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RESEARCH ARTICLE

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Single-chamber pacemakers: with or without leads? Cost-effectiveness and cost-utility analyses

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ABSTRACT

Introduction: The evolution in pacemaker technologies has led to improvements in size, weight, functionality, and durability, even as the battery and electrode-based structural configuration has remained essentially the same.

Objective: To compare the cost-effectiveness and cost-utility of conventional and leadless pacemakers.

Material and methods: We conducted a retrospective observational study of 403 patients randomly implanted with a conventional or leadless pacemaker (1 June 2015–31 January 2020) in the Hospital-University Complex of Santiago de Compostela (Galicia, NW Spain).

Results: Conventional and leadless pacemakers were implanted in 244 and 159 patients, respectively. Leadless pacemakers were superior to the conventional pacemakers in terms of both cost-effectiveness and cost-utility, with incremental cost-effectiveness ratios of 6,263.38 euros per gained life year and of 5,210.71 euros per quality-adjusted life year, respectively.

Conclusions: Leadless pacemakers have fewer complications than conventional pacemakers and, although the device itself is more expensive, the leadless pacemaker is more cost-effective in around 90% of cases.

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Conventional pacemaker; leadless pacemaker; cost-effectiveness analysis; cost-utility analysis

1. Introduction

Single-chamber atrial or ventricular stimulation has resulted in survival rates of 93% in the first year and 66% in the fifth year [1]. Continuous technological advances since the first intravenous pacemaker (based on an electrode, generator, and implantable energy source) have led to improvements in weight, size, functionality, durability, materials and monitoring. Pacemaker implantations are estimated to increase by around 5% annually in the coming years, mainly due to population ageing and an increase in heart-related pathologies.

Currently, around 36,441 pacemakers per year are implanted in Spain [2], of which around 40% are pacemakers with single-chamber pacing, mainly (99.7%) VVIR pacemakers with right ventricular stimulation. In 2014, the cardiac electrostimulation field evolved radically with the introduction of a leadless pacemaker consisting of a single device incorporating both generator and electrode [3,4]. This change modified both the implantation technique and the profile of potential complications during and after implantation. The health benefits of the leadless pacemaker are similar to those for the conventional pacemaker [5–7], although potential implantation complications differ particularly in the immediate postoperative period: tamponade and vascular complications for leadless devices compared to infection/endocarditis, pneumothorax, haematoma, electrode dislocation, and lead dysfunction for conventional pacemakers.

The existence of two interventions with similar indications, but different costs and complication rates requires a comparative cost-effectiveness analysis to support decisions regarding the allocation of healthcare

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resources [8]. Since, to the best of our knowledge, few studies have evaluated and compared costs, whether of the device itself, hospitalization or monitoring, we attempt in this paper to fill this gap.

The rest of the paper is organised as follows. Section 2 describes the studied population and our statistical analyses. The results and discussion of them appear in Sections 3 and 4, respectively. Finally, Section 5 is devoted to some conclusions.

2. Material and methods

2.1. Study population

In 2015, a leadless pacemaker was implanted for the first time in Spain in the Hospital-University Complex of Santiago de Compostela (CHUS) located in Galicia's capital city (NW Spain). The CHUS is a tertiary-level specialist care hospital, whose cardiology service is a reference for the immediate region's population (344,358 persons). However, since Galician Instruction 7/13 grants patients free choice regarding haemodynamic and electrophysiology services, the potential hospital catchment is the entire population of Galicia, i.e. 2,744,661 inhabitants.

Our retrospective observational study included all 403 patients implanted with a pacemaker in the period 1 June 2015 – 31 January 2020 in any of the CHUS cardiac electrophysiology rooms: 244 implanted with a conventional pacemaker and 159 with a leadless pacemaker. The decision as to pacemaker type (conventional or leadless) was at the physician's discretion. Patient clinical data were obtained from their electronic medical records.

Economic data for the two devices were obtained from the CHUS Management Control Service. When specific intervention costs were unavailable, the average cost was taken as the 2,200.08 euros established by the Galician Regional Health Service (SERGAS) [9] for implantation alone, i.e. excluding the costs of the pacemaker device, hospital stay, pharmaceutical expenditure, and diagnostic and pre-and post-implant monitoring tests. Hospitalization, pharmaceutical, and test costs are similar for the two types of devices [9].

2.2. Statistical analysis

We performed a cost-effectiveness analysis, which consisted of numerically determining the relationship between the net cost of the intervention and of complications and its net benefit for the patient, measured in terms of potential gained life years (GLYs). This analysis was suitable for comparing the two pacemaker types, as they have identical objectives and indications, but differ in terms of costs and potential complications due to differences in implantation techniques. A Markov chain [10] was implemented that calculated survival probability for the five years post-implantation. The outcome quantified was death or survival; in other words, the optimal strategy was that which maximized survival, measured as GLYs over a five-year horizon, contrasted with implantation cost plus complications cost.

We also performed a cost-utility analysis [11] for the two pacemaker types to calculate quality-adjusted life years (QALYs) [12]. Quality of life (QoL) results for the 36-Item Short Form Health Survey (SF-36) were converted into EuroQoL format (using an algorithm described elsewhere [13]) and annual probability of survival was multiplied by QoL results to obtain the QALYs.

To strengthen the statistical robustness of our results for both pacemaker types, a Montecarlo sensitivity analysis [14] was also performed to simulate the impact of mortality on the cost-effectiveness and cost-utility analyses. In addition, a two-sample t-test assuming equal variances was performed to evaluate whether mortality differences were random or due to differences in the pacemakers.

All procedures were conducted in accordance with the Decree 63/2013 of 11 April 2013 regulating research ethics committees in Galicia (Euroregion Galicia-Northern Portugal), approved in writing by the institutional ethical review committee (Research Ethics Committee of Santiago-Lugo), and conducted under the authority of Project Licence 2021/164.

SPSS (V.21) was used to conduct the descriptive statistical analyses.

3. Results

The baseline characteristics of our sample are described in Table 1. As observed, patients implanted with conventional pacemakers were older and had higher rates of cardiomyopathy and arterial hypertension than the patients implanted with leadless pacemakers.

For the conventional and leadless pacemakers, average procedure time was 99 and 110 min, respectively, and mean (standard deviation [SD]) fluoroscopy time was 4 min (SD 9 s) and 8 min (SD 3 s), respectively.

Mortality unrelated to the intervention was 11 patients (4.5%) with conventional pacemakers, and 18 patients (11.3%) with leadless pacemakers. Implant-related mortality was 2 patients with leadless pacemakers and 0 patients with conventional pacemakers. We performed an analysis of the independence of the

Table 1. Study sample.

	Pacemaker type		
	Conventional ($n=244$)	Leadless ($n=159$)	*p*-value
Men	60.2%	59.1%	0.8217
Women	39.8%	40.9%	
Mean age	83.31	79.15	0.000
Age >75 years	82.8%	78.6%	0.296
AH	76.2%	80.5%	0.312
DM	29.5%	35.2%	0.229
IC	32.0%	24.5%	0.108
COPD	16.4%	17.6%	0.750
CI	17.6%	21.4%	0.881
CM	27.9%	48.4%	0.000
CRF	34.8%	17.6%	0.000
Arteriopathy	8.6%	7.5%	0.705
Valvulopathy	38.1%	42.1%	0.651

AH, arterial hypertension; DM, diabetes mellitus; IC, ischaemic cardiopathy; COPD, chronic obstructive pulmonary disease; CI, cardiac insufficiency; CM, cardiomyopathy; CRF, chronic respiratory failure.

samples of the two types of pacemaker and their relationship with mortality using the Student t test. Table 2 summarizes the results.

As observed, implant-related mortality differences between the two samples were not due to the pacemaker type but to the hazard (Student t-test =1.75503296; critical value of t (one-tailed) =1.64867194; critical value of t (two-tailed) =1.96591234).

3.1. Cost-effectiveness and cost-utility analyses

The only major complication directly related to 244 conventional pacemaker implants was four cases (1.6%) of pneumothorax (minor complications such as hematomas were not taken into account), costed at 10,793.25 euros each. For the 159 leadless pacemaker implants, the only major complication was one case (0.6%) of pericardial effusion, costed at 13,878.7 euros.

Conventional pacemaker cost was calculated per patient as 2,194.8 euros (device), plus 176.94 euros (cost of four pneumothorax complications distributed over 244 patients), plus 2,200.08 euros (SERGAS standard intervention cost). This yields a total cost of 4,572.54 euros per conventional pacemaker. Similarly, leadless pacemaker cost was calculated per patient as 8,485.2 euros (device), plus 87.29 euros (cost of one pericardial effusion complication distributed over 159 patients), plus 2,200.08 euros (SERGAS standard intervention cost). Thus, the total cost of each leadless pacemaker amounts to 10,773.29 euros.

Our complications rates for leadless pacemakers and for conventional pacemakers (2.9% each) – somewhat lower than those reported in recently published studies (4.0% and 6.8% [15], respectively) – would suggest that the leadless pacemaker is safer for the patient than the conventional pacemaker.

Table 2. Two-sample t-test assuming equal variances.

	EXITUS-MICRA	*EXITUS-VR*
Mean	0.0125786163522013	0
Variance	0.0124990048563012	0
Observations	159	243
Pooled variance	0.00493710691823899	
Hypothetical difference of means	0	
Degrees of freedom	400	
t-statistic	1.75503296	
P (T<=t) one-tailed	0.0400096	
Critical value of t (one-tailed)	1.64867194	
P (T<=t) two-tailed	0.08001921	
Critical value of t (two-tailed)	1.96591234	

Table 3. Cost-effectiveness analysis.

Pacemaker	GLYs	Cost (€)	Incremental GLYs	Incremental cost (€)	ICER
Leadless	4.54	10,773.29	0.99	6,200.75	6,263.38
Conventional	3.55	4,572.54			

GLY, gained life year; ICER, incremental cost-effectiveness ratio.

Table 4. Cost-utility analysis.

Pacemaker	QALYs	Cost (€)	Incremental QALYs	Incremental cost (€)	ICER
Leadless	3.38	10,773.29	1.19	6,200.75	5,210.71
Conventional	2.19	4,572.54			

QALY, quality-adjusted life year; ICER, incremental cost-effectiveness ratio.

The results of the cost-effectiveness and the cost-utility analyses are summarized in Tables 3 and 4, respectively. The leadless pacemaker was more expensive but also more effective according to both the cost-effectiveness and cost-utility analyses: the incremental cost-effectiveness ratio (ICER) of 6,321.02 euros was below the acceptability threshold of 10,000 euros per GLY, while the ICER of 5,293.21 euros was also below the acceptability threshold of 20,000 euros per QALY.

3.2. Montecarlo simulation

The Montecarlo sensitivity analyses, depicted in Figure 1 (cost-effectiveness) and Figure 2 (cost-utility), corroborate the results: the cost-effectiveness and cost-utility of the leadless pacemaker were 89.10% and 99.9%, respectively.

3.3. Survival probability analysis

The probability of post-implant survival for the conventional pacemaker was 91.39% in the first year, gradually dropping to 53.28% by the fifth year. In comparison, the probability of post-implant survival for the leadless pacemaker was 95.60% in the first year, dropping only to 87.44% by the fifth year. Two

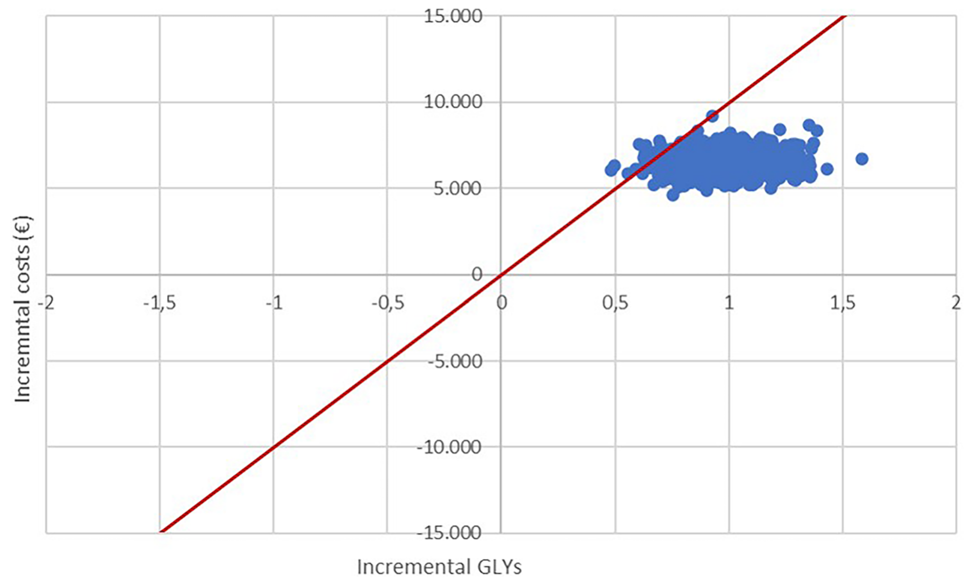

Figure 1. Montecarlo analysis. Cost-effectiveness in gained life years (GLYs).

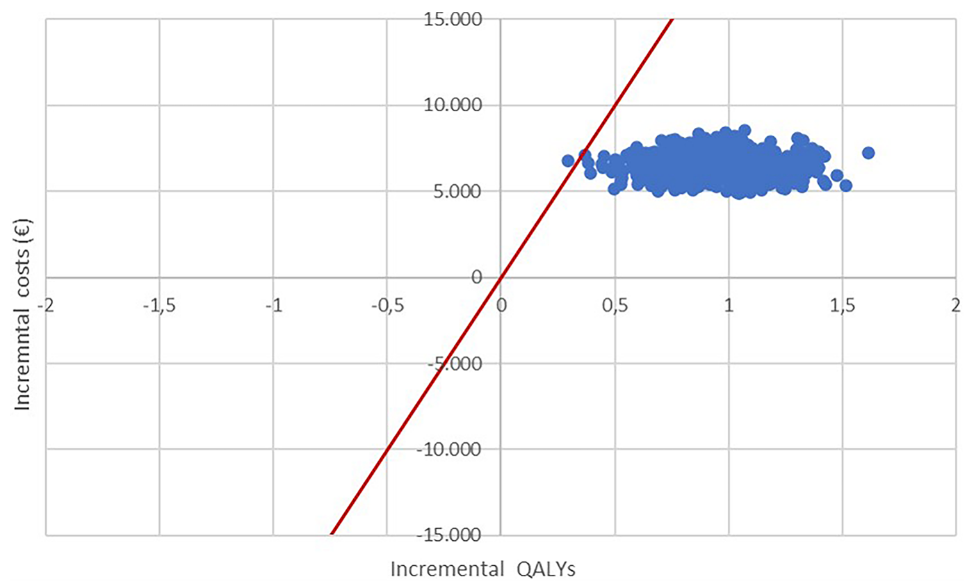

Figure 2. Montecarlo analysis. Cost-utility in quality-adjusted life years (QALYs).

results are therefore noteworthy. First, over all the years following implantation the probability of survival with the leadless pacemaker is unequivocally higher than with the conventional pacemaker. Second, the difference between the probability of survival with the leadless pacemaker and with the conventional pacemaker is greater the further away we are from the year of implantation. Figure 3 illustrates these results.

4. Discussion

Cost analyses of conventional and leadless pacemakers is information of major relevance in the care of patients in any healthcare system. As far as we are aware, no studies to date have reported or calculated cost differences between conventional and leadless pacemakers. Using real-world data for a tertiary hospital, we performed cost-effectiveness and cost-utility analyses of conventional and leadless pacemakers. As shown, although more costly than the conventional pacemaker, the leadless pacemaker may confer an overall benefit in reducing acute and long-term complications.

Regarding studies of costs and complications associated with the leadless pacemaker, most studies focus exclusively on complications. However, we included complications costs in this study, given that they are an indirect cost. Over the long term, leadless pacemakers could be anticipated to improve in cost-effectiveness,

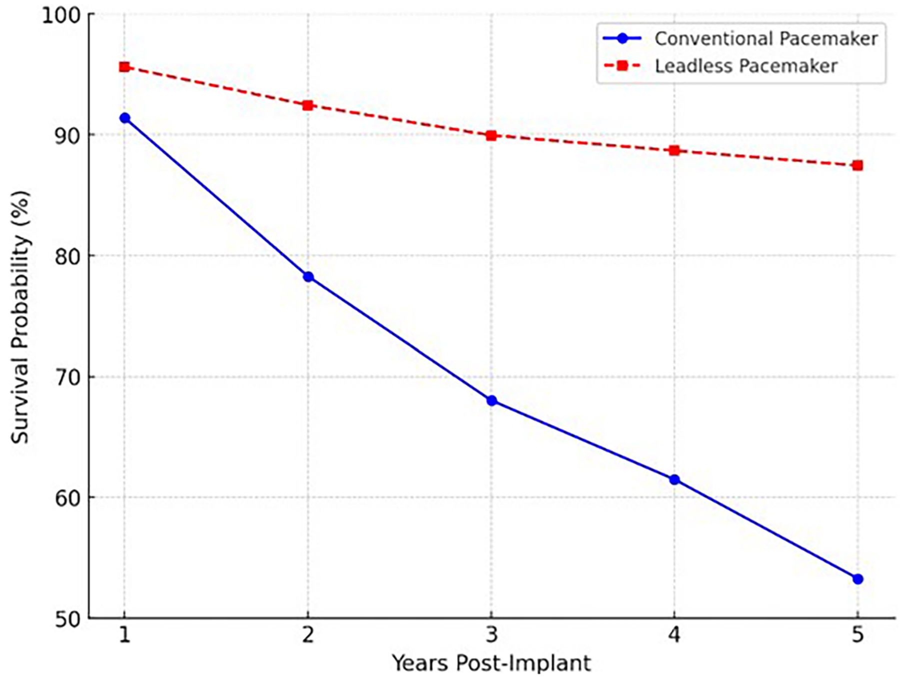

Figure 3. Survival probabilities for the conventional and leadless pacemakers.

given the longer battery life and possible reduction in overall complications, although this remains a 'known unknown' at present.

In our comparative study, despite not initially obtaining the expected results for the leadless pacemaker from the perspective of associated complications, the leadless pacemaker is theoretically safer and faster. This result is similar to those obtained in numerous studies of conventional implants and the few studies published on leadless pacemakers. Of note is the fact that leadless pacemakers are typically implanted in more severely ill patients in the real world, which has implications when comparing them to conventional pacemakers. In the absence of randomization, careful adjustment and propensity matching is required to infer conclusions from these studies, since the baseline characteristics of leadless vs conventional pacemaker recipients are different.

Note that selection bias may be present in our study since very fragile patients with a life expectancy of <6 months are typically implanted with conventional pacemakers. This could explain the greater mortality trend in those patients and may have influenced the analysis. Nevertheless, since the reason for death was not device-related, we believe that it did not affect either cost-effectiveness or cost-utility. For the leadless pacemakers, the elimination (or mitigation) of some of the complications commonly encountered with conventional pacemakers (such as pneumothorax and pocket- and lead-related issues) might be a key factor associated with the better complications profile. Those results remain consistent when adjusted for the pericardial effusion rate and the overall safety of leadless pacemakers.

Our complications rate for both groups seems to be aligned with current data, at 1.2% overall. Darlington et al. [16] reported a rate of 3.11% for patients in India who received a leadless pacemaker. Reynolds et al. [17], after 6 months' follow-up of 725 patients implanted with a leadless pacemaker, reported a rate of 3.8%. For a German multicentre study of 4,355 followed-up patients who had undergone a conventional implant between 2006 and 2011, Kirkfeldt et al. [18] reported a rate of 5.8%. However, Roberts et al. [19] reported complications in 13 patients (1.51%) for 795 patients after 30 days of follow-up after implantation of a leadless pacemaker.

Regarding comparative costs, an Australian study of 1,595 patients with a similar complications rate to that of our analysis (1%), a single-chamber pacemaker cost AUD 2,000 and a leadless pacemaker cost AUD 11,000, representing an 18% difference [20], compared to the 41.98% difference in our study. In a Norwegian study, Faguerlund et al. [21] concluded that substituting single-chamber pacemakers with leadless pacemakers for all patients scheduled for the intervention would result in an additional cost of NOK 27,386,992 by the fifth year, and an ICER that was significantly higher than the Norwegian cost-effectiveness level. However, our research, contrasting with the Norwegian study, reports ICER values that indicate the cost-effectiveness of each technique.

While our study has the limitations inherent to all observational studies, our design allowed us to reach relevant conclusions. Moreover, in surgery, observational studies comparing the procedure and overall patient management (type 2 study) or comparing surgery versus non-surgery (type 3 study), provided they are conducted in a methodologically sound manner, can reach conclusions similar to those of randomized trials [22], especially since the creativity that characterizes surgery and that has allowed important advances cannot be captured by randomized trials [23].

While single-centre studies usually recruit too few patients to be scientifically feasible, they have the advantages that they offer the flexibility of approach necessary for clinicians and scientists to develop new treatments and are an important source of new therapeutic ideas [24,25].

4.1. Limitations

While our results for complications are similar to those of other authors, we can hypothesize about possible biases. It has been amply demonstrated that complications are directly related to the experience of the professional who performs the technique. Even though the leadless pacemakers were implanted in our patients by two professionals classified as experts – having been previously trained in the technique and having passed the learning criterion stipulated by the company (at least 10 implants without complications) – we believe that a comparison with professionals with over a decade of experience of hundreds of cases of conventional implants cannot be considered a level playing field.

The vast numbers of our patients have undergone conventional pacemaker implants. Therefore, most studies on complications – and so indirectly related to part of our objective – are based on a far larger sample of patients than in our study, which would explain the important differences in results.

The price of innovative leadless pacemakers is set by the manufacturer, whereas price is established through competition for conventional pacemakers. The fact that newer devices will be included in future public tenders will almost certainly lead to a reduction in price.

Our study only considered economic variables reflecting pacemaker implantation and the first months of follow-up, i.e. we did not consider battery replacement. However, if battery depletion were considered, there would be important differences in the current replacement cost. While the fungible material used for the two interventions is similar, the specific material implantable in the devices differs. In the conventional device with leads, only the battery is replaced, so the cost calculated at the time of the implant would have to be discounted relative to the value of the electrode that is not changed when replacing the battery. In the leadless device, in contrast, since there is no electrode, the cost is the cost as calculated for the implant.

While the durability of batteries in leadless devices is stated to be similar to that for conventional devices, that value is currently only known from laboratory tests under ideal conditions. From experience with conventional devices, we know that readings of threshold-type stimulation, percentage stimulation, and impedance parameters at the time of the implant and in the initial follow-up visits depend directly on battery consumption; the readings are therefore not stable and may vary throughout the life of the patient, leading to significantly modified durability (most typically shortened).

For all these reasons, while our initial findings regarding complications are similar to those published to date, they need to be interpreted with care. To correct all possible biases, further studies are required based on progressively increasing the number of patients and following up over longer periods.

5. Conclusions

Cost-effectiveness analyses are not yet standard in the incorporation of new technologies. Few studies to date describe the cost-effectiveness of innovative leadless pacemakers, yet this kind of analysis is crucial information for healthcare managers and professionals. As for complications, our results for leadless pacemakers (2.9%) are slightly lower than those recently published studies (4.0%). Despite its novelty and the smaller samples, the leadless pacemaker would appear to be safer than the conventional pacemaker. The good safety and complications profile of the leadless pacemaker comes at a price, however, as it cost 8,485.2 euros in our study, compared to 2,194.8 euros for the conventional pacemaker. Given the novelty of the leadless pacemaker technology, however, we suggest that our conclusions be interpreted with care.

Authors' contributions

José Ramón Lago-Quinteiro participated in the design of the study, performed part of the literature review and helped to draft the manuscript. Manel Antelo participated in the design of the study, performed part of the literature review and helped to draft the manuscript. Vicente Caballer-Tarazona participated in the design of the study and helped to draft the manuscript. José Luis Martínez-Sande performed part of the literature review and helped to draft the manuscript.

Javier García-Seara performed part of the literature review and helped to draft the manuscript. Moisés Rodríguez Manero participated in the design of the study and helped to draft the manuscript. Francisco Reyes-Santias conceived of the study, its design, performed part of the literature review and coordinated the draft of the manuscript. José Ramón González-Juanatey participated in the design of the study and coordinated the draft of the manuscript. All authors have read and approved the final version of the manuscript.

Disclosure statement

No potential conflict of interest was reported by the author(s).

Ethics approval and consent to participate

The ethics committee (Comité de Ética de la Investigación de Santiago-Lugo) exempted the requirement of participant consent due to the retrospective nature of the study and the use of anonymized data. The study had adhered to the principles stated in the 'Declaration of Helsinki'.

Availability of data and supporting materials section

Data are available on reasonable request. The authors declare that they had full access to all the data in this study and they take full responsibility for the integrity of the data and the accuracy of the data analysis.

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References

[1] Otero Rodríguez R, de Juan Montiel J, Roldan Pascual T, et al. Guías de práctica clínica de la Sociedad Española de Cardiología en marcapasos. Rev Esp Cardiol. 2000;53:947–966.
[2] Pombo Jiménez M, Cano Pérez O, Fidalgo Andrés ML, et al. Registro Español de Marcapasos. XIII Informe Oficial de la Sección de Estimulación Cardíaca de la Sociedad Española de Cardiología (2015). Rev Esp cardiol. 2016;69(12):1190–1203.
[3] Roberts PR, Clementy N, Al Samadi FMD, et al. A leadless pacemaker in the real-world setting: the micra transcatheter pacing system post-approval registry. 2017.
[4] Bernabei MA. The micra transcatheter pacing study: the making of a revolution in pacemaking. J Lancaster Gen Hosp. 2014;9(3):75–79
[5] Paana T, Nammas W, Karjalainen PP, et al. Transcatheter leadless pacemaker implantation in a patient with recurrent complications following transvenous pacemaker systems. J Cardiol & Cardiovasc Ther. 2017;5(4):56–58.
[6] Jennett B. Assessment of clinical technologies. Ice for provision and use. Int J Technol Assess Health Care. 1988;4(3):435–445. doi: 10.1017/s0266462300000374.
[7] Thomas JG. The lives of a cell. New York: Viking Press; 1974.
[8] Pampillón Olmedo R. El déficit tecnológico español. Madrid: Instituto de Estudios Económicos; 1991.
[9] Diario Oficial de Galicia (DOGA). Decreto 54/2014 del 30 de Abril por el que se establecen las tarifas de los servicios sanitarios en los centros dependientes de Servizo Galego de Saúde y en fundaciones públicas sanitarias. Available at 96, 21 May 2014. https://www.xunta.gal/dog/Publicados/2014/20140521/AnuncioC3K1-140514-0001_es.html.
[10] Grimmett G, Stirkatzer D. Markov chains. Probability and random processes. 3rd ed. New York, USA: Oxford University Press; 2001. p. 213–220.
[11] Brooke BS, Kaji AH, Itani KM. Practical guide to cost-effectiveness analysis. JAMA Surg. 2020;155(3):250–251. doi: 10.1001/jamasurg.2019.4392.
[12] Cabanas-Grandío P, García Campo E, Bisbal F, et al. Quality of life of patients undergoing conventional vs leadless pacemaker implantation: a multicenter observational study. J Cardiovasc Electrophysiol. 2020;31(1):330–336. doi: 10.1111/jce.14322.
[13] Ara R, Brazier J. Deriving an algorithm to convert the eight mean SF-36 dimension scores into a mean EQ-5D preference-based score from published studies (where patient level data are not available). Value Health. 2008;11(7):1131–1143. doi: 10.1111/j.1524-4733.2008.00352.x.
[14] Doubilet P, Begg CB, Weinstein MC, et al. Probabilistic sensitivity analysis using monte carlo simulation. Med Decis Making. 1985;5(2):157–177. doi: 10.1177/0272989X8500500205.
[15] Cui D, Liao Y, Du J, et al. A meta-analysis of major complications between traditional pacemakers and leadless pacemakers. CVIA. 2021;5(3):145–153. doi: 10.15212/CVIA.2019.0596.
[16] Darlington D, Brown P, Carvalho V, et al. Efficacy and safety of leadless pacemaker: a systematic review, pooled analysis and meta-analysis. Indian Pacing Electrophysiol J. 2022;22(2):77–86. doi: 10.1016/j.ipej.2021.12.001.
[17] Reynolds D, Duray GZ, Omar R, et al. Leadless intracardiac transcatheter pacing system. N Engl J Med. 2016;374(6):533–541. doi: 10.1056/NEJMoa1511643.
[18] Kirkfeldt RE, Johansen JB, Nohr EA, et al. Complications after cardiac implantable electronic device implantations: an analysis of a complete, nationwide cohort in Denmark. Eur Heart J. 2014;35(18):1186–1194. doi: 10.1093/eurheartj/eht511.
[19] Roberts PR, Clementy N, Al Samadi F, et al. A leadless pacemaker in the real-world setting: the Micra Transcatheter Pacing System Post-Approval Registry. Heart Rhythm. 2017;14(9):1375–1379. doi: 10.1016/j.hrthm.2017.05.017.
[20] Chen D, Burgess N, Maddern G. Micra™ single chamber transcatheter pacing system leadless pacemaker. Health Technology Assessment (HTA) decision summary. South

Australian Policy Advisory Committee on Technology (SAPACT). Adelaide: Government of South Australia; 2018.

[21] Fagerlund BC, Harboe I, Giske L, et al. The micraTM transcatheter pacing system, a leadless pacemaker. In patients indicated for single-chamber ventricular pacemaker implantation: a single technology assessment from the Norwegian Institute of Public Health (Folkehelseinstituttet). Oslo: Norwegian Institute of Public Health; 2018.

[22] Ayloo S, Roh Y, Choudhury N. Laparoscopic versus robot-assisted cholecystectomy: a retrospective cohort study. Int J Surg. 2014;12(10):1077–1081. doi: 10.1016/j.ijsu.2014.08.405.

[23] Beks RB, Houwert RM, Groenwold RHH. Meerwaarde van observationeel onderzoek in chirurgie [Added value of observational studies in surgery: the hierarchical structure of study designs requires a more refined approach]. Ned Tijdschr Geneeskd. 2017;161: d 1493.

[24] Steering Committee of the Physician's Health Study Research Group. Final report on the aspirin component of the ongoing Physicians' Health Study (1989). N Engl J. Med. 1989;321(3): 129–135.

[25] Sackett DL. Rules of evidence and clinical recommendations on the use of antithrombotic agents (1992). Chest. 1989;95(2):2S–4S. doi: 10.1378/chest.95.2_Supplement.2S.