Acute Evaluation of the Post Atrial Stimulation Evoked Response at Various Sites

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Summary

Previous studies have confirmed the efficacy and reliability of ventricular autocapture. There is less experience with detecting the atrial evoked response. This study aims at evaluating the ability to detect the local atrial evoked response and to define possible implantation areas, using conventional VVI Regency SC+ pacing technology. Twenty patients (age 75.7 ± 11.7 years, 7 female) undergoing dual-chamber pacemaker implantation were enrolled for standard clinical indications. Regency pacemaker systems for atrial evoked response measurement were connected to titanium-nitride coated Tendril DX 1388T leads. The atrial evoked response was recorded in 3 different areas: the atrial septum, the lateral atrial free wall, and the right appendage. Atrial pacing thresholds and P-wave amplitudes were analyzed in the same positions. An atrial evoked response was detected in 11/20 patients (55 %): in 3 at the atrial septum, 3 at the lateral atrial free wall, and 7 at the right appendage. In 2 patients, the atrial evoked response was recorded at 2 different sites. The mean atrial-evoked response amplitude was 2.16 ± 0.61 mV. The mean atrial pacing threshold of the 11 patients with atrial-evoke response detection was 0.7 ± 0.2 V, compared to 0.95 ± 0.55 V if the atrial evoked response was not recorded (p = 0.01). The mean P-wave amplitude was 3.30 ± 0.95 mV (compared to 2.24 ± 1.30 mV; p = 0.02). There was no correlation between the atrial-evoked response amplitude and the P-wave amplitude. Ventricular filters were used for atrial-evoked response recording. The authors suggest that the use of special atrial filters might improve atrial-evoked response detection results. Other implantation sites, including the atrial septum, should be explored if no atrial evoked response can be detected at the lateral atrial free wall or the right appendage. In the future, it should be possible to use atrial-evoked response analysis to measure chronic atrial thresholds and adapt pacing amplitudes, thereby limiting energy drain and optimizing patient safety.

Key Words

Atrial evoked response, P-wave amplitude, atrial pacing threshold, atrial septum, lateral atrial free wall, right appendage

Introduction

The evoked response is defined as the electrical reaction of myocardial cells to an efficient stimulation. It is composed of the sum of myocardial action potential signals [1]. This signal has been measured and used in pacemakers since 1973 [2-6]. For 4 years, St. Jude Medical (USA) has been marketing a single-chamber pacemaker designed to incorporate an automatic threshold adaptation, or autocapture. This device proved to be safer, more reliable and also more economical [7,8]. The benefits of autocapture are presently limited to the ventricle. The study of the evoked response at the atrial level, while feasible, is still in its beginnings [9,10]. Our study had the purpose to determine the probability of detecting an atrial evoked response (AER), using the technology developed by St. Jude Medical, and to find out whether AER sensing is a function of the implant site.

Material and Methods

Patients

Twenty consecutive patients (7 females), mean age 75.75 ± 11.7 years, with a valid dual-chamber pace-

Patient	Age/Sex	Indication	Diagnosis	Left atrium size (mm)	Right atrium size (mm)	AR drugs
1	82/M	sd / css	ihd	35.3	33.35	no
2	42/M	parox. avb	dilated cm	48.5	37	no
3	83/M	css	ihd	32.4	32.6	no
4	60/F	sd / parox. avb	-	40.94	30.29	amiodarone flecainide
5	84/F	css	-	31.8	26.9	no
6	73/F	perm. avb	-	29.08	27.3	no
7	88/M	sd / ccs	-	33.7	31.35	no
8	86/F	perm. avb	ht	nd	nd	no
9	74/F	sd / parox avb	ht / ihd	39.1	34.5	amiodarone
10	72/M	perm. avb	ht	39.95	38.4	no
11	62/M	sd / parox. avb	ihd	37.75	42.5	no
12	84/M	sd / parox. avb	-	37	32.7	no
13	63/M	brady-tachy synd.	-	43	38	no
14	87/F	avb / css	ht	41.2	37.3	no
15	88/M	sd	dilated cm	nd	nd	no
16	83/F	parox. avb	ht / ihd	nd	nd	no
17	83/M	sd / css	ht	37.16	42.5	no
18	73/M	css	ht	30.6	20.15	no
19	73/M	perm. avb	-	nd	nd	flecainide digoxine
20	75/M	perm. Avb	ihd	nd	nd	no

Table 1. Main patient data. avb = atrioventricular block; cm = cardiomyopathy; css = carotid sinus syndrome; ht = hypertension; ihd = ischemic heart disease; nd = not determined; parox. = paroxysmal; perm. = permanent; sd = sinus dysfunction; synd. = syndrome.

maker implant indication (ACC/AHA task force Class I or II) were enrolled after giving their informed consents. We excluded patients with supraventricular rhythm disturbance at implant time. The indications are itemized in Table 1. Cardiomyopathy, most often of ischemic or hypertensive origin, was present in 65 % of the cases. Whenever possible, an echocardiography (US Diasonics Wingmed CFM 750) was performed in order to measure the right and left atrial diameters. The technique used a parasternal cut, great axis, and four cavities. Any antitachyarrhythmia treatment was maintained.

Pacing Method

Two surgeons were involved in this study. The implant procedure was absolutely typical and performed according to the implanting surgeon's usual technique, except that 3 atrial zones were systematically evaluated: the interatrial septum (AS), the lateral atrial free wall (LFW), and the right atrial appendage (RA). The AS was always tested first, the fixation being performed at the coronary sinus ostium. The AS was localized by introducing a lead into the coronary sinus, then withdrawing it and positioning it near the ostium, and also by looking for

negative P-waves in the lower leads during pacing. The following measurements were systematically performed for all 3 sites:

- Pacing threshold amplitude, unipolar at 0.5 ms pulse width (ERA 300, Biotronik, Germany).
- P-wave amplitude measured peak-to-peak on the bipolar traces collected at a Hellige-Midas (USA) electrophysiology bay after elimination of the ancillary filters and amplitude limiters. Low 30 Hz and high 300 Hz filtering was maintained. The amplitude obtained corresponded to the average of 4 or 5 recorded signals.
- Evoked response and lead polarization amplitudes, recorded using a Regency SC + 2402 L pulse generator (St. Jude Medical) that acted as an external pacemaker. This pulse generator was insulated in a can with three outlets: one anode and one cathode connector used for bipolar sensing of the AES; and a third outlet used for pacing in a distal unipolar mode. The pulse generator can was connected to the atrial lead via two sterile connecting cables (Figure 1). This device was produced by the St. Jude Medical company in Issy les Moulineaux, France. The AER was always recorded last, 10 min after lead fixation in its site. The AER signal (expressed in mV) and the residual polarization were then measured separately, using the pacemaker and a sensing window set between 15 and 62 ms after a biphasic pulse. Both measurements were made according to the device sensitivity. The polarization was measured after a 4.5 V/0.5 ms pulse. The various parameters and the signal filtering are not programmable. Autocapture is allowed according to the evoked response/polarization ratio. The evoked response amplitude must be 4 times higher than the polarization amplitude. Evoked response and polarization occur simultaneously because they are induced by the same pacing pulse. They are synchronous (Figure 2). Interrogation and results display were performed using an APS II external programmer (St. Jude Medical), after positioning the programming head over the pacemaker and launching the "Evoked response measurement" program. Three consecutive measurements were performed in this manner at each implant site, at a pacing rate higher than the sinus rhythm in order to eliminate fusion beats. The obtained value was the average of the 3 measurements. Evoked response sensing was defined as possible whenever the programmer displayed an AER value (Figure 3), even when this result was indicated as inadequate to recommend autocapture algorithm activation. Otherwise, the impossibility to proceed with the measurement was displayed (Figure 4). Whenever the residual polarization amplitude was higher than the AER, the search was declared negative. When the polarization was significant (> 4 mV) but remained below the AER signal amplitude, the estimated value of the latter was calculated as the difference between measured AER and polarization amplitude. This approximation was made possible by programming the pacing parameters to 4.5 V/0.37 ms; polarization and AER measurements were then performed at the same pacing amplitude. Because the measurements are automatic, the results cannot be influenced by the user's expertise. At the end of the procedure, the atrial lead was repositioned based on the best pacing and sensing parameters.

Leads

Only one type of screw-in retractable helix bipolar silicon leads was used at the atrial level: the Tendril DX 1388 T (St. Jude Medical), a low-polarization, titanium nitride, steroid-eluting lead.

Statistical Analysis

All values are indicated as mean ± standard deviation. The Wilcoxon test was used to compare the populations in terms of age, P-wave amplitude, and AER signal. The standard Mann and Whitney test was used for

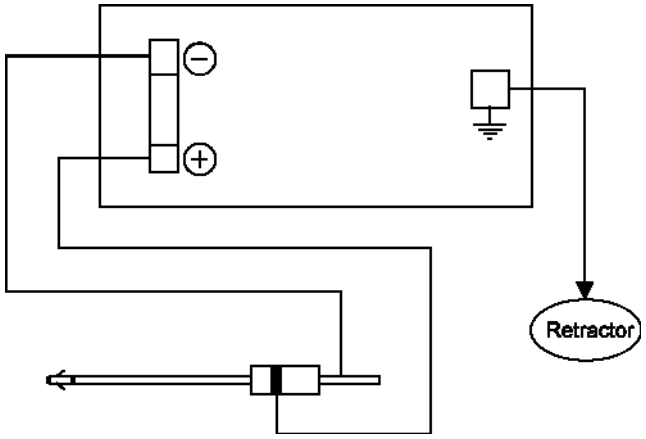

Figure 1. Technique for recording the AER (= atrial evoked response) in bipolar mode after unipolar stimulation.

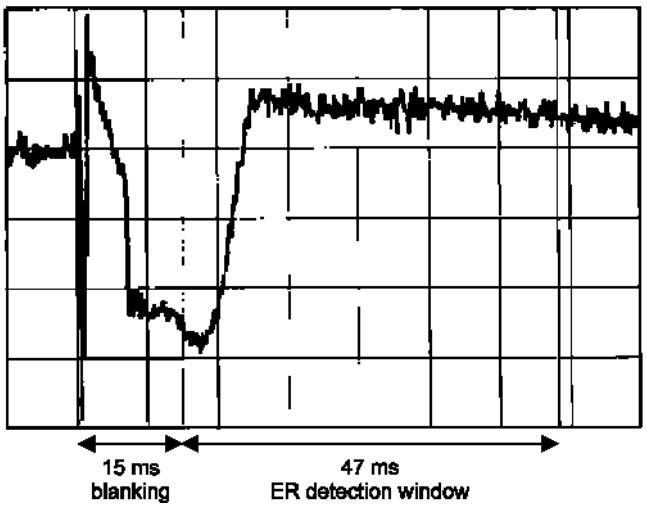

Figure 2. Evoked response sensing.

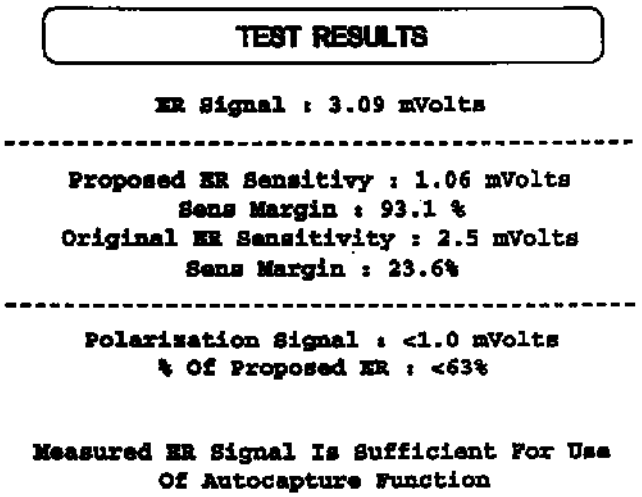

Figure 3. An example of an AER and polarization measurement with the St. Jude Medical system. Sens = sensitivity.

the threshold parameters. Chi-square testing was used to compare the qualitative variables. A value of $p < 0.05$ was considered as significant.

Results

This study confirms that the AER can be measured, using the unmodified technique developed by the manufacturer (Table 2). Detection was possible in 11 out of 20 patients (55 %) if several sites were tested. The AER signal was sufficient to enable autocapture in only 2 patients out of 11 (# 7 and 9). In three other cases, an intermittent response could be noted. However, the signal amplitude was too low to allow quantification, and the response was declared negative. The detection site is variable. The AER was detected in:

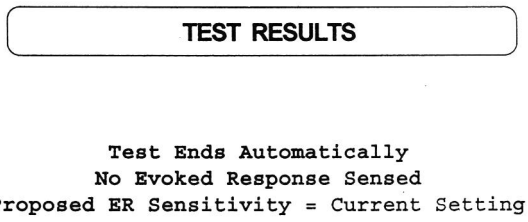

Figure 4 . An example where no AER was detected. ER = evoked response.

- the LFW in 3 cases.
- the RA in 7 cases.
- the AS in 3 patients.

Only in 2 patients, an AER signal was evidenced in two different locations:

- in one case, at the level of LFW and of the RA.
- in the other case, at the level of the RA and of the AS.

The mean amplitude of the AER was 2.16 ± 0.61 mV, with no significant differences between the 3 sites.

A correlation between existence of an AER, low pacing threshold, and higher P-wave amplitude measurement seems logical, but has not yet been described. When an AER was observed, the pacing thresholds were statistically lower (0.7 ± 0.2 V vs. 0.95 ± 0.5 V, $p = 0.01$), and the recorded P-wave amplitudes were higher (3.3 ± 0.95 mV vs. 2.24 ± 1.3 mV, $p = 0.02$) (Table 3). In 84.6 % of the cases (11/13), the P-wave amplitude was ≥ 3 mV whenever AER detection was possible.

On the other hand, there is no correlation between the presence of an AER and age, gender, potential cardiopathy, or atrial dimensions. The lead resistance did not have any bearing on the AER findings.

Finally, there was no correlation between the AER amplitude and the intrinsic P-wave amplitude (Figure 5) ($p = 0.55$).

Residual polarization typically remained < 1 mV. Higher polarization values (> 4 mV) were observed with two leads.

Patient	Posit. AER	Thr. LFW	Pwa LFW	AER LFW	Thr. AP	Pwa AP	AER AP	Thr. AS	Pwa AS	AER AS	Polariz.
1	1	0.9	2	-	0.6	3	-	0.5	3.3	1.6	0
2	0	1.3	2	-	1.7	3.2	-	1.7	1.4	-	0
3	0	0.6	1.4	-	0.5	1.2	-	0.8	1.3	-	0
4	1	3.9	3.25	-	0.8	3.25	-	1	3.2	2.71	0
5	0	0.6	2	-	0.7	1.5	-	0.7	1.8	-	0
6	1	0.4	7.4	-	0.5	3.9	2.12	0.9	1.5	-	0
7	1	0.6	3	2.81	0.6	3	-	1.4	0.55	-	0
8	0	2	0.8	-	0.9	0.4	-	0.9	1.7	-	0
9	1	0.8	3.5	2.66	0.6	3.5	2.81	0.6	2.4	-	0
10	1	0.8	3.5	-	0.6	3.5	0.68	1	2.3	-	1
11	0	1	1.5	-	0.8	2.3	-	1	1.6	-	0
12	1	0.8	1.8	-	0.6	5.2	2.61	1.3	1.5	-	0
13	1	0.8	4.5	1.9	0.7	1.6	-	1	0.7	-	0
14	0	0.7	1.4	-	0.7	2.2	-	0.7	1	-	0
15	0	0.5	2.6	-	0.7	4.2	-	0.9	1.2	-	0
16	1	1	1.6	-	1.1	1.8	1.98	0.9	2.25	-	0
17	1	0.5	5	-	0.6	3	2.24	0.9	1.6	1.62	0
18	0	0.7	2.5	-	0.6	4	-	1.5	4.5	-	1
19	1	1	2.2	-	0.5	3	2.4	1	1	-	0
20	0	0.7	2.2	-	0.9	4	-	0.9	2	-	0

Table 2. Main data concerning AER, P-wave amplitude, and atrial pacing threshold. AS = atrial septum; Pwa = P-wave amplitude; LFW = lateral free wall; thr. = threshold; AP = appendage; polariz. = polarization.

An atrial pathology (sinus dysfunction, atrial rhythm disturbance) was often observed whenever an AER was present (8/11 patients). Conversely, AER detection was not possible in 7 of 9 patients with a presumably "healthy" atrium (discrete HB, carotid sinus syndrome).

Discussion

Previous Reports

Ten years ago, two authors already demonstrated the possibility to detect an evoked response following atrial pacing and showed that this response was present in all patients. In our study, such a signal was measured in only 55 % of the cases. A number of explanations can be proposed:

- The used technology is different: Curtis first tested a triphasic pacing system to limit the polarization artifacts [11], and then used bipolar pacing and sensing [9]. Livingston [9] used unipolar pacing and sensing with passive or active fixation leads. Pacing was followed by a brief "short-circuiting" to modify the pacemaker's output impedance and to make a larger part of the residual post-pacing polarization disappear. In the system developed by St. Jude Medical, the residual polarization is limited by using low polarization titanium nitride leads [12] and a biphasic pulse.
- In this study, the AER amplitude was measured 10 min after lead fixation. This may have led to a mixture of the AER potential (positive) and the lesion current (negative), resulting in a composite signal of very low amplitude.
- The pacemaker used to measure the AER is of the SSI type. However, the autocapture algorithm is authorized only in ventricular pacing using a specific signal filtering. In the study conducted, we applied a technique developed for the ventricle to

	AER+	AER-	p
Age (years)	75.9 ± 8.9	75.5 ± 15.15	NS
Left atrial size (mm)	36.58 ± 4.4	38.3 ± 6.8	NS
Structural heart disease	45.45 %	88.8 %	NS
Atrial threshold (V)	0.7 ± 0.2	0.95 ± 0.55	p = 0.01
Atrial sensing (mV)	3.30 ± 0.95	2.24 ± 1.30	p = 0.02

Table 3. Comparison between positive and negative AER.

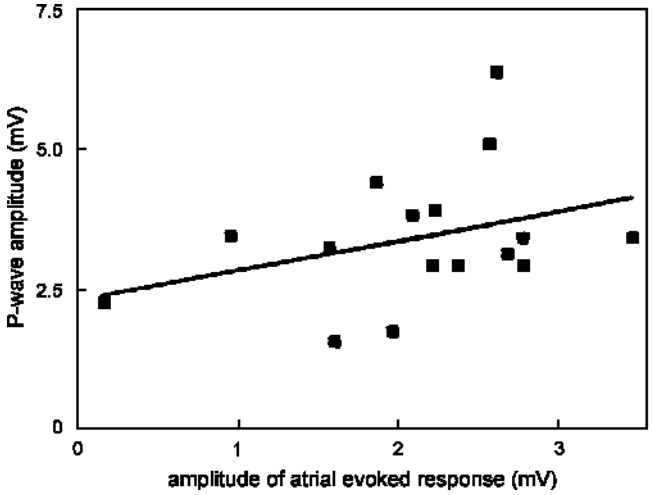

Figure 5. The amplitudes of the AER and the P wave show no correlation.

the atrium. Since the AER signal morphology can be significantly modified by a change of the filtering frequency [10], some responses may not be detected. The use of specially designed atrial filters might improve the results.

- The paced signal morphology can differ according to the potential presence of an underlying atrial pathology, which is not specified by Curtis and Livingston.

Major Findings

- This study confirms that AER detection is possible in 55 % of patients.
  The mean AER signal amplitude varies widely from one study to the other: from 1 mV to 3.1 ± 1.4 mV with a mean AER amplitude of 2.16 ± 0.61 mV in this report. Our results are intermediate. Here again, many causes can be proposed to explain these differences.
- The used pacing and sensing techniques differ, both in the two original studies and in ours. It seems that inferior results correspond to unipolar sensing.
- Signal amplitudes are not measured in the same manner. Endocardial traces were used in the original studies [9,10]. In our experience, the pacemaker delivers a number that is an averaged value and cannot be verified because there is no possibility to obtain an associated graphical representation. There remains a false negative risk.
- The quality of the atrial substratum can also be questioned. Many of our patients were elderly, and over 50 % suffered from atrial rhythm disturbances.
  The existence of an atrial pathology in the group where an AER was detected seems paradoxical. The patients with an "a priori" healthy atrium displayed higher pacing thresholds, lower P-wave amplitudes, and less frequent AERs. Therefore, one can question whether organic atrial lesions were really absent in this elderly population, and it is possible that local conduction disorders actually promote AER detection.

It has already been demonstrated that there is no correlation between the amplitudes of the R wave and the evoked response in the ventricle [13]. The same was also observed in the atrium.

Presently, it is difficult to define what would be a preferred implant site to sense AERs. Even though the RA seems to be the most appropriate site, the sample size of our study is actually too small to give an answer. In the event of failure, it is thus necessary to test other atrial sites including the AS.

Limitations

Due to the current of injury which occurs at the time of fixation, the use of an active fixation lead may not always be associated with good immediate AER signals.

In the long run, it should be possible to use this AER analysis to measure chronic atrial thresholds and adapt pacing amplitudes, thereby limiting energy drain and optimizing patient safety.

Acknowledgement

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