VIA MEDICA
ORIGINAL ARTICLE
2015, Vol. 22, No. 3, 241–246
DOI: 10.5603/CJ.a2014.0088

ISSN 1897–5593

Differences in the yield of the implantable loop recorder between secondary and tertiary centers

Francisco Javier Lacunza-Ruiz[1], Angel Moya-Mitjans[2], Jesús Martínez-Alday[3], Gonzalo Barón-Esquivias[4], Ricardo Ruiz-Granell[5], Nuria Rivas-Gándara[2], Susana González-Enríquez[6], Juan Leal-del-Ojo[7], Natalie Garcia-Heil[8], Arcadi García-Alberola[1]

[1]Hospital Universitario Virgen de la Arrixaca, Murcia, Spain
[2]Hospital Universitario Vall d´Hebron, Universidad Autónoma de Barcelona, Spain
[3]Hospital de Basurto/Clínica Vicente San Sebastian, Bilbao, Spain
[4]Hospital Virgen del Rocío, Sevilla, Spain
[5]Hospital Clínico de Valencia, Valencia, Spain
[6]Hospital Marqués de Valdecilla, Santander, Spain
[7]Hospital de Valme, Sevilla, Spain
[8]Scientific and Clinical Department, Medtronic Iberica SA, Spain

Abstract

Background: *The implantable loop recorder (ILR) is a useful tool for diagnosis of syncope or palpitations. Its easy use and safety have extended its use to secondary hospitals (those without an Electrophysiology Lab). The aim of the study was to compare results between secondary and tertiary hospitals.*

Methods: *National prospective and multicenter registry of patients with an ILR inserted for clinical reasons. Data were collected in an online database. The follow-up ended when the first diagnostic clinical event occurred, or 1 year after implantation. Data were analyzed according to the center of reference; hospitals with Electrophysiology Lab were considered Tertiary Hospitals, while those hospitals without a lab were considered Secondary Hospitals.*

Results: *Seven hundred and forty-three patients (413 [55.6%] men; 65 ± 16 year-old): 655 (88.2%) from Tertiary Centers (TC) and 88 (11.8%) from Secondary Centers (SC). No differences in clinical characteristics between both groups were found. The electrophysiologic study and the tilt table test were conducted more frequently in Tertiary Centers. Follow-up was conducted for 680 (91.5%) patients: 91% in TC and 94% in SC. There was a higher rate of final diagnosis among SC patients (55.4% vs. 30.8%; $p < 0.001$). Tertiary Hospital patients showed a trend towards a higher rate of neurally mediated events (20% vs. 4%), while bradyarrhythmias were more frequent in SC (74% vs. 60%; $p = 0.055$). The rate of deaths and adverse events was similar in both populations.*

Conclusions: *Patients with an ILR in SC and TC have differences in terms of the use of complementary tests, but not in clinical characteristics. There was a higher rate of diagnosis in Secondary Hospital patients.* (Cardiol J 2015; 22, 3: 241–246)

Key words: implantable loop recorder, registry, secondary centers, tertiary centers

Address for correspondence: Francisco Javier Lacunza-Ruiz, MD, Cardiology Department. Hospital Universitario Virgen de la Arrixaca, Ctra Madrid Cartagena sn. El Palmar. Murcia 30120, Spain, tel: +34 678 44 72 11, fax: +34 968 36 95 58, e-mail: javierlacunzaruiz@gmail.com

Received: 10.06.2014 Accepted: 22.10.2014

Introduction

The implantable loop recorder (ILR) is a valuable tool for the diagnosis of clinical situations associated with paroxysmal arrhythmias. Since the first cases in 1998 [1], several studies have documented the role of the ILR in the research of syncopal episodes [2], palpitations [3], atrial fibrillation [4], risk stratification in infarction [5], or the study of cryptogenic stroke [6].

The majority of these studies have been conducted in tertiary centers of reference, with a highly selected population and high degree of specialization, which might introduce a certain bias, both regarding population and in results obtained. The ease of device implantation has extended its use among general cardiologists, and has allowed its use as a first line tool in centers without an Electrophysiology Lab. Neither the indications nor the results of the device in this setting have been described. The objective of the present study is to compare the results of the ILR (Reveal Plus/ /DX/XT®, Medtronic, Inc.) in a non-selected patient population from centers with and without Electrophysiology Lab.

Methods

This is a sub-study of the Reveal Spanish Registry [7], which was designed as a prospective, observational and multicenter study on a national level. All centers where ILR devices are inserted were invited to take part. All patients who had a Reveal Plus® or Reveal XT-DX® implanted between April 2006 and December 2008 were included. No exclusion criteria were implemented, and the device parameters were programmed according to the choice of each professional conducting the procedure.

Those centers with an Electrophysiology Lab were defined as Tertiary Centers (TC group), while centers without an Electrophysiology Lab were defined as Secondary Centers (SC group).

Structural heart disease and bundle branch block were defined according to the definitions of previously published studies [8, 9].

Baseline data, as well as data about electrogram interpretation, final diagnosis and treatment, were included in the database as provided by the corresponding local investigator. Event was defined as the presentation of syncope, pre-syncope or palpitations which reproduced the patient's symptoms, or the presence of a significant arrhythmia detected by the device, as defined in clinical guidelines [10]. Any event considered significant by the responsible physician and which led to a final diagnosis was considered a diagnostic event.

Follow-up visits were scheduled according to the investigators' preference. Follow-up was ended when a diagnostic event occurred, or at the end of the follow-up period. For those patients without any events, follow-up at least of 12 months was requested.

Data were collected in electronic format or in paper forms, if it was required by the center. Electrograms could be sent in an electronic format to the Research Committee for its interpretation, if the physician considered it necessary. All data were stored in a database created for that purpose (MS Access Microsoft Corporation 2003). All those abnormal or inconsistent data were subject to a new analysis by the Research Committee.

Statistical analysis

Continuous variables are presented as mean and standard deviation or median (range), if distribution is not normal. Qualitative variables were analyzed using frequency and percentage tables. Comparison between arms was conducted with Student's t-test or Mann-Whitney test for continuous variables, and with χ^2 or Fisher's exact test for proportions. The hypothesis was considered significant if the value of p was below 0.05. The SPSS program (v16.0.1, Chicago, Ill, USA) was used for analysis.

Results

Study centers and population

Forty centers took part in the registry; out of these, 30 (75%) were TCs and 10 (25%) were SCs. Seven hundred and forty-three ILRs were implanted: 655 (88.2%) in TCs, and 88 (11.8%) in SCs.

The baseline characteristics of the study population, and the results of tests conducted, classified according to the type of center, appear on Table 1. No significant differences were observed in terms of gender, age, prevalence of hypertension or diabetes, between both groups, nor in prevalence of structural heart disease (35% vs. 30%), left ventricular ejection fraction, or bundle branch block.

Cases were classified into four categories, according to the reason for implantation: single syncope, recurrent syncope, pre-syncope, and others (which included the rest of causes for implantation). Both populations presented a similar distribution in terms of cause for implantation (Table 1).

Table 1. Baseline characteristics, test performed, events, diagnosis, and treatment of patients according to the type of hospital.

	Tertiary Centers	Secondary Centers	P
Patients	655	88	
Age [years]	64.7 ± 16.5	67.1 ± 14.5	0.271
Gender (men)	364 (55.6%)	49 (55.7%)	0.966
Left ventricular ejection fraction:			0.365
> 55%	460 (70.2%)	67 (76.1%)	
35–55%	75 (11.5%)	10 (11.4%)	
< 35%	8 (1.2%)	0 (0%)	
No data	112 (17.1%)	11 (12.5%)	
Structural heart disease	197 (30.1%)	31 (35.2%)	0.325
Hypertension	307 (46.9%)	45 (51.1%)	0.347
Diabetes	105 (16.0%)	14 (15.9%)	0.830
Bundle branch block (BBB)	158 (24.1%)	25 (28.4%)	0.381
Right BBB	40 (6.1%)	6 (6.8%)	
Left BBB	55 (8.4%)	9 (10.2%)	
Others	63 (9.6%)	10 (11.4%)	
Electrophysiologic study:			0.001
Normal	245 (37.4%)	13 (14.8%)	
Pathologic	45 (6.9%)	8 (9.1%)	
Non performed	365 (55.7%)	67 (76.1%)	
Carotid sinus massage:			
Performed	330 (50.4%)	32 (36.3%)	0.013
Head up tilt test:			0.07
Positive	72 (11.0%)	10 (11.3%)	
Negative	139 (21.2%)	10 (11.3%)	
Non performed	444 (67.8%)	68 (77.3%)	
Cause of implant:			0.355
Recurrent syncope	501 (76.5%)	67 (76.1%)	
Single syncope	98 (15.0%)	9 (10.2%)	
Presyncope	34 (5.2%)	9 (10.2%)	
Others	22 (3.3%)	3 (3.4%)	
Lost patients	58 (8.8%)	5 (5.7%)	0.417
Events*	275 (46.6%)	50 (60.2%)	0.015
Final diagnosis*	184 (30.8%)	46 (55.4%)	< 0.001
Final treatment*	166 (27.8%)	45 (54.2%)	< 0.001
Diagnosis of the event**:			0.084
Bradyarrhythmia	110 (59.8%)	34 (73.9%)	
Tachyarrhythmia	25 (13.6%)	7 (15.2%)	
Neuromediated	37 (20.1%)	2 (4.3%)	
Other	12 (6.5%)	3 (6.5%)	

*Percentages refer to patients with follow-up; **Percentages refer to patients with final diagnosis

Diagnostic tests

Carotid sinus massage (CSM) was conducted more frequently in the TC group (50 vs. 36%, p = = 0.020), though no differences were found in the age of both populations. There was a trend to perform tilt table test more frequently in TCs (33% vs. 22%; p = 0.07), and, as expected, the electrophysiologic study (EPS) was conducted more frequently in

patients with the ILR implanted in TCs. The most common finding among patients with abnormal EPS results was first or second degree atrioventricular block (n = 16), followed by induced supraventricular tachycardias (n = 15).

Follow-up

All results refer to the patients with follow-up data (680 patients; 591 from TCs (91%) and 89 (94%) from SCs). The baseline characteristics of 63 patients without follow-up showed no differences from those of the rest of the population. The average duration of follow-up was 321.5 ± 174.4 days for patients from TCs and 274.6 ± 190.5 days for SC patients (p = 0.02).

There were 414 events (350 in TCs and 64 in SCs) in 325 patients (275 TC patients and 50 SC patients) (47% vs. 60% p = 0.015). The number of events per patient was similar in both populations (1.3 vs. 1.2). The type of event recorded (syncope, pre-syncope, palpitations and automatic activations) had a similar distribution between both groups.

A final diagnosis was obtained in 184 patients (30.8%) from TCs and 46 (55.4%) from SCs (p < 0.001). The average time to diagnosis was similar in both groups (212 ± 193 days in SCs vs. 225 ± 175 days in TCs; p = 0.662).

The type of final diagnosis was different in both groups. In the TC group, the rate of neurally mediated events was higher (20% vs. 4%; p = 0.006), while bradyarrhythmias were more frequent in the SC group (74% vs. 60%; p = 0.035). The proportion of events due to tachycardia or other causes was similar in both groups.

A similar proportion of patients with final diagnosis received specific treatment in both populations (90% in TCs and 98% in SCs).

Mortality

Eighteen (2.4%) deaths were recorded during follow-up (55.5% male patients; age 72.7 ± 8.5); 10 (55.5%) of these patients had structural heart disease, and 7 (38.9%) presented abnormalities in their electrocardiograms. The cause of death could only be confirmed in 4 cases; 17 cases came from TCs (2.5% vs. 1.1%, p = 0.7).

Discussion

As far as we know, this is the first study which has compared ILR results between SC and TC. Results show that the performance of the device seems to be higher in those centers without Electrophysiology Lab, probably due to the different diagnostic strategies used in both populations.

Regarding baseline characteristics of the population, both groups present similar data in terms of age, distribution by gender, and comorbidities (diabetes, hypertension, bundle branch block), and the primary cause for implantation in both groups was recurrent syncope. The prevalence of structural heart disease in our population (30%) was similar to that in previous studies (28–33%), and so were the rest of baseline characteristics [11, 12]. We did not find significant differences between patients from TCs and SCs.

Diagnostic tests

The tests conducted in both populations show important differences, not only regarding EPS data, but also in other tests; this shows that a different diagnostic strategy was used in each group.

As expected, there were no significant differences in the use of echocardiography. EPS (44% vs. 26%, p < 0.05) were conducted more frequently in TCs, probably due to their higher availability. Something similar happened with the tilt table test, with a significant trend to be performed more frequently at TCs (33% vs. 22%; p = 0.07).

Even though the CSM is a simple clinical maneuver, it was more frequently conducted in TCs (50% vs. 36%; p < 0.05), even when there were no differences between ages of both populations. The explanation for this could lie in a higher familiarity among TC physicians with this test, or a higher adherence to clinical guidelines. However, the rate of patients with CSM in both groups was higher to the one reported in previous studies (36% in the PICTURE Registry [11]) or in studies about syncope conducted in Emergency Units in Spain (0.4% in the GESINUR Study [13]).

Results of the ILR

The study showed significant differences in the final diagnosis rate among SC patients (55% with final diagnosis) vs. TC patients (31% diagnosis). The main difference lies in the presence of a higher number of bradycardias in the SC group. There are reasons which might explain this fact; thus, the more frequent use of EPS in TCs could have detected a group of patients with higher risk of bradycardia, as patients with first grade infra-Hisian block, or with prolonged sinus node recovery time, with direct indication for pacemaker instead of ILR. Something similar could be applied to CSM, more frequent in TCs. Finally, even though both groups presented a similar rate of patients with recurrent syncope, the total number

of syncopes and the presentation pattern in these patients was not ascertained, and could be different in both both groups. These results probably indicate that the selection of population is conducted differently in both types of centers; this may have a direct impact on the performance obtained, not so much due to a different cost–effectiveness of the device, but because a different initial population has been studied in each of them (SC vs. TC).

Diagnosis rates in the TC group are very similar to those described in previous studies (28% [11], 24% [12]) with similar populations. However, the lack of previous studies in the patient population from SC does not allow making any comparisons.

The type of final diagnosis was also different between both cohorts; the TC group presented a prevalence of neurally mediated events (20% vs. 4%), while the SC group presented more events associated with bradycardias (74% vs. 60%). Patient selection may play a role in these findings, as those patients more prone to suffering severe bradycardias might have been previously excluded in TCs through the use of EPS. Another possible explanation could be a different interpretation of the bradycardia mechanisms, and consequently of the final diagnosis, depending on each center. In SCs, the arrhythmic etiology of events with bradycardia could be more frequently accepted, while those same registries could be interpreted as neurocardiogenic in TCs.

The treatment rate in both cohorts was very similar, though logically pacemakers were more frequently implanted in the SC group, according to the predominant interpretation of the bradycardiac episodes in these centers.

One important aspect is device safety; as previously described, there were no differences in mortality rate between both groups. This fact can be explained by the low number of deaths, as well as by the previous selection of patients conducted by the researchers, who would use the ILR only when a low risk of fatal events was accepted. The global rate of mortality is similar to the one in other previous publications, which ranges between 3.9% and 5% [12, 14].

Limitations of the study

The Spanish Reveal Registry is an observational registry and therefore, results should be interpreted as such. However, this information may complement data from controlled and randomized studies, and may be more accurate regarding what happens in daily clinical practice.

Given the low number of electrograms sent to the database, it is impossible to use them for the interpretation of events, and most diagnoses rely only on the clinical judgment of the responsible physicians.

Even though patients lost during follow-up may introduce a bias in the study results, there were similar rates of loss in both groups; and, moreover, our loss figures are consistent with those reported by other authors [11], and seem difficult to improve in this type of studies.

Conclusions

Patients considered for ILR implantation have a similar demographic and clinical profile in centers with and without EPS availability but a different diagnostic strategy used, with EPS and CSM conducted more often in TCs, resulting in a different selection of the final population receiving the device, which probably explains the higher rates of final diagnosis obtained in patients from SCs. In both populations, bradyarrhythmias were the most frequent events, though the rate of events of an assumed neurocardiogenic origin was significantly higher in TCs.

Although the strategy of using an ILR in these patients seems to be safe in both populations, even when no invasive tests are conducted before implantation, the low number of events precludes a detailed analysis of this important issue.

Acknowledgements

Participant centers and researchers: Clínica Universitaria de Navarra (Ignacio García Bolao), Complejo Hospitalario de Jaén (Miguel Ángel Arias), Fundación Hospital Son Llatzer (Tomás Ripoll Vera), Hospital Xeral de Vigo (Xulio Beiras), Hospital 12 de Octubre (Fernando Arribas/ /María López Gil), Hospital Arnau de Vilanova (José Sotillo), Hospital Clínico de Valencia (Ricardo Ruiz Granell), Hospital Clínico San Carlos (Julián Villacastín), Hospital Costa Del Sol (Francisco Ruiz Mateas), Hospital de Basurto/Clínica Vicente San Sebastián (Jesús Martínez Alday/María Fe Arcocha), Hospital de Donostia (Rafael Telleria), Hospital de Fuenlabrada (Alejandro Curcio), Hospital de León (Marisa Fidalgo), Hospital de Mérida (Javier Tejada Ruiz), Hospital de Orense (José Miguel Martínez-Escauriaza Alonso), Hospital de Santiago (José Luis Martínez Sande), Hospital de Tortosa (I. Lechuga), Hospital de Valme (Mª Dolores García Medina), Hospital de Zafra (Francisco Andrade), Hospital del Mar (Julio Martí), Hospital Francisco

de Borja (Plácido Orosa/Cathelyne Lawers), Hospital General de Albacete (Jesús F. García Sacristán), Hospital General de Castellón (Alejandro Navarro), Hospital General de Ciudad Real (Juan Benezet), Hospital General Yagüe (Javier García/Javier Martín), Hospital Gregorio Marañón (Felipe Atienza), Hospital Juan Canalejo (Luisa Pérez), Hospital Juan Ramón Jiménez (Rafael Barba Pichardo), Hospital Marqués de Valdecilla (Susana González), Hospital Puerta de Hierro (Jorge Toquero), Hospital Puerta del Mar (Lucas Cano), Hospital Ramón y Cajal (Antonio Hernández Madrid), Hospital Río Hortega (Benito Herreros/Juan Francisco Muñoz), Hospital San Pedro de Alcántara (J.M. Larrazabal Murillo), Hospital Universitario de Canarias (Aníbal Rodríguez), Hospital Universitario de Getafe (Agustín Pastor), Hospital Universitario Infanta Cristina (Juan José García Guerrero), Hospital Universitario La Paz (José Luis Merino Llorens), Hospital Universitario Vall D'hebron (Ángel Moya), Hospital Virgen de La Arrixaca (Arcadio García Alberola, Francisco J. Lacunza Ruiz), Hospital Virgen de La Macarena (Ernesto Díaz), Hospital Virgen de La Victoria (Javier Alzueta), Hospital Virgen del Rocío (Eduardo Arana, Gonzalo Barón-Esquivias).

Conflict of interest: Natalie García-Heil belongs to the Scientific and Clinical Department Medtronic Iberica SA. The rest of the authors declare not to have any other conflict of interest.

References

1. Krahn AD, Klein GJ, Yee R, Norris C. Final results from a pilot study with an implantable loop recorder to determine the etiology of syncope in patients with negative noninvasive and invasive testing. Am J Cardiol, 1998; 82: 117–119.
2. Krahn AD, Klein GJ, Yee R, Takle-Newhouse T, Norris C. Use of an extended monitoring strategy in patients with problematic syncope. Reveal Investigators. Circulation, 1999; 99: 406–410.
3 Giada F, Gulizia M, Francese M et al. Recurrent unexplained palpitations (RUP) study: Comparison of implantable loop recorder versus conventional diagnostic strategy. J Am Coll Cardiol, 2007; 49: 1951–1956.
4. Montenero AS, Quayyum A, Franciosa P et al. Implantable loop recorders: A novel method to judge patient perception of atrial fibrillation. Preliminary results from a pilot study. J Interv Card Electrophysiol, 2004; 10: 211–220.
5. Huikuri HV, Mahaux V, and Bloch-Thomsen PE. Cardiac arrhythmias and risk stratification after myocardial infarction. Pacing Clin Electrophysiol, 2003; 26: 416–419.
6. Merce J, Garcia M, Ustrell X, Pellisé A, de Castro R, Bardají A. Loop recorder implantable subcutáneo: Una nueva herramienta en el diagnóstico del ictus criptogénico. Rev Esp Cardiol, 2013; 66: 665–666.
7. Lacunza-Ruiz F, Moya-Mitjans A, Martínez-Alday J et al. Implantable loop recorder allows an etiologic diagnosis in one-third of patients. Circ J, 2013; 77: 2535–2541.
8. Brignole M, Menozzi C, Moya A et al. Mechanism of syncope in patients with bundle branch block and negative electrophysiological test. Circulation, 2001; 104: 2045–2050.
9. Menozzi C, Brignole M, Garcia-Civera R et al. Mechanism of syncope in patients with heart disease and negative electrophysiologic test. Circulation, 2002; 105: 2741–2745.
10. Brignole M, Alboni P, Benditt DG et al. Guidelines on management (diagnosis and treatment) of syncope: Update 2004. Eur Heart J, 2004; 25: 2054–2072.
11. Edvardsson N, Frykman V, Mechelen R et al. Use of an implantable loop recorder to increase the diagnostic yield in unexplained syncope: Results from the PICTURE registry. Europace, 2011; 13: 262–269.
12. Entem F, Enriquez S, Cobo M et al. Utility of implantable loop recorders for diagnosing unexplained syncope in clinical practice. Clin Cardiol, 2009; 32: 28–31.
13. Baron-Esquivias G, Martinez-Alday J, Martin A et al. Epidemiological characteristics and diagnostic approach in patients admitted to the emergency room for transient loss of consciousness: Group for syncope study in the emergency room (GESINUR) study. Europace, 2010: 12: 869–876.
14. Brignole M, Menozzi C, Maggi R et al. The usage and diagnostic yield of the implantable loop-recorder in detection of the mechanism of syncope and in guiding effective antiarrhythmic therapy in older people. Europace, 2005; 7: 273–279.