Conventional single-chamber pacemakers versus transcatheter pacing systems in a “real world” cohort of patients: A comparative prospective single-center study

Jose Luis Martinez-Sande a, Javier Garcia-Seara a, Laila Gonzalez-Melchor a,*, Moises Rodriguez-Manero a, Aurora Baluja b, Xesus Alberte Fernandez-Lopez a, Jose Ramon Gonzalez Juanatey a

a University Clinical Hospital of Santiago de Compostela, Cardiology Department, Santiago de Compostela, Spain
b University Clinical Hospital of Santiago de Compostela, Anesthesiology Department, Santiago de Compostela, Spain

ARTICLE INFO

Article history:
Received 1 October 2020
Received in revised form
29 November 2020
Accepted 24 December 2020
Available online 5 January 2021

Keywords:
Leadless
Transcatheter pacemaker
Transvenous
Complications

ABSTRACT

Purpose: Despite the developments in conventional transvenous pacemakers (VVI-PM), the procedure is still associated with significant complications. Although there are no prospective clinical trials that compared VVI-PM with transcatheter pacemaker systems (TPS).

Methods: This is a prospective, observational, single-center study that included all patients with an indication for a single-chamber pacemaker implant within a 4-year period. All clinical, ECG and echocardiographic characteristics at implant, electrical parameters, associated complications and mortality were analyzed. A Cox survival model and a Bayesian cohort analysis were performed for differences in complication rates between groups.

Results: There were 443 patients included (198 TPS and 245 VVI-PM). The mean age was 81.5 years (TPS group, 79.2 ± 6.6 years; VVI-PM group, 83.5 ± 8.9 years). There was a male predominance in TPS group (123, 62.1% vs. 67, 27.3%; p < 0.001). The presence of systolic dysfunction and renal insufficiency were more frequent in VVI-PM group than in TPS patients. Mean follow-up was 22.3 ± 15.9 months. In a multivariable paired data the TPS group presented fewer complications than VVI-PM group (HR = 0.39 [0.15–0.98], p-value 0.013), but major complications were not different (6, 3% vs 14, 5.6% respectively, p = 0.1761). There was no difference in the mortality rate between the groups. The TPS group had less risk than VVI-PM group to have a complication, with a 96% of probability.

Conclusions: TPS patients had a lower overall complication rate than VVI-PM patients including matched-pair samples using a Bayesian analysis. These results confirm the safety profile of TPS in clinical practice.

Copyright © 2021, Indian Heart Rhythm Society. Production and hosting by Elsevier B.V. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

1. Introduction

Despite the advancements in conventional transvenous pacemakers, the procedure is still associated with significant complications, which are mostly related to the transvenous lead and the subcutaneous generator pocket, with short-term complication rates as high as 8%–12% [1—3]. Some of the most frequent complications are pneumothorax, cardiac tamponade, pocket hematoma, lead dislodgement, venous obstruction, tricuspid regurgitation, and endocarditis [4]. To address these issues, leadless transcatheter pacemaker systems (TPS) have been gradually developed. The two leadless systems that are currently available have demonstrated comparable performance and safety results [5], and although pneumothorax and pocket/lead infection did not occur, the leadless procedure is also associated with femoral vascular complications, the need to reposition the device intraoperatively, and a moderate risk of cardiac perforation resulting in pericardial effusion. The TPS MICRA (Medtronic Inc.®) has the same implant indications as single chamber pacemakers (VVI-PM), with similar functionality and features, including rate adaptive pacing,
remote monitoring capabilities, and automated pacing capture threshold management [6]. Previous series have described a rate of 1.5% for short-term major complications [7] and up to 4% for midterm follow-up [8]. The risk of major complications in TPS appears to be much lower (up to 48%) than with conventional transvenous pacemakers [9]. However there are no clinical trials comparing conventional pacemakers with TPS in a prospective fashion, TPS seems to have a lower rate of major complications [6] and a satisfactory performance at midterm- and long-term follow-up [10] compared to historic cohorts of VVI-PM. In addition, there is little information about safety issues in middle-volume centers. The aim of this study was to prospectively compare the clinical characteristics, electrical performance, and related complications between TPS and a matched cohort of patients who were referred for VVI-PM implantation by the same operators and during the same period of time.

2. Methods

This is a prospective, observational, single-center study that included all patients with an indication for a single-chamber pacemaker implant, according to the current guidelines [11], within a 4-year period (from June 1, 2015 to December 31, 2019) in an experienced center. The choice between a conventional transvenous pacemaker or TPS was made according to physician discretion after discussion with the Electrophysiologist Unit and considering the clinical characteristics and age of the patient. TPS was encouraged in those patients who were at a higher risk of infection or who had difficult vascular access or abandoned electrodes. TPS implantation was performed via femoral access according to the manufacturer’s recommendations. VVI-PMs were implanted by cephalic dissection or subclavian puncture, and the choice of approach was based on the operator preference and all leads implanted were of active fixation. At implant, clinical characteristics, electrocardiographic, echocardiographic, and electrical parameters were collected in all patients. Follow-up in patients with TPS was performed systematically at 1, 3, 6, and 12 months and every year thereafter if uneventful. Patients with VVI-PM were scheduled for follow-up visits at 3 months after the procedure and yearly thereafter.

2.1. Complications

All complications and mortality were analyzed. Device-related complications were classified as minor or major. Major complications included the following: i) severe deterioration of clinical status; and/or ii) a life threatening event that required intervention that prolonged hospitalization or death; iii) vascular (aneurysm, pseudoaneurysm, arteriovenous fistula, hematoma and/or hemorrhage); iv) thoracic complications (pneumothorax); v) pericardial effusion and/or tamponade; vi) stimulation related failures (capture failure, electrode dislodgment); and vii) complications from the pacemaker pocket (infection or hematoma).

2.2. Statistical analysis

The statistical analysis was descriptive for categorical variables and included the frequency, percentage, mean, and standard deviation (SD) in numeric variables. The level of statistical significance was defined as p < 0.05. Complications data were paired by propensity score matching of age, left ventricular ejection fraction (LVEF), heart failure, anticoagulation, and renal failure. For the matched data, a Cox regression analysis was performed to analyze the complications. Multiple hypothesis testing was addressed with the Benjamini–Hochberg procedure. A Bayesian cohort analysis was used to estimate the probability of complications in both pacemaker groups with a binomial distribution. For prior probabilities, two possibilities were chosen. The first possibility was more skeptical (non-informative) prior (between −50% and +50%) for the risk difference between the TPS and VVI-PM groups. The second prior distribution was based on the difference found in the cohort of 1817 patients that was published by El-Chami [6] in 2018. Hence, the prior probability (between −27% and −52%) was the risk difference of the TPS group compared to the VVI-PM group. The risk followed a normal distribution, centered in −0.37 with a SD of 0.125. The baseline risk followed an uniform prior distribution (conservative, non-informative). The posterior distribution was calculated using the Metropolis–Hastings algorithm with 40,000 iterations and 2,000 burn-in iterations in two Markov chains. Statistical calculations were performed using the survival, Matchit and rjags packages for R v.3.5 and SPSS v.19.

Table 1
Baseline patient characteristics.

|                      | VVI-PM n = 245 (%) | TPS n = 198 (%) | P     |
|----------------------|--------------------|----------------|-------|
| Age                  | 83.6               | 79.2           | <0.00001 |
| Men                  | 67 (27.3)          | 123 (62.1)     | <0.00001 |
| Hypertension         | 155 (63.3)         | 160 (80.8)     | <0.000001 |
| Diabetes             | 63 (25.7)          | 69 (34.8)      | 0.3662  |
| COPD                 | 33 (13.5)          | 34 (17.1)      | 0.2795  |
| Renal disease        | 86 (35.1)          | 36 (18.2)      | 0.00007 |
| Cardiomyopathy       | 68 (27.7)          | 95 (48)        | 0.00001 |
| Ischemic cardiopathy | 39 (15.9)          | 43 (21.7)      | 0.1181  |
| Heart failure        | 67 (27.3)          | 46 (23.2)      | 0.3232  |
| LVEF                 | 56.9 (8.6)         | 59.8 (7.9)     | 0.000252 |
| Peripheral arteriopathy | 16 (6.5)      | 12 (6.1)        | 0.8398  |
| Valvular disease     | 80 (32.6)          | 87 (43.9)      | 0.0148  |

COPD: chronic obstructive pulmonary disease, TAVI: transcatheter aortic valve implantation, LVEF: left ventricular ejection fraction.

Table 2
TPS and VVI-PM total complications.

|                      | TPS (%) | VVI-PM (%) | P     |
|----------------------|---------|------------|-------|
| TOTAL COMPLICATIONS  | 7 (3.5) | 21 (8.6)   | 0.0303 |
| Major complications  | 6 (3)   | 14 (5.6)   | 0.1761 |
| Minor complications  | 1 (0.5) | 7 (2.8)    | 0.0645 |
| VASCULAR COMPLICATION| 4 (2)   | 4 (1.6)    | 0.7607 |
| Bleeding             | 0       | 0          |       |
| Puncture hematoma    | 0       | 0          |       |
| Arteriovenous fistula| 3 (1.5) | 0          |       |
| Pseudoaneurysm       | 1 (0.5) | 0          |       |
| Hemotorax            | 0       | 1 (0.4)    |       |
| Pneumothorax         | 0       | 3 (1.2)    |       |
| CARDIAC PERFORATION  | 2 (1)   | 0          | 0.1992 |
| Pericardial effusion | 1 (0.5) | 0          |       |
| Tamponade            | 1 (0.5) | 0          |       |
| PACING               | 1 (0.5) | 4 (1.6)    | 0.2639 |
| Dislodgement         | 0       | 3 (1.2)    |       |
| Threshold elevation  | 1 (0.5) | 0          |       |
| Pacemaker syndrome   | 0       | 1 (0.4)    |       |
| Electrode Fracture   | 0       | 0          |       |
| POCKET RELATED       | 0       | 12 (4.9)   | NA    |
| Hemorata             | 0       | 10 (4.1)   |       |
| Skin ulcer risk      | 0       | 2 (0.8)    |       |
| ENDOCARDITIS         | 0       | 1 (0.4)    | 1     |

NA, not analyzed.
3. Results

3.1. Baseline characteristics

There were 443 patients who underwent a pacemaker implantation from June 1, 2015 to December 31, 2019 who were included, and 198 patients were in the TPS group while 245 patients were in the VVI-PM group. Mean age was 81.5 years (TPS group, 79.2 ± 6.6 years; VVI-PM group, 83.5 ± 8.9 years). There was a male predominance in the TPS group (123, 62.1%) and a female predominance in the VVI-PM group (178, 72.6% and p < 0.0001). There were also statistically significant differences regarding the presence of LV systolic dysfunction, renal insufficiency, and oral anticoagulation prescriptions between VVI-PM and TPS patients (Table 1). At the time of the procedure, the vast majority of patients were in atrial fibrillation (388, 87.6%; slow ventricular response 253, 57.2%; atrioventricular block 101, 22.8%; or fast ventricular response 34, 7.7%) or left atrial flutter (15, 3.4%). Ninety one (37.1%) pacemakers in the VVI-PM group were implanted by cephalic venodissection and 154 (62.8%) were implanted by subclavian puncture. In both groups, three patients had a previous pacemaker extraction, three patients with VVI-PM and four patients in the TPS group presented with a history of an infection. Average fluoroscopy time was significantly different between the groups: 6.09 ± 5.1 min in the TPS group versus 4.04 ± 7.02 min in the VVI-PM group (p < 0.001). The median time of fluoroscopy in between the groups was of 5.13 min in the TPS group versus 3.3 min in the VVI-PM group.

3.2. Outcomes

The mean follow-up was 22.3 ± 15.9 months. The TPS were located as follows: 51 in apex, 122 in mid-septum and 25 in the outflow tract and the VVI-PM ventricular leads: 239 in apex, 5 in mid-septum and 1 in outflow tract. The TPS group reported significantly lower total complications than the VVI-PM group (7, 3.5% vs. 21, 8.6% respectively, p = 0.0303). However, there were no differences in major complications between the groups (6, 3% vs. 14, 5.6% respectively, p = 0.1761) (Table 2). In a multivariable analysis of data matched by age, LVEF, chronic heart failure, anticoagulation status, and chronic kidney disease, the TPS group presented fewer complications than the VVI-PM group (Hazard ratio (HR) = 0.39, confidence interval (CI) 95%: 0.15–0.98; p = 0.013) (Fig. 1A). The most frequent complications in patients with TPS were vascular (4, 2%), and associated with heart effusion (2, 1%). In patients with VVI-PM, the most frequent complications were pocket generator-related (12, 4.9%), pneumothorax (3, 1.2%), and electrode dislodgement (3, 1.2%) (Table 2). During the follow-up, 62 patients died (14%), including 18 in the TPS group (9.1%) and 44 in the VVI-PM group (17.5%) with significant difference between the groups (p = 0.007) (Table 3). Only one of the deaths was pacemaker related in the TPS group, even though there was no statistically significant difference in the paired analysis (Fig. 1B).

3.3. Non-informative prior in terms of differences in complications

After the Bayesian analysis, the mean posterior probability of complications for the VVI-PM group was 9.8% (credible interval [CrI] at 95%: 5.6–15%), while that in the TPS group was 4.6% (CrI at 95%: 1.9–8.5%). The posterior probability of having fewer complications in the TPS group than in the VVI-PM group was of 96.4% (Fig. 2A).

---

Table 3

| Cause                     | VVI-PM (%) | TPS (%) | p       |
|---------------------------|------------|---------|---------|
| Total mortality           | 44 (17.9)  | 18 (9.1)| 0.007476|
| Cardiac                   |            |         |         |
| Heart failure             | 1 (0.4)    | 1 (0.5) | 0.879791|
| Endocarditis              | 1 (0.4)    | 0       | 1       |
| Non-cardiac               |            |         |         |
| Pneumonia                 | 10 (4.1)   | 8 (4)   | 0.982566|
| Respiratory failure       | 5 (2)      | 2 (1)   | 0.387096|
| Stroke                    | 5 (2)      | 2 (1)   | 0.387096|
| Chronic kidney disease    | 3 (1.2)    | 0       | 0.2568  |
| Sepsis/infected pressure  | 2 (0.8)    | 0       | 0.5045  |
| Sepsis/Urinary tract      | 0          | 1 (0.5) | 0.447   |
| Lung cancer               | 2 (0.8)    | 0       | 0.5045  |
| Prostate cancer           | 1 (0.4)    | 0       | 1       |
| Epilepsy/Dementia         | 2 (0.8)    | 0       | 0.5045  |
| Bleeding of digestive trac| 2 (0.8)    | 0       | 0.5045  |
| Volvulus                  | 1 (0.4)    | 0       | 1       |
| Intestinal ischemia       | 1 (0.4)    | 0       | 1       |
| Bone fractures             | 1 (0.4)    | 1 (0.5) | 0.879791|
| Unknown                   | 7 (2.9)    | 3 (1.5) | 0.344446|

Fig. 1. Kaplan-Meier plots of time to event in matched data. A: risk of complications; B: risk of death.
they were associated with the implant procedure. As observed in term related complications occurred frequently in both groups, and probability of lower complications in the TPS group was 96%. Short-term probability of complications to one or the other group, the PM group. Even based on a priori probabilities that assign the same prior probability for TPS based on a previous study showed that the TPS group had fewer complications than the VVI-PM group. In the present study, we analyzed the clinical characteristics and short and mid-term follow-up visits, with an average threshold at implant of 0.55 ± 0.26 V/0.24 ms (n = 198), and it was 0.56 ± 0.31 V/0.24 ms (n = 119). The average impedance at implant was 779.8 ± 211 Ω, and it was 584 ± 102 Ω, 580.5 ± 91 Ω, and 538.8 ± 91 Ω at 12, 24, and 36 months. The average amplitude at implant was 10.7 mV ± 4.6, and it was 13.5 mV ± 4.6, 14.5 mV ± 4.9, and 12.9 mV ± 5.2 at 12, 24, and 36 months (Fig. 3).

The stimulated QRS duration in conventional VVI pacing were of: 175.9 ms (±19.3) and in LPS-PM of: 153.1 ms (±14), with a significant difference between the groups (p < 0.00001). LV function at follow-up in the VVI-PM group was of 56.4 (±5.9) and in LPS-PM of 58 (±5), with only one case of cardiomyopathy in the VVI group (0.4%).

3.4. Optimistic prior for TPS based on a previous study

The mean posterior probability of complications for the VVI-PM group was 11% (CrI at 95%: 6.5–16.6%), while that in the TPS group was 4.1% (CrI at 95%: 1.7–7.5%). Considering the data from a previous cohort, the posterior probability of having fewer complications in the TPS group than in the VVI-PM group was of 99.3% (Fig. 2B).

Electrical parameters in patients with TPS were stable at the short and mid-term follow-up visits, with an average threshold at implant of 0.55 ± 0.26 V/0.24 ms (n = 198), and it was 0.56 ± 0.31 V/0.24 ms (n = 119), 0.56 ± 0.32 V/0.24 ms (n = 73), and 0.61 ± 0.47 V/0.24 ms (n = 42) at 12, 24 and 36 months. The average impedance at implant was 779.8 ± 211 Ω, and it was 584 ± 102 Ω, 580.5 ± 91 Ω, and 538.8 ± 91 Ω at 12, 24, and 36 months. The average R amplitude at implant was 10.7 mV ± 4.6, and it was 13.5 mV ± 4.6, 14.5 mV ± 4.9, and 12.9 mV ± 5.2 at 12, 24, and 36 months (Fig. 3).

The stimulated QRS duration in conventional VVI pacing were of: 175.9 ms (±19.3) and in LPS-PM of: 153.1 ms (±14), with a significant difference between the groups (p < 0.00001). LV function at follow-up in the VVI-PM group was of 56.4 (±5.9) and in LPS-PM of 58 (±5), with only one case of cardiomyopathy in the VVI group (0.4%).

4. Discussion

In the present study, we analyzed the clinical characteristics and mid-term follow-up complications between TPS and a cohort of VVI-PM patients. Our results revealed an elderly population with a high rate of co-morbidities in both groups. Overall, there were fewer complications in the TPS group than in the VVI-PM group. In a matched patient analysis, the TPS group also had a lower complications rate. Additionally, Bayesian analysis in our sample showed that the TPS group had fewer complications than the VVI-PM group. Even based on prior probability that assigns the same probability of complications to one or the other group, the posterior probability of lower complications in the TPS group was 96%. Short-term related complications occurred frequently in both groups, and they were associated with the implant procedure. As observed in other studies of conventional endovascular pacemakers, the incidence of complication is still substantial, and most complications occurred early after pacemaker implantation [12]. The most common cause was lead-related re-intervention, especially for vascular access and lead dislodgment [13]. In our study, the rate of dislodgment was 1.2% in the VVI-PM group. These data seem consistent with the series of single-lead pacemakers in the Danish Registry, in which the dislodgment rate was 1.2% [14], and the FOLLOWPACE study, which showed dislodgement rate of 3.3% [12] (this study also included dual-chamber pacemakers). No patients in the TPS group had device dislodgment, the IDE Registry reported two cases of device dislodgement out of 1817 TPS patients (0.12%), and one of them had embolization. Both devices were successfully retrieved [6]. In the TPS group, the vascular access complication rate was 2%, while that in the VVI-PM was 1.6%. The vascular complication rate in the IDE Registry was lower (0.61%) compared with our results [6]. These data emphasize the importance of a careful vascular access and consideration of ultrasound guidance or venography for venous puncture, especially in an elderly population. In the VVI-PM group, pocket-related adverse events were the most frequent complication (4.9%), although the incidence of reoperation was low, especially for hematomas that were mostly managed conservatively. This finding was consistent with the conservative management of hematoma in other series (rate of hematoma, 2.97%; required surgical drainage, 0.07%) [12]. Many patients were taking oral anticoagulation agents during pacemaker implantation (80.1%). This was not surprising because our cohort consisted of elderly patients with atrial fibrillation and multiple comorbidities. However, anticoagulation was not an independent factor for complications. There was a high rate of overall mortality (62 patients, 14%), and one case was related to pacemaker endocarditis in the TPS group, which was similar to other TPS series with a procedure-related death rate of up to 0.28% [6]. The mortality rate at follow-up was attributed to the characteristics of the population in which age and multiple co-morbidities played an important role [15–17].

However, our study had the expected limitation that was not a randomized trial, and the choice of each pacemaker was based on the patients’ clinical conditions. Furthermore, the number of
patients included and the follow-up probably underestimates the infectious complications, particularly in VVI-PM group, according to other published studies [18]. Additionally, pocket-related complications that are more likely to be presented in mid- and long-term follow-up were not well represented in this study.

Finally, as published by Gupta and cols, as well as other studies, the stimulated QRS duration difference between the groups, could be related to the different location predominant in each type of PM, considering that RV mid-septal and RVOT septal pacing were associated with significantly lower QRS duration as compared with apical pacing [19,20].

5. Conclusions

TPS patients had a lower overall complication rate than VVI-PM patients including matched-pair samples using a Bayesian analysis. These results confirm the good safety profile of TPS in daily clinical practice.

CRediT authorship contribution statement

Jose Luis Martinez-Sande: Conceptualization, Investigation, Visualization, Writing - original draft. Javier Garcia-Seara:
Declaration of competing interest

The authors whose names are listed certify that they have NO conflict of interest and NO affiliations with or involvement in any organization or entity with any financial interest (such as hono-

raria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

References

[1] Epstein AE, DiMarco JP, Ellenbogen KA, Estes NA, Freedman RA, Gettes LS, Glinn AM, Gregoratos G, Hammers SC, Hayes DL, Hlatky MA, Newby LK, Page RL, Schoenfeld MH, Silka MJ, Stevenson LW, Sweeney MO. ACC/AHA 2008 guidelines for device-based therapy of cardiac rhythm abnormalities: a report of the American college of cardiology/American heart association task force on practice guidelines (writing committee to revise the ACC/AHA/NASPE 2002 guideline update for implantation of cardiac pacemakers and antiar-

rhythmia devices). Circulation 2008;117:e350–e408.

[2] Ellenbogen KA, Wilkoff BL, Kay GN. Clinical cardiac pacing, defibrillation and resynchronization therapy. Philadelphia, PA: WB Saunders Company; 2000.

[3] Andersen HR, Nielsen JC, Thomsen PE, Thuesen L, Mortensen PT, Vesterlund T, Pedersen AK. Long-term follow-up of patients from a randomised trial of atrial versus ventricular pacing for sick sinus syndrome. Lancet 1997;350:1210–6.

[4] Toff WD, Camm AJ, Skehan JD. United Kingdom Pacing and Cardiovascular Events Trial Investigators. Single-chamber versus dual-chamber pacing for high-grade atrioventricular block. N Engl J Med 2005;353:145–55.

[5] Martinez-Sande JL, García-Seara J, Rodríguez-Mañero M, Fernández-López X, González-Melchor L, Redondo-Díezeg A, et al. Marcapasos transcendente sin cables Micra. Resultados del implante y seguimiento a medio plazo en un centro. Rev Esp Cardiol 2017;70:275–81.

[6] El-Chami M, Al-Samadi F, Clementy N, Garvec C, Martinez-Sande JL, Piccini J, et al. Updated performance of the Micra Transcather pacemaker in the real-world setting: a comparison to the investigational study and a transvenous historical control. Heart Rhythm 2018;15(12):1800–7.

[7] Roberts P, Clementy N, Samadi F, Garvec C, Martinez-Sande JL, Iacopino S, et al. A leadless pacemaker in the real-world setting: the Micra transcatheter pacing system postapproval registry. Heart Rhythm 2017;14:1375–9.

[8] Reynolds D, Dray GZ, Omar R, Soejima K, Neuzil P, Zhang S, et al. A Leadless intracardiac transcatheter pacing system. N Engl J Med 2016;374:535–41.

[9] Duray G, Ritter P, El-Chami M, Narasimhan C, Omar R, Tosoana J, et al. Long-

term performance of a transcatheter pacing system: 12-Month results from the Micra transcatheter pacing study. Heart Rhythm 2017;14(5):702. 290.

[10] El-Chami M, Al-Samadi F, Clementy N, Garvec C, Martinez-Sande JL, Piccini J, et al. Updated performance of the Micra Transcatheter pacemaker in the real-

world setting: a comparison to the investigational study and a transvenous historical control. Heart Rhythm 2018;15(12):1800–7.

[11] Brignole M, Auricchio A, Baron-Esquivias G, Bordachar P, Boriani G, Breit-

hardt OA, et al. ESC Guidelines on cardiac pacing and cardiac resynchronization therapy: the Task Force on cardiac pacing and resynchronization therapy of the European Society of Cardiology (ESC). Developed in collaboration with the European Heart Rhythm Association (EHRA). Eur Heart J 2013;34:2281–329. 2013.

[12] Udo EO, Zuihoff NP, Van Hemel NM, De Cock C, Hendriks T, Doevendans PA, et al. Incidence and predictors of short- and long-term complications in pacemaker therapy: the FOLLOWPACE study. Heart Rhythm 2012;9:728–35.

[13] Kirkleidt R, Johansen JB, Nielsen JC. Complications with conventional VVI pacing: an analysis of a complete, contemporary cohort in Denmark. Europace 2017;19(Suppl_3), iii3.

[14] Vamos M, Erath JW, Benz AP, Bari Z, Duray GZ, Hohlnsler SH. Incidence of cardiac perforation with conventional and with leadless pacemaker systems: a systematic review and metaanalysis. J Cardiovasc Electrophysiol 2017;28:336–46.

[15] Cano O, André A, Alonso P, Osca J, Sancho-Tello MJ, Olagüe J, et al. Incidence and predictors of clinically relevant cardiac perforation associated with sys-

tematic implantation of active fixation pacing and defibrillation leads: a single center experience with over 3800 implanted leads. Europace 2016;19:96–102.

[16] Hsu JC, Varosy PD, Bao H, Dewland TA, Curtis JP, Marcus GM. Cardiac perfo-

ration from implantable cardioverter-defibrillator lead placement: insights from the national cardiovascular data registry. Circ Cardiovasc Qual Outcomes 2013;6:582–90.

[17] Boriani G, Savelieva I, Dan GA, Debaro JC, Ferro C, Israel CW, et al. Chronic kidney disease in patients with cardiac rhythm disturbances or implantable electrical devices: clinical significance and implications for decision making-a position paper of the European Heart Rhythm Association endorsed by the Heart Rhythm Society and the Asia Pacific Heart Rhythm Society. Europace 2015;17:1109–96.

[18] Klug D, Balde M, Pavin D, Hidden-Lucet F, Clementy J, Sadoul N. Risk factors related to infections of implanted pacemakers and cardioverter-defibrillators: results of a large prospective study. Circulation 2007;116(12):1349–55.

[19] Gupta A, Parakh N, Bansal R, Verma S, Roy A, Sharma G, et al. Correlation of pacing site in right ventricle with paced QRS complex duration. Indian Pacing Electrophysiol J 2018;18:210–6.

[20] Sharma F, Guleria V, Bhadraway P, Datta R. Assessing safety of leadless pacemaker (MICRA) at various implantation sites and its impact on paced QRS in Indian population. Indian Heart J 2020;72:376–82.