeed, Figs. 1-3 display a notable overlapping between the values corresponding to each patients group.

Finally, the classification tree was useless to improve the group classification. Although in a first step SampEn was used to generate two branches, the remaining parameters were discarded to generate additional nodes.

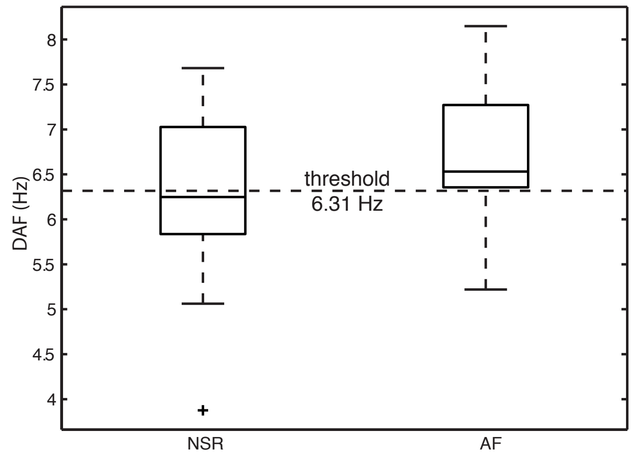

Figure 2. Box-and-whisker diagram for DAF considering the patient's rhythm at six months after Cox-Maze surgery.

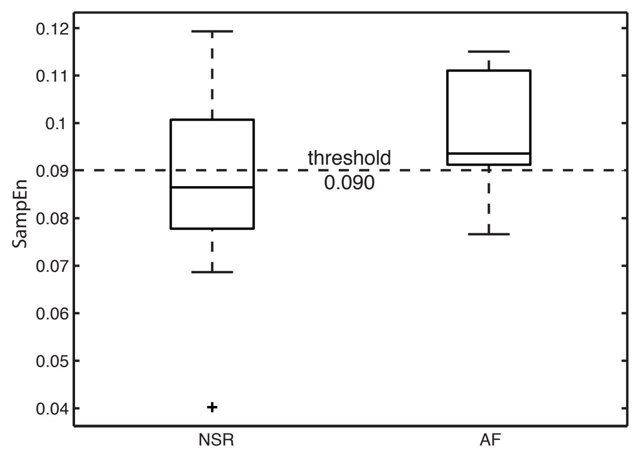

Figure 3. SampEn box-and-whisker diagram for the patient's rhythm at six months after Cox-Maze surgery.

4. Discussion

Previous works have analyzed the ability of fWP, DAF and SampEn to predict the patient's rhythm at the moment of the discharge [5]. Results revealed the fWP as a powerful risk predictor of developing AF immediately after Cox-Maze surgery. Moreover, DAF and SampEn also provided notably high accuracy values greater than 70%, reporting statistically significant differences between patients resulting in AF and those in NSR. In contrast, in the present work the same metrics have not reported statistically significant differences between patient groups, their discriminant ability being considerably reduced. Indeed, the diagnostic accuracy for the fWP has provided a decrease of 20%, approximately.

Although this discriminant ability deterioration of the parameters may have several causes, the most probably is the pharmacological or electrical cardioversion applied to the patients in AF at three months of follow-up [4]. This procedure is able to alter atrial substrate for synchronizing atrial cells and restoring NSR [16], thus hindering the discriminant ability of preoperative predictors. In fact, the reduced specificity values observed for the analyzed metrics could be a consequence of the NSR restoration through cardioversion in a considerable number of patients. Nonetheless, further studies on wider databases are required to confirm this assumption. To this respect, the analysis of postoperative ECG recordings could also reveal useful information.

5. Conclusion

The analysis of fWP, DAF and SampEn from the preoperative ECG did not reveal a significant ability to predict successfully the patient's rhythm at six months after the Cox-Maze surgery. The alteration of atrial substrate by pharmacological or electrical cardioversion during the patient's follow-up seems to be the main reason for this result. Nevertheless, further analyses are needed to clarify this question.

Acknowledgements

Work funded by TEC2010–20633 from the Spanish Ministry of Science and Innovation and PPII11–0194–8121 from Junta de Comunidades de Castilla-La Mancha.

References

[1] Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, Hindricks G, Kirchhof P, ESC Committee for Practice Guidelines-CPG, Document Reviewers. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation–developed with the special contribution of the European Heart Rhythm Association. Europace Oct 2012;14(10):1385–413.

[2] Melby SJ, Zierer A, Bailey MS, Cox JL, Lawton JS, Munfakh N, Crabtree TD, Moazami N, Huddleston CB, Moon MR, Damiano RJ. A new era in the surgical treatment of atrial fibrillation: the impact of ablation technology and lesion set on procedural efficacy. Ann Surg Oct 2006; 244(4):583–592.

[3] Gaynor SL, Schuessler RB, Bailey MS, Ishii Y, Boineau JP, Gleva MJ, Cox JL, Damiano RJ. Surgical treatment of atrial fibrillation: predictors of late recurrence. J Thorac Cardiovasc Surg Jan 2005;129(1):104–111.

[4] Hornero F, Montero JA, Canovas S, Bueno M. Biatrial radiofrequency ablation for atrial fibrillation: epicardial and endocardial surgical approach. Interact Cardiovasc Thorac Surg Dec 2002;1(2):72–77.

[5] Hernández A, Alcaraz R, Hornero F, Rieta JJ. Role of fibrillatory waves amplitude as predictors of immediate arrhythmia termination after maze surgery of atrial fibrillation. In Computing in Cardiology (CinC), 2012. 2012; 661–664.

[6] Petrutiu S, Ng J, Nijm GM, Al-Angari H, Swiryn S, Sahakian AV. Atrial fibrillation and waveform characterization. A time domain perspective in the surface ECG. IEEE Eng Med Biol Mag 2006;25(6):24–30.

[7] Sörnmo L, Laguna P. Bioelectrical signal processing in cardiac and neurological applications. Amsterdam: Elsevier Academic Press, 2005.

[8] Alcaraz R, Rieta JJ. The application of nonlinear metrics to assess organization differences in short recordings of paroxysmal and persistent atrial fibrillation. Physiol Meas Jan 2010;31(1):115–130.

[9] Alcaraz R, Rieta JJ. Adaptive singular value cancelation of ventricular activity in single-lead atrial fibrillation electrocardiograms. Physiol Meas Dec 2008;29(12):1351–1369.

[10] Holm M, Pehrson S, Ingemansson M, Sörnmo L, Johansson R, Sandhall L, Sunemark M, Smideberg B, Olsson C, Olsson SB. Non-invasive assessment of the atrial cycle length during atrial fibrillation in man: introducing, validating and illustrating a new ECG method. Cardiovasc Res Apr 1998; 38(1):69–81.

[11] Alcaraz R, Rieta JJ. A review on sample entropy applications for the non-invasive analysis of atrial fibrillation electrocardiograms. Biomedical Signal Processing and Control 2010;5(1):1 – 14.

[12] Richman JS, Moorman JR. Physiological time-series analysis using approximate entropy and sample entropy. Am J Physiol Heart Circ Physiol Jun 2000;278(6):H2039–H2049.

[13] Alcaraz R, Abásolo D, Hornero R, Rieta JJ. Optimal parameters study for sample entropy-based atrial fibrillation organization analysis. Comput Methods Programs Biomed Jul 2010;99(1):124–32.

[14] Palus M, Hoyer D. Detecting nonlinearity and phase synchronization with surrogate data. IEEE Eng Med Biol Mag 1998;17(6):40–45.

[15] Breiman L, Friedman J, Stone CJ, Olshen RA. Classification and Regression Trees. Chapman & Hall/CRC, 1984.

[16] Gall NP, Murgatroyd FD. Electrical cardioversion for AF-the state of the art. Pacing Clin Electrophysiol Apr 2007; 30(4):554–67.

Address for correspondence:

Antonio Hernández Alonso
Biomedical Synergy. Electronic Eng. Dept. 7F
Universidad Politécnica de Valencia
Camino de Vera s/n. 46022 Valencia (Spain)
e–mail: anheral@upv.es