WAVELET COEFFICIENTS PREDICTORS FOR MAINTENANCE OF SINUS RHYTHM AFTER ELECTRICAL CARDIOVERSION IN PATIENTS WITH PERSISTENT ATRIAL FIBRILLATION

Raquel Cervigón*, César Sánchez*, Francisco Castells**, Jose Manuel Blas*, José Millet**

*DIEEA. Universidad de Castilla-La Mancha, Cuenca, España.
**BET. Universidad Politécnica Valencia, Valencia, España.

raquel.cervigon@uclm.es

Abstract: Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. In a substantial number of patients AF recurs after efective electrical cardioversion (ECV). The aim of this study was to identify predictors for successful ECV and maintenance of sinus rhythm after a first ECV in patients with persistent AF.

We investigated the predictive power of coefficients obtained with Continuous Wavelet Transform (CWT) respect to defibrillation outcome. CWT was applied to Lead V1, and in determinates scales of the transformation, some differences were observed between the two groups.

A logistic regression model was constructed, determining the calibration with the Homer-Lemeshow test and the discrimination with the area under the ROC Curve.

These proposed protocols calibrates and discriminates well and accurately differentiates patients with recurrent AF from those without. This technique can be used as an important independent predictor for maintenance of sinus rhythm after electrical cardioversion in patients with persistent AF, it complements existing clinical parameters and contribute to the interpretation of AF recurrence risk. [1]

Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia. Its incidence increases with age, being relatively uncommon under the age of 50 but occurring in 2% to 4% of the population after the age of 65, with doubling of the risk of AF with each advancing decade of life. [3] It is the most common cause of embolic stroke and is associated with pronounced morbiliy an mortality. [4][5] Furthermore, AF can significantly impair quality of life due to symptoms of palpitations and decreased cardiac output.

Patients with AF are heterogeneous. [2] It may be associated with significant underlying heart disease, but may also occur in the absence of any demonstrable disease.

The mechanisms responsible for the initiation and perpetuation of the arrhythmia are incompletely understood. The most widely accepted theory of AF mechanisms was proposed by Moe [7][8] as early as 1962. It postulated that AF perpetuation is based on the continuous propagation of multiple wavelets wandering throughout the atria. Other studies [8] affirm that a premature atrial beats during normal sinus rhythm facilitate the induction of the arrhythmia, and could promote early AF reinitation following cardioversion. It constitutes the basis of the concept that AF tends to perpetuate itself: "AF begets AF". [9]

Traditionally, AF has been diagnosed clinically based on an irregular pulse and thus in terms of its ventricular consequences rather than in its own right. On ECG, AF is confirmed by the replacement of consistent P waves of varying frequency, amplitude and morphology.

Electrical cardioversion (ECV) has become routine therapy [10] for AF patients since its introduction in 1962. Lately, intracardiac and transoephageal cardioversion [11] have provided alternatives to traditional external ECV, often where it has failed. However these techniques are technically more difficult and may have a greater risk of complications.

External shocks are given in an attempt to convert AF to sinus rhythm with a higher acute success rate. Despite successful conversion of AF to sinus rhythm, the recurrence of AF after cardioversion is a major and largely unpredictable clinical problem, only about 25% [12][13] of the patients remain in sinus rhythm in the absence of antiarrhythmic treatment, and little is known about mechanisms responsible immediate recurrence or AF following the use of the different cardioversion techniques.

Currently, it is not possible to predict the response to treatment of this arrhythmia. Many recent studies have shown that atrial fibrillatory cycle length may be used as an index of the average atrial myocardial refractoriness, [14][15][17] and it is possible to estimate from the surface ECG, through power spectrum analysis of QRS reduced ECG for detection of atrial fibrillatory activity, to predict outcome of ECV, but its effective power is unclear. A lot of variables have been proposed: age, sex, functional class, left ventricular

This work was supported by Castilla-La Mancha research scheme (Ref: PAC-05-008-1) and from Consellería of University-Business and Science of the Generalitat Valenciana (Ref: IIARC0/2004/249).

ISSN: 1727-1983

ejection fraction, AF duration and antiarrhythmic drugs [25] though their role for prediction of outcome following cardioversion is controversial, [16][18][19][20][21][23][24] being left atrial size [22], the most common parameter used to guide therapy.

The present study was conducted in patients with persistent AF after successful ECV to extract parameters from ECG signal alone or in combination with anatomical atrial parameters that could predict the outcome of ECV.

Materials and Methods

Materials

The subjects of this study were 34 consecutive patients who restored sinus rhythm after first elective external ECV for persistent AF and AF recurrences were checked 6 weeks after cardioversion.

This database includes from 34 patients different clinical characteristic (Table 1) and the registers diagnosed with AF sampled at 1KHz recorded before application ECV belong to the cardiac Electrophysiological Laboratory of the University Clinic Hospital of Valencia.

Table 1: Clinical characteristic of patients

Parameters		Sinus Rhythm (n=15)	Recurrence AF (n=19)
Men, n (%)		9 (60.0)	15 (78.9)
Underlying heart disease n(%)		3 (20.0)	5 (26.3)
AF duration (months)		9.5±17.2	10.48±33.1
Antiarrhythmic	Amiodarone	12	16
	Flecainida	3	3
Left atrial diameter		42±5.9	45.6± 4.5

ECG Preprocessing

Preprocessing is used over ECG recordings to improve the later analysis stages. The ECG is preprocessed since the spectral content of interest in the residual ECG is well below 40 Hz. [11]

All signals were sampled at 1 kHz and were pre-processed using a band-pass filter with cut-off frequencies of 1 and 40 Hz to remove baseline wandering and reduce thermal noise.

Continuous Wavelet Transform Processing

Wavelet Transform has become a valuable analysis tool in the last years because of its ability to localize simultaneously local spectral and temporal information within a signal. It overcomes some of the limitations of the more widely used Fourier Transform, which only contains globally averaged information and has the potential to lose transient or location-specific features within the signal.

Wavelet analysis is essentially comparing the signal with a chosen wavelet, in our case mexhican wavelet; and recording the coefficients that indicate the correlation of the signal to the wavelet.

In the Continuous time Wavelet Transform (CWT) the wavelet coefficients are evaluated for infinitesimally small shifts of translation as well as scale factors. This approach provides a more accurate time localization of the abnormality or the defect in the signal.

CWT to lead V1 and frequency domain analysis using a Welch periodogram of 4096 points and a Hamming window with an overlap of 50% were applied.

Using mexhican wavelet, in a determinate scale was found difference between the two groups. Power spectrum of these signals were determined and some parameters were extracted: mean peak frequency, amplitude of the mean peak, amplitude of the second frequency and concentration around main frequency.

In the following figures are represented in time and frequency domain, signals belong to our database, the first one (Figure 1) corresponds with AF recurrence and the second one (Figure 2) with maintenance in the sinus rhythm after the application of a successful ECV.

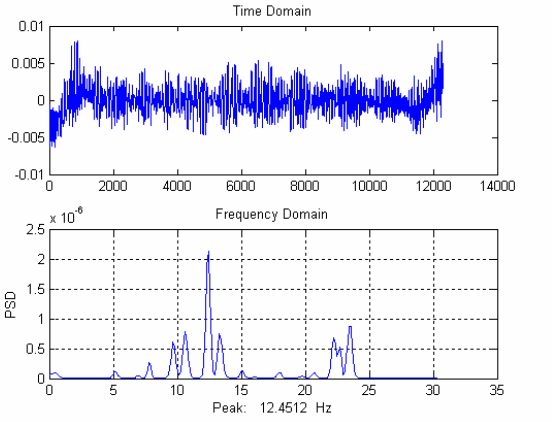

Figure 1: CWT mexhican wavelet coefficients at 500 scale (AF recurrence)

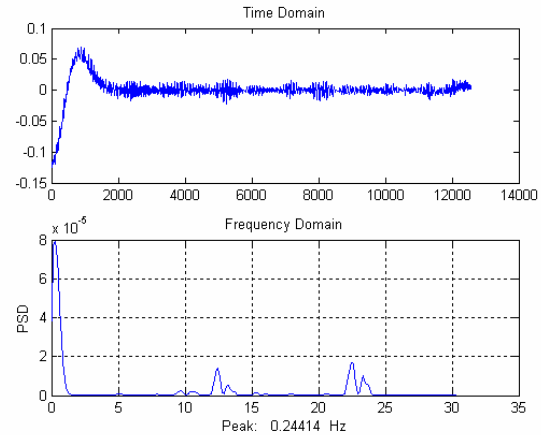

Figure 2: CWT mexhican wavelet coefficients at 500 scale (sinus rhythm maintenance)

ISSN: 1727-1983

The same process was proposed to evaluate on the residual signal after cancellation of the QRST, that only contained Atrial Activity (AA).

We used a validate method of extraction called Template Matching Subtraction (TMS), this technique cancels Ventricular Activity (VA) in the ECG involves direct suppression of QRS-T complex through the subtraction of a mean QRS-T template.

After extraction, CWT was applied to AA signal and the same coefficient that to the original ECG signal were calculated. The results were not as favourable as in the preceding analysis.

Statistical Analysis

The preceding method generates parameters that were tested to see their effective power of prediction.

Values of parameters extracted alone or in combination with anatomical atrial parameters were evaluated.

The Kruskal Wallis test was used to determine whether there was any significant difference between the groups.

A logistic regression model was constructed, determining the calibration with the Homer-Lemeshow test and the discrimination with the area under the ROC Curve was performed to assess the correlation between parameters and AF recurrence. The reference model was built by forced entry variables followed by removal of the ones with no significant partial correlation.

Results

Cardioversion restored sinus rhythm in all of the patients in the study, but at 4 weeks only 15 (44.11%) remained in sinus rhythm. The proposed analysis was applied to all of the registers and the variables obtained from the original ECG alone of in combination with clinic parameters were statistically evaluated (Table 1) to determine if they could be statistically significant ($p<0.05$) in the prediction of recurrences. Variables obtained from AA signal were not statistically significant and not were employed in the following analysis.

Table 2: Extracted variables Kruskal Wallis Test

Parameters	Chi square	Significant
Main Frequency (Fp)	14.210	0.0001
Amplitude low frequency (Alow)	8.693	0.003
Amplitude frequency 5-20Hz (Amed)	7.040	0.008
TamAur*0.001/Alow	12.769	0.005
TamAur*Fp	7.991	0.0001

Receiver operating characteristic (ROC) analysis curves were used to validate the usefulness of this parameters in diagnosing recurrence of AF versus non recurrence of this arrhythmia. Area measures discrimination were used for its ability of the test to correctly classify those with and without the disease. The discrimination showed an area under the ROC curve (Table 3) that proposed as variables to make a better differentiation: 'Fp', 'TamAurFp' and 'TamAurAlow'.

Table 3: ROC curve analysis

Parameters	Area	Asympt. Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
Main Frequency (Fp)	0.821	0.002	0.677	0.965
Amplitude low frequency (Alow)	0.798	0.003	0.636	0.960
Amplitude frequency 5-20Hz (Amed)	0.768	0.008	0.603	0.934
TamAur* 0.001/Alow	0.786	0.005	0.061	0.951
TamAur*Fp	0.861	0.0001	0.739	0.984

These variables were introduced in a logistic regression analysis and only two of them were described by logistic regression model, because their high correlation. These variables were: Fp>0.24Hz (OR 22.63, IC95% 2.08-246.21, p=0.001); Atrial Diameter>43mm (OR 7.06, IC95% 1.01-48.99, p=0.03).

Discussion

The role of identification patients at risk of developing AF recurrence has been studied in numerous publications, being validated and used in the clinic procedure specific variables as are: left atrial size and AF duration, that are included in our database.

In this study were analysed several ECG signal belong patients diagnosed with AF before ECV, follollowing within 3 month after successful ECV application to know their evolution.

The proposed method was apply to find a parameter that could predict this evolution. The found variables with more efficiency in prediction AF recurrence were: 'Fp' (main frequency), 'Alow' (second frequency amplitude) and 'Amed' (main frequency amplitude).

It has propposed the combination of anatomical parameters and the variables generate with our method. The original database (Table 1) is composed by some of them mentioned clinic validated parameters, as 'time evolution' or 'left atrial size'. Both were analyzed and the variable 'time evolution' was rejected because of being in almost all the cases over 6 weeks that it is established by numerous studies [22] so that exist remodelling.

ISSN: 1727-1983

The resulting variables were validate (Table 2), and the more significative were: 'Fp' (main frequency), 'TamAurFp' (left atrial size × main frequency) and 'TamAurAlow' (Amplitude low frequency / left atrial size), both with a significacion lower to 0.05.

The reference logistic model takes into account two original variables: 'Fp' and 'TamAur' that discriminate well and accurately differentiates patients with recurrent AF versus without, with a 82.35% capacity of prediction.

The specifity in prediction of sinus rhythm maintenance was 90.09 % and the sensibility in the prediction of recurrences was 78.26%. These results can be obserbed in Figure 3 and Figure 4 where numerical variables are been transformed into binary or dichotomy variables.

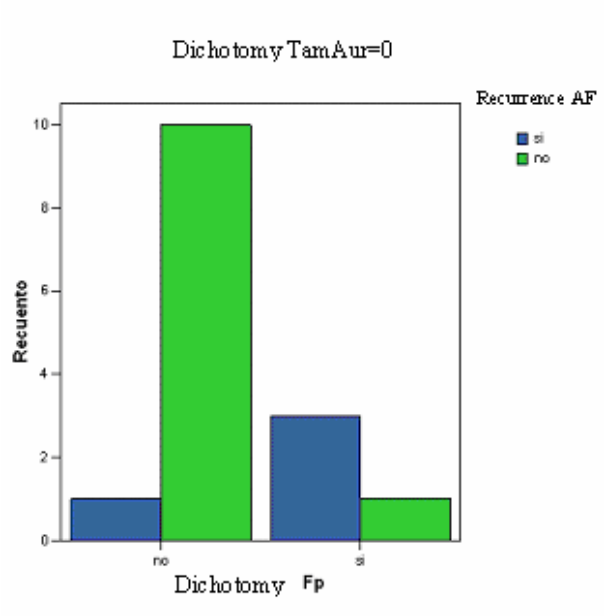

Figure 3: Fp (cross point DichotFp 5.3710) variable analysis for AF recurrences when left atrial size <45mm

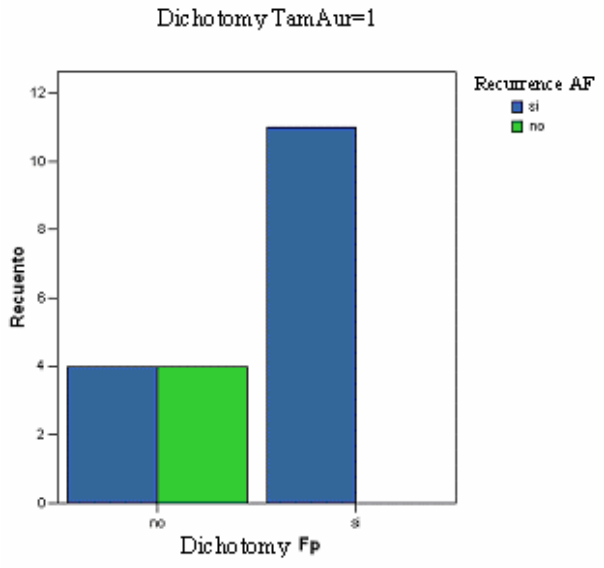

Figure 4: Fp (cross point DichotFp 5.3710) variable analysis for AF recurrences when left atrial size >45mm

Conclusions

The present study identified some parameters as predictors of AF recurrence versus non recurrence, extracted to ECG signal. The combination of these parameters and anatomical measurements improve the prediction of maintenance of sinus rhythm following ECV. The proposed protocol calibrates and discriminates well and accurately differentiates the two groups of patients.

Nevertheless, these results must take with caution, since the number of samples is very small and should be necessary studies with more extensive samples to confront the results obtained in this work.

It is necessary a deeper investigation, but the finding suggests that it is possible that inside ECG signal should contain hidden informacion that with a tool as, wavelet transmorf could be extracted. It should contribute to a best knowledge of the mechanisms of the studied arrhytmy and to the interpretation of AF recurrence risk with the enormous advantages of a non-invasive method.

References

[1] MALLAT S. A Wavelet Tour of Signal Processing, Academic Press, 1998.

[2] KANNEL WB, ABBOTT RD, SAVAGE DD. Epidemiologic features of chronic atrial fibrillation: the Framingham study. N. Engl. J. Med. 1982;306:1018-1022.

[3] BENJAMIN E.J., LEVY D., VAZIRI S.M. Independent risk factors for atrial fibrillation in a population-based cohort. The Framingham Heart Study. JAMA. 1994;271:840-844.

[4] WHISNANT JP, WIEBERS DO, PETTY GW, O'FALLON WM, SICKS JD, WIEBERS DO. Comparison of population-based models of risk factors for TIA and ischemic stroke. *Neuroloy*. 1999;53:532-536.

[5] BENJAMIN EJ, WOLF PA, D'AGOSTIO RB, SILBERSHATZ H, KANNEL WB, LEVY D. Impact of atrial fibrillation on the risk of death: te Framingham Heart Study. *Circulation*. 1998;98:946-952.

[6] STRIDH M, SÖRNMO L., MEURLING C.J., OLSSON S.B., "Characterization of Atrial Fibrillation Using the Surface ECG: Time-Dependent Spectral Properties". IEEE. Trans. BioMed. Eng. 2001;48:19-21.

[7] MOE G. K., "On the multiple wavelet hypothesis of atrial fibrillation, "*Archives Internationales de Pharmacodynamie et de Therapie*, vol. 140, pp. 183–188, 1962.

[8] ALLESSIE MA, LAMMERS WJEP, BONKE FI M, AND HOLLEN J, "Experimental evaluation of Moe's multiple wavelet hypothesis of atrial fibrillation," in *Cardiac Electrophysiology and Arrhythmias*, D. P. Zipes and J. Jalife, Eds.

ISSN: 1727-1983

Orlando, FL: Grune and Straton, 1985, pp. 265–275.

[9] WIFFELS MCEF, KIRCHHOF CJHJ, DORLANND R, ALLESSIE MA. AF BEGETS AF: a study in awake chronically instrumented goats. Circulation 1995;92:1954-1968.

[10] FUSTER V, RYDEN LE, ASINGER RW, et al. ACC/AHA/ESC guidelines for the management of patients with atrial fibrillation: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the European Society of Cardiology (committee to develop guidelines for the management of patients with atrial fibrillation). Journal of the American College of Cardiology 2001;38(4):1266i–1266lxx.

[11] LAUER MS, EAGLE KA, BUCKLEY MJ, DE SANTIS RW. Atrial fibrillation following coronary artery bypass surgery. *Prog Cardiovasc Dis* 1989;31:367-78.

[12] LAU CP, AYERS GM. Long-term outcome in patients with chronic atrial fibrillation after successful internal cardioversion. *Am J Cardiol* 1999;83:607–9.

[13] VALENCIA J, CLIMENTE VE, MARTÍN F, MONMENEU JV, MARTINEZ JG, MARTINEZ MA, IBÁÑEZ A, GARCIA A, AND SOGORD F. Eficacia de la cardioversión programada en la fibrilación auricular. comparación de dos esquemas de tratamiento: cv eléctrica frente a cv farmacológica. *Revista Española de Cardiología*, 55(2):113{20, 2002.

[14] BOLLMANN A, HUSSUER D, STEINERT R, STRIDH M, SOERNMO L, OLSSON B, POLYWKA D, POLLING J, GELLER C, AND KLEIN H. Ecocardiographic and electrocardiographic predictors for atrial fibrillation recurrence following cardioversion. *Cardiovasc Electrophysol*, 14:162-165, 2003b.

[15] BOLLMANN A. Electrical remodeling of the atrium in an anatomic model of atrial flutter. In Argentine Federation of Cardiology, editor, *2nd Virtual Congress of Cardiology*, 2001.

[16] LEVY S, RICARD P, LAU CP, *et al*. Multicenter low energy transvenous atrial defibrillation (XAD) trial results in different subsets of atrial fibrillation. *J Am Coll Cardiol* 1997;29:750–5.

[17] MEURLING C, SORNMO L, STRIDH M, AND OLSSON B. Non invesive assessment of atrial fibrillation (af) cycle length in man: potential application for studyimg af. *Ist Super Sanita*, 37(3):341-349, 2001.

[18] BARBARO V, BARTOLINI P, CALGAGNINI G, CENSI F, MACIOCE R, AND MICHELUCCI A. Efect of atrial fibrillation organization on internal debrillation threshold. In *Ist. Super Sanita*, volume 37, pages 377-381, 2001.

[19] BOLLMAN T, MENDE M, NEUGEBAUER A, AND PFEIFER. Atrial Fibrillatory frecuency predicts atrial de fibrillation threshold and early arrhythmia recurrence in patients undergoing internal cardioversion of persistent atrial fibrillation. PACE, 25:1179-1184, 2002.

[20] BOTTO GL, POLITI A, BONINI W, BROFFONI T, AND BONATTI T. External cardioversion of atrial fibrillation: of paddle position on technical efficacy and energy requirements. *Heart*, 82:726-730, 1999.

[21] CHING-TAI T, SHIH-ANN D, WEN-CHUNG Y, YU-AN D, MAU-SONG T, AND TSA-IR K. Spectral analysis of chronic atrial fibrillation and its relation to minimal de fibrillation energy. *PACE*, 25:1747-1751, 2002.

[22] SOPHER SM, MURGATROYD FM, SLADE AKD, *et al*. Low energy internal cardioversion of atrial fibrillation resistant to transthoracic shocks. *Heart* 1996;75:635–8.

[23] ORTIZ JA, AVILA MC, OCHOA C, FUENTE L DE LA, MORENO JC, CAMPO F DEL, AND VILLAFRANCA JL. Factores predictores independientes del éxito agudo y al año de la cardioversión eléctrica en pacientes con fibrilación auricular crónica. *Revista Española de Cardiología*, 54:958-964, 2001.

[24] VAN GELDER IC, CRIJNS HJGM.Cardioversion of atrial fibrillation and subsequent maintenance of sinus rhythm. *PACE* 1997;20:2675–83.

[25] FYNN SP, TODD DM, HOBBS JC, ARMSTRONG KL, FITZPATRICK AO, And GAR-RATT CJ. Effect of amidarome on dispersion of atrial refractoriness and cycle length in pacientes with atrial fibrillation. *Cardiovasc Electrophysol*, 14: 485-491, 2003.

ISSN: 1727-1983