

Dynamic Changes in Intracardiac Resistance as a Predictive Marker during Internal Cardioversion of Atrial Fibrillation

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Abstract

Intracardiac resistance (ICR) is an important determinant of treatment success during internal cardioversion of atrial fibrillation (AF). However, there is limited data on dynamic changes in ICR as a predictor of cardioversion outcome. In this retrospective study, thirty patients with persistent AF were randomised to treatment with a biphasic or monophasic energy step-up cardioversion protocol (50V-to-300V in 50V steps). ICR was computed for each patient and a student t-test used to investigate the significance of dynamic changes in ICR between successive shocks delivered. For both biphasic and monophasic waveforms, all patients who cardioverted exhibited a significant reduction in ICR between the first and third shock ($p < 0.01$ and $p < 0.003$, respectively). Yet, critically, a significant reduction in ICR was absent for all patients who failed to cardiovert ($p > 0.05$ for both waveforms). A statistically significant decrease in ICR during the first three shocks was identified as a predictive marker for successful cardioversion outcome.

1. Introduction

Atrial Fibrillation (AF) is one of the most common cardiac arrhythmias encountered in medical practise. AF occurs in approximately 0.65% of the population between the ages of 45-64 years and has a prevalence of 9% among those over 80 years of age [1]. It is currently estimated to affect approximately 4.5 million people in Europe and over 2.2 million people in the USA. AF is one of the leading causes of stroke, with the associated after care costs identified as almost entirely preventable. Consequently, the need for the continued investigations and improvements in AF associated therapies remains self evident [2,3]. Intracardiac impedance (ICR) has long been identified as one of the major determinants of the minimum energy required for successful internal cardioversion; as ICR is inversely related to the electrical current density and energy delivered to the cardiac

substrate. Studies on the effect of changes in transthoracic electrical impedance during external defibrillation have been carried out for transthoracic cardioversion of AF and knowledge gained has led to significant advancements in the understanding of optimum shock waveforms and treatment protocols for transthoracic cardioversion therapy [4-6]. However, there is a paucity of similar studies that have examined the dynamic variation in ICR during internal cardioversion of AF. Hence, the objective of this study was to further analyse and extend upon our previous investigations [7] into dynamic variations of ICR within the time domain during internal cardioversion of AF and to investigate the relationship to treatment outcome.

2. Methods

2.1. Study population

Thirty patients with persistent AF were recruited for the study; with exclusion criteria as previously reported [7,8].

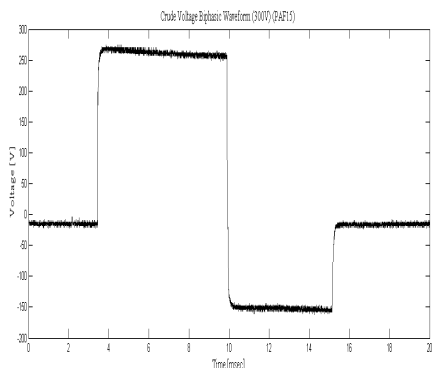
2.2. Cardioversion protocol

The cardioversion procedure was carried out in a cardiac catheterisation laboratory. Prior to the procedure, intravenous midazolam was administered for adequate sedation. Using venous access, a St. Jude 6F Inquiry™ internal cardioversion catheter (St Jude. Medical, St. Paul, MN, USA) was located in the distal coronary sinus and right atrial appendage (verified via fluoroscopy in multiple views) [8]. In order to verify system operation, a 50V test shock was initially delivered to a purely resistive 47Ω dummy load. Patients were then randomised to treatment with a step-up energy cardioversion shock protocol (50V to 300V in 50V steps (Table 1)) using either a biphasic very-low-tilt rectilinear (B-VLTR) chronosymmetric (6ms/6ms) amplitude asymmetric (negative phase at 50% amplitude) waveform, or a monophasic very-low-tilt (M-VLTR) rectilinear

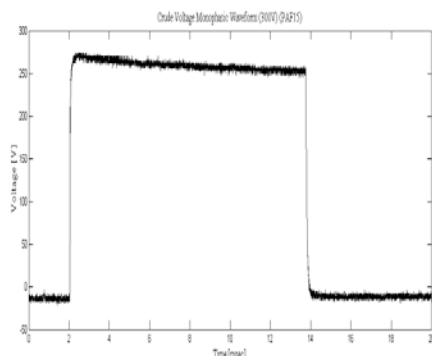
waveform (12ms) (Figure 1 (a) and (b), respectively).

Table 1. Step up cardioversion protocol with voltage and estimated shock energies [7].

Step	Study Arm 1 Biphasic, 6/6 (ms)		Study Arm 2 Monophasic, 12 (ms)	
	Voltage	Energy (J)	Voltage	Energy (J)
S1	50	0.38	50	0.6
S2	100	1.5	100	2.4
S3	150	3.38	150	5.4
S4	200	6	200	9.6
S5	240	8.62	240	13.8
S6	280	11.75	280	18.81
S7	300	18.5	300	21.6



(a)



(b)

Figure 1. Very-low-tilt internal cardioversion shock waveforms: (a) biphasic (B-VLTR, 6/6ms duration; amplitude asymmetric), (b) monophasic (M-VLTR, 12ms duration; amplitude symmetric) [7].

A minimum of 60s was allowed between shocks. Cardioversion success was defined as the restoration of sinus rhythm for a period of 30s or greater. Patients who failed to cardiovert were crossed over to the opposite arm of the study. Patients who cardioverted before the third shock were excluded from this particular ICR retrospective study. Post procedure, all patients were monitored in the cardiology ward; with blood pressure, pulse and saturation checked every two hours for the first six hours and then every four hours until discharge. In addition, the venous access site was closely monitored for signs of haematoma. Routine bloods, Troponin T, CK-MB were also checked every twelve hours and immediately prior to discharge (twenty four hours post procedure). All patients were required to undergo a follow-up review within three months [8].

2.3. Signal recording

A two channel digital oscilloscope (Tektronix TDS 3014 manufactured by Tektronix Inc., Beaverton, Oregon, USA) and a current probe (Fluke 80i-110s manufactured by Fluke Inc., Washington, USA) were used to measure simultaneously the voltage and current during shock delivery.

2.4. Signal Processing

Data was retrospectively grouped into the four categories shown in Table 2.

Table 2. Retrospective patient data groupings.

Title	Description
Group-I	Biphasic - Successful Cardioversion
Group-II	Biphasic - Failed Cardioversion
Group-III	Monophasic - Successful Cardioversion
Group-IV	Monophasic - Failed Cardioversion

The magnitude of ICR (Z_{AV}) was then calculated as the ratio of voltage (V) to current (I) at every discrete sample point of V and I within the shock delivery time window averaged over 4ms for both B-VLTR (positive phase only) and M-VLTR waveforms.

$$Z_{AV} = \frac{\sum V/I}{n} [\Omega]$$

where n is the number of sampled points in a 4ms window commencing 1ms after the initial rising edge.

A standard student t-test (two-tailed paired distribution) was used to investigate the significance of variation in ICR between successive electrical shocks delivered with differences considered significant for $p < 0.05$. In addition, variation of ICR early within a shock ($E-\Delta Z_T$) was defined in units of ohms per second (Ω/s) as the linear impedance slope ($Z(m)$) over time in the early part of the shock waveform pulse (1-5ms); processed for the positive phase in the case of the biphasic waveform. Similarly, variation of ICR late within a shock ($L-\Delta Z_T$) was defined in units of ohms per second (Ω/s) as the linear slope ($Z(m)$) over time in the late part of the shock waveform pulse (7-11ms); processed for the negative phase in the case of the biphasic waveform [7]. For both $E-\Delta Z_T$ and $L-\Delta Z_T$ the slope $Z(m)$ was calculated using standard statistical linear regression and at least 1000 data points within the identified time windows:

$$y = mx + c$$

$$m = \frac{S_{xy}}{S_{xx}}$$

$$S_{xy} = \sum xy - \frac{\sum x \sum y}{n}$$

$$S_{xx} = \sum x^2 - \frac{(\sum x)^2}{n}$$

where x,y are the time and corresponding $Z(t)$ data point pairs during a time segment of the voltage (V) and current (I) signals captured by the digital oscilloscope and n is the number of data points within the associated time interval.

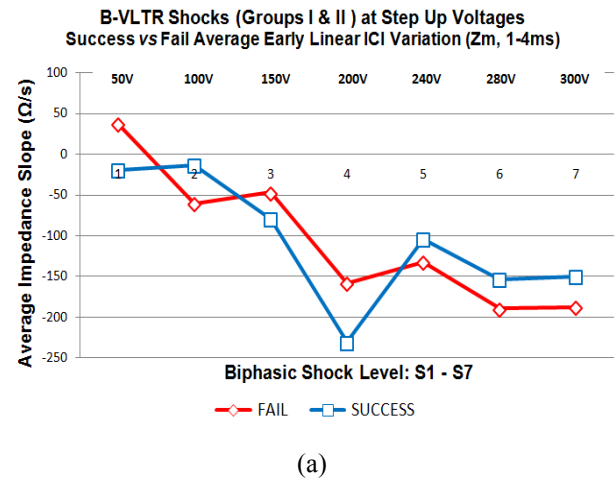
3. Results

Variation of ICR over time between successive electrical shocks (ΔZ_T) delivered was calculated and analyzed for statistical significance across all groups within both arms of the study (Table 3). For both the biphasic and monophasic treatment protocols, all patients who cardioverted exhibited a significant reduction in ICR (Z_{AV}) between the first shock (S1) and third shock (S3) (Group-I: $\Delta Z_T(S1 \rightarrow S3) = 4.95\Omega$ (SD=2.71), $p < 0.01$ and Group-III: $\Delta Z_T(S1 \rightarrow S3) = 5.00\Omega$ (SD=1.62), $p < 0.003$). However, critically, a significant reduction in ICR between the first and third shock was absent for all patients who failed to cardiovert (Group-II : $\Delta Z_T(S1-S3) = 3.30\Omega$ (SD=5.63 Ω), $p > 0.05$ and Group-IV: $\Delta Z_T(S1-S3) = 8.12\Omega$ (SD=6.61 Ω), $p > 0.05$, respectively). Note that for the latter pair of groups SD values are relatively high with respect to the mean values.

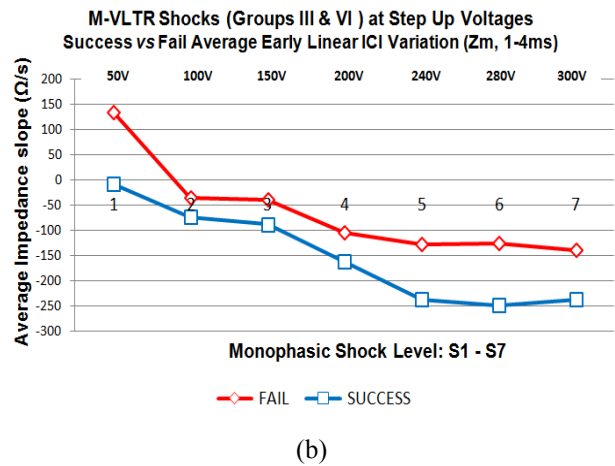
As previously described in the methods section, variation of ICR within a shock over time was also estimated using linear regression; estimated in units of

Table 3. Dynamic variation in ICR during cardioversion.

Group	ΔZ_T (Ω) S1 -> S3 (p-value)	ΔZ_T (Ω) S3 -> S4 (p-value)	ΔZ_T (Ω) S4 -> S5 (p-value)
Group-I (n=5)	4.95±2.71 $p < 0.009$	0.11±2.04 $p > 0.147$	2.22±1.61 $p > 0.100$
Group-II (n=6)	3.30±5.63 $p > 0.154$	0.02 ±1.61 $p > 0.891$	-1.18±3.50 $p > 0.254$
Group-III (n=5)	5.00±1.62 $p < 0.003$	-0.04±2.80 $p > 0.952$	1.03±3.20 $p > 0.264$
Group-IV (n=5)	8.12 ±6.61 $p > 0.051$	0.92±3.40 $p > 0.404$	-0.12±3.35 $p > 0.775$



(a)



(b)

Figure 2. (a) and (b): Average values of $E-\Delta Z_T$ for (a) Group-I, Group-II (biphasic: success versus fail) and Group-III, Group-IV (monophasic: success versus fail).

ohms per second (Ω/s) as the linear slope (m) of $Z(t)$ over time in the early part of the shock waveform pulse ($E-\Delta Z_T$: 1-5ms; positive phase for B-VLTR waveform) and late dynamic part of the shock waveform ($L-\Delta Z_T$: 7-11ms; negative phase for B-VLTR waveform). However, using this approach, no significant correlation of linear variation in ICR to clinical outcome was detected (neither within individual patient shock sequences or across any of the data groups previously defined). Yet, for completeness, the contrasting average values of $E-\Delta Z_T$ for Group-I versus Group-II [Figure 2(a): B-VLTR waveform (success versus fail)] and Group-III versus Group-IV [Figure 2(b): M-VLTR waveform (success versus fail)] are presented.

4. Discussion

This study reveals the prognostic attributes of intracardiac resistance variation metrics and can be used as a predictive marker during internal cardioversion of AF. Here a significant decrease in intracardiac resistance within the time domain was identified as positive predictors of success in both arms of the study (B-VLTR and M-VLTR waveforms using a step-up treatment protocol). The phenomena is observed to be linear for the first three shocks delivered; the effect becoming considerably less pronounced thereafter. Moreover, the reproducibility of these observations across both arms of the study (with significantly different efficacy rates) provides an indication of the electrophysiological nature of the trends observed.

Several factors can influence intracardiac resistance such as the position and dimensions between defibrillation electrodes, type of electrode, the electro-mechanical interface between the catheter and cardiac substrate and the phase of respiration during shock delivery [5,6,8]. However, in mitigation, all of these variables were kept constant in this study; the same defibrillator system (including catheter type) was used throughout, the defibrillation catheter was positioned in the same anatomical position for each patient (with changes in the distance between the defibrillation electrode poles due to different sized cardiac substrates accounted for via the comparative analysis techniques used), while each cardioversion shock was electronically synchronised to the R wave of the electrocardiogram (ECG) via the defibrillator system.

Ideally, a larger sample number for each group in Table 3, would have enhanced the power of this retrospective study. Nevertheless, if a Bonferroni correction is used to account for the statistical comparison between the two arms of study ($p < 0.025$ for significance) then ICR changes in groups II and IV would be placed further away from statistical significance.

5. Conclusions

The data suggests that for both biphasic and monophasic based internal cardioversion protocols, a significant decrease in ICR during the first three shocks delivered can be used as a predictive marker for cardioversion outcome.

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