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REVIEW ARTICLE

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Complications of leadless vs conventional (lead) artificial pacemakers – a retrospective review

Yasar Sattar [a], Waqas Ullah [b], Sohaib Roomi [b], Hiba Rauf [c], Maryam Mukhtar [d], Asrar Ahmad [b], Zain Ali [b], Muhammad Shan-Ul- Abedin [e] and M Chadi Alraies [f]

[a]Internal Medicine, Icahn School of Medicine at Mount Sinai-Elmhurst Hospital, New York, USA; [b]Internal Medicine, Abington Jefferson Health, Abington, PA, USA; [c]Internal Medicine, Dow University Health Sciences, Karachi, Pakistan; [d]Internal Medicine, Fauji Foundation Hospital, Rawalpindi, Pakistan; [e]Internal Medicine, King Edward Medical College, Lahore, Pakistan; [f]Detroit Medical Center, Wayne State University, Detroit, Michigan, USA

ABSTRACT

Background: Leadless pacemakers (LPM) are introduced in cardiovascular market with a goal to avoid lead- and pocket-associated complications due to conventional artificial pacemakers (CPM). The comparison of LPM and CPM complications is not well studied at a case by case level.

Methods: Comprehensive literature was searched on multiple databases performed from inception to December 2019 and revealed 204 cases that received LPM with a comparison of CPM. The data of complications were extracted, screened by independent authors and analyzed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.).

Results: The complications of CPM were high in comparison to LPM in terms of electrode dislodgement (56% vs 7% of cases, p-value < .0001), pocket site infection rate (16% vs 3.4%, p-value = 0.02), and a lead fracture rate (8% vs 0%, p-value = 0.04). LPMs had a statistically non-significant two-times high risk of pericardial effusion (8%) compared to CPMs (4%) with a p-value = 0.8.

Conclusion: LPMs appear to have a better safety profile than CPMs. There was a low pocket site and lead-related infections in LPM as compared to CPM. However, LPM can have twice the risk of pericardial effusion than CPMs, but this was not statistically significant.

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Conventional pacemaker; traditional pacemaker; leadless pacemaker; Micra transcatheter pacing system (Medtronic); Nanostim® leadless cardiac pacemaker; St. Jude Medical; St. Paul

1. Introduction

In the USA, annually about one million de novo pacemakers are inserted and more than 200,000 pacemakers are replaced [1,2]. Since the invention of the pacemaker in the 1950s, there has been robust evolution in the technology of these devices, such as small battery size with a long half-life, quality, the number of leads, rate and voltage responsiveness. Despite these revolutionary changes, pacemakers face a wide array of complications such as pocket and lead infections, perforation, cardiac tamponade, and pulmonary complications [3,4]. Other long-term complications include lead failure, lead fracture, endocarditis, tricuspid regurgitation, and insulation abnormalities [4,7]. A new type of pacemaker, the leadless pacemaker (LPM), was introduced as an initial concept in animals in the 1970s [8]. Subsequent human studies showed that LPMs have a major complication rate of only 2.7%, major complications are 63% lower than complications with conventional transvenous pacemakers (CPMs) at 12 months follow-up [9]. Further studies substantiated these findings leading to the Food and Drug Administration approval of LPMs in the USA in December 2016 [10]. We sought to determine the safety of these novel pacemakers in our review.

2. Methods

2.1. Search strategy

A literature search for relevant articles was performed from inception to December 2019. We searched PubMed, Ovid (MEDLINE), and the Cochrane Central Register of Controlled Trials using medical subject headings (MeSH) and keywords like 'Artificial pacemaker,' 'Lead pacemaker,' 'Wire pacemaker,' 'Single chamber pacemaker,' 'Dual chamber pacemaker,' 'Conventional pacemaker,' 'Transvenous pacemaker,' 'Cardiac pacing device,' 'Cardiac Resynchronization Therapy,' ''Permanent leadless cardiac pacemaker,' ''Nanostim transcatheter pacing system,' and 'Micra transcatheter pacing system.' The terms from the two subsets were combined in 1:1 combination using Boolean operators, and final results from all the possible combinations were downloaded into an EndNote library. A thorough

CONTACT Waqas Ullah waqasullah.dr@gmail.com Internal Medicine, Icahn School of Medicine at Mount Sinai-Elmhurst Hospital, Abington, PA 19001, USA

search through the reference list of the articles published. The full search strategy is shown in the PRISMA diagram (Figure 1), and supplemental table 1.

2.2. Study selection and selection criteria

Cases reporting CPM- or LPM-related complications were selected. The titles and abstracts of the included articles were reviewed independently by three authors (HR, YS, and WU). The studies that met title/abstract screening inclusion criteria were deemed for full-text reading, and subsequent variable of interest was extracted and analyzed.

2.3. Inclusion criteria

Patients with age >18 received pacemaker with any reported indication, cases that used LPM with reported complications, cases with CPM that underwent any complications, and either subsequently got CPM replaced with LPM insertions.

2.4. Exclusion criteria

Patients with age <18, no indication of a pacemaker, and neither CPM nor LPM, no reported complication of CPM, or LPM.

2.5. Statistical analysis

Frequencies of individual complications across the studies were combined and reported. Descriptive analysis of continuous variables was recorded as mean and standard deviation. The comparison between categorical data was performed using Pearson's chi-squared test. A *P* value of less than.05 was considered significant. The statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.)

3. Results

A study population included 204 reported cases. The mean age of patients with CPM and LPM was 71and 64 years, respectively. The male-to-female ratio was about 2:1 in both CPM and LPM. About 14% of patients had lead pacemaker implantation whereas 86% of patients had LPM implantation. The most frequent overall complication experienced with pacemaker implantation was pericardial effusion in 8% of patients followed by hematoma and perforation in 7% of patients.

We stratified the complications based on the type of pacemaker and found that electrode dislodgement was seen significantly higher in CPM group (CPM vs LPM: 56% vs 7%, p-value = 0.00). Site infection was higher in CPM (pocket site = 16% of cases, p-value = 0.02) in CPM, whereas LPM had lower site infection (right ventricular site infection = 3.4% of cases (patients),

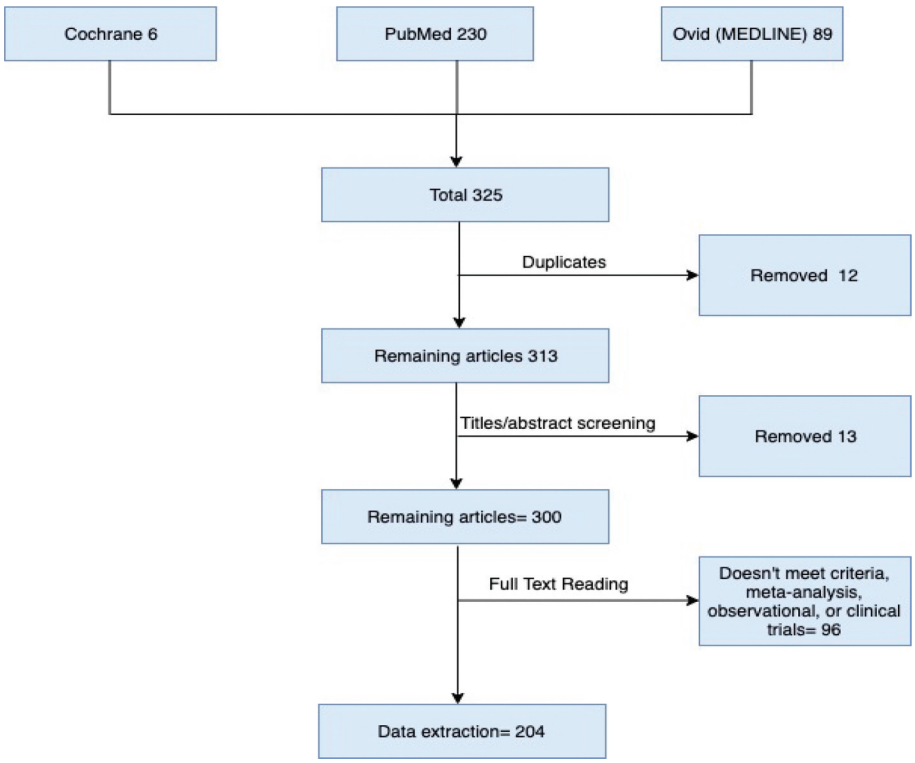

Figure 1. Preferred reporting items for systematic review and meta-analysis (PRISMA) flow diagram showing search strategy.

p-value = .02). CPMs had a significantly 8% higher incidence of lead fracture as compared to LPM with a p-value = 0.04. There was no significant difference seen between CPM and LPM for complications such as pericardial effusion (8% vs 4%, p-value = 0.8), hematoma (8% vs 7.4%, p-value = 0.58), and thrombosis (4% vs 4%, p-value = 0.66). A detailed comparison of the complications is given in supplemental table 2. The combined complications of any artificial pacemaker including lead and leadless in our patient population are shown in bar chart below in Figure 2. The percentage complications of conventional (lead) pacemakers and leadless pacemakers are shown in Figures 3 and 4.

4. Discussions

The CPM includes single-chamber, dual-chamber pacemakers, biventricular, and rate-responsive pacemakers [1]. Currently, there are two LPMs available, including a Micra transcatheter Pacing system (Medtronic, Dublin, Ireland) and the Nanostim® Leadless Cardiac Pacemaker (St. Jude Medical, St. Paul, MN). LPMs are inserted percutaneously via a catheter-guided femoral vein approach. Both Medtronic and St. Jude Medical LPMs differ in size, proximity to the myocardium, and responsiveness [11]. LPMs are implanted in the right ventricle directly for sensing and pacing; therefore, they are believed to decrease the risk of lead-associated infection but can have potentially higher risks of perforation and cardiac tamponade.

Complications associated with any artificial pacemaker are shown above in Figure 2. CPM had a higher proportion of lead fracture, lead infection, and site in comparison to LPM. The risk of other minor complications was comparable between the two groups and included perforation (4% vs 7.4%, P-value = .45), surgical revision (4% vs 4.6%, p-value = 0.68), mitral regurgitation (0% vs 1.1%, p-value = .76). The detailed comparison data of complications between LPM and CPM are shown above in Figures 3 and 4.

Our findings were consistent with previously reported studies stating better efficacy and safety of LPMs are promising. The results of the Micra study found that LPM has a 48% lower complication rate, 47% fewer annual hospitalizations, and 82% lower pacemaker re-insertion rate compared to CPM [12]. Our results endorse not only previous findings but also highlight rare LPM-associated complications.

The complications of pacemakers can be broadly classified into the lead, pulse generator, arrhythmic, and miscellaneous complications.

4.1. Lead complications

The complications of CPMs include lead infection, lead failure, lead fracture, lead dislodgement, tricuspid regurgitation, increased defibrillator threshold, endocarditis, and sepsis. The cardiac mortality due to CPM can be associated with 31% of deaths [5,13]. Lead complications due to CPMs also include lead noise or loss of insulation. The lead can be extracted using mechanical snares or laser technology; this has been associated with injury to the vessels or endocardium [14,15].

The FOLLOWPACE study and Danish registry reported the rate of lead dislodgement in CPMs and LPMs to be 3.3% and 1.2%, respectively [16]. The LEADLESS II trial showed similar results including device dislodgement (1.7%), cardiac perforation (1.3%), and higher pacing thresholds requiring device

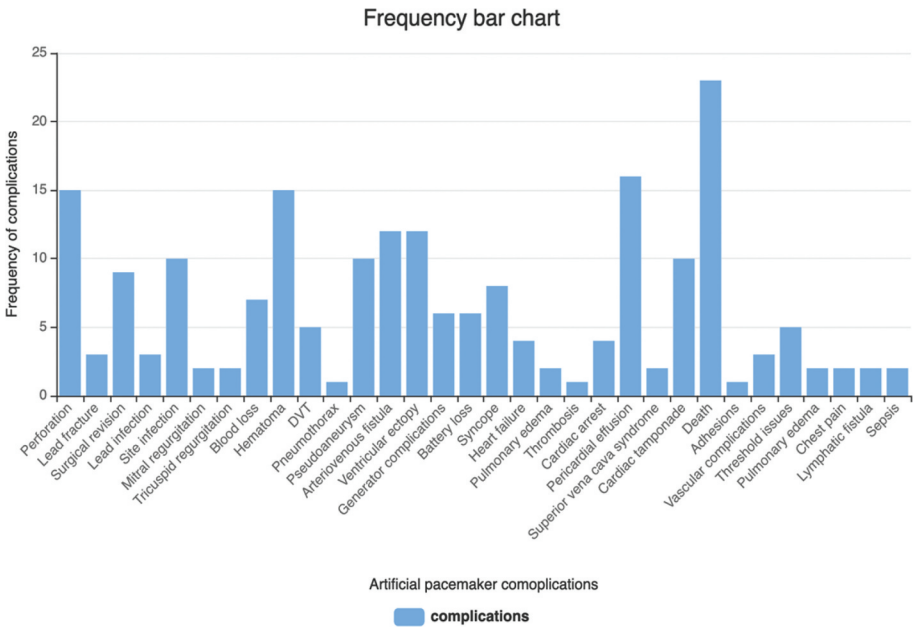

Figure 2. Bar chart showing frequency of complications secondary to artificial pacemakers including conventional or leadless.

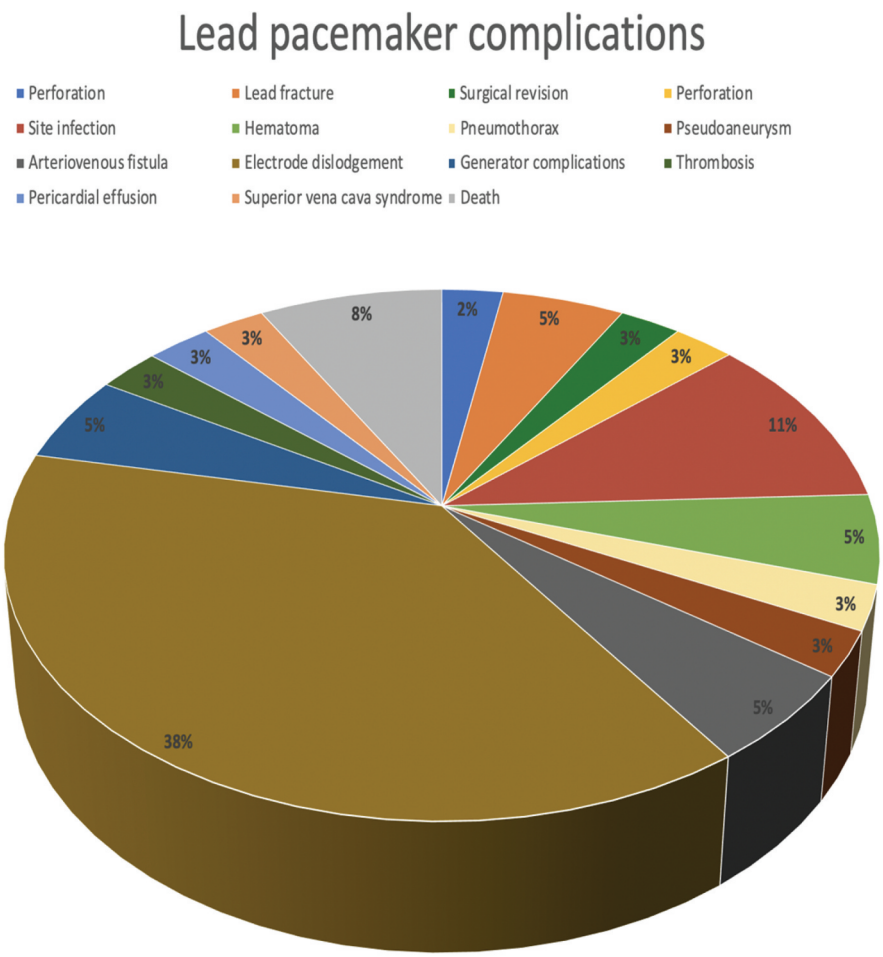

Figure 3. Pie chart showing percentage complications secondary to conventional (lead) pacemakers in our study population.

repositioning (1.3%). These results are consistent with our review showing a higher rate of lead fracture and infections. Also, lead dislodgment rate was negligible in LPMs compared to CPMs. Valvular complications secondary to lead impaction on the tricuspid valve or the direct impact of the LPM were also reported in both groups, but these complications were not significantly different between the two groups (LPM 0% vs CPM 1.1%, P = .76).

4.2. Generator complications

Pulse generator complications are uncommon and account for less than 2% of the complications [17]. Generator complications can be periprocedural including hematoma, infection of the pocket, device dislodgement, cardiac perforation, pericardial effusion, and cardiac tamponade [18]. In CPMs, a subcutaneous pocket at the site of the device is the source of local infection, erosion, and bacteremia in 1% to 2% of cases [19,21]. LPMs are associated with low rates of infection in general due to the absence of a subcutaneous pocket and the small surface area of LPMs. Infection associated with LPMs can be procedurally related including abdominal wall infection, infected groin hematoma, and sepsis [9]. In our study, both the CPMs and LPM have almost the same percentage of peri-procedural hematoma formation (8% vs 7.4%, P-value = 0.58). In the LEADLESS II trial, 6.5% of the 526 patients were reported to have a hematoma due to cardiac perforation, and 1.3% of that 6.5% subgroup had pacemakers implanted in the ventricle through right ventricular sensing and pacing [22]. Another prospective study named Micra investigational device exemption (IDE) had 719 pacemaker implants and reported cardiac perforation in 1.5% of the cases [23]. In our study, we found a higher but statistically insignificant pericardial effusion risk with LPMs of 8% (p-value = 0.05) compared to CPMs at 4.2% [24]. In the LEADLESS trial, at a one-year follow-up, the Nanostim device was shown to have stable pacemaker electricity, rate responsiveness, and without any device-related complications [25]. Overall, our analysis showed no significant difference in the CPM- and LPM-associated generator complications (8% vs 2.3%, P-value = 0.16) or threshold/electromagnetic complication (0% vs 2.8%, p-value = 0.51), respectively.

4.3. Miscellaneous

Rare complications secondary to pacemakers can include heart failure, pulmonary oedema, pericardial effusion, venous thrombo-embolism/deep venous thrombosis (DVT), pulmonary embolism, lymphatic

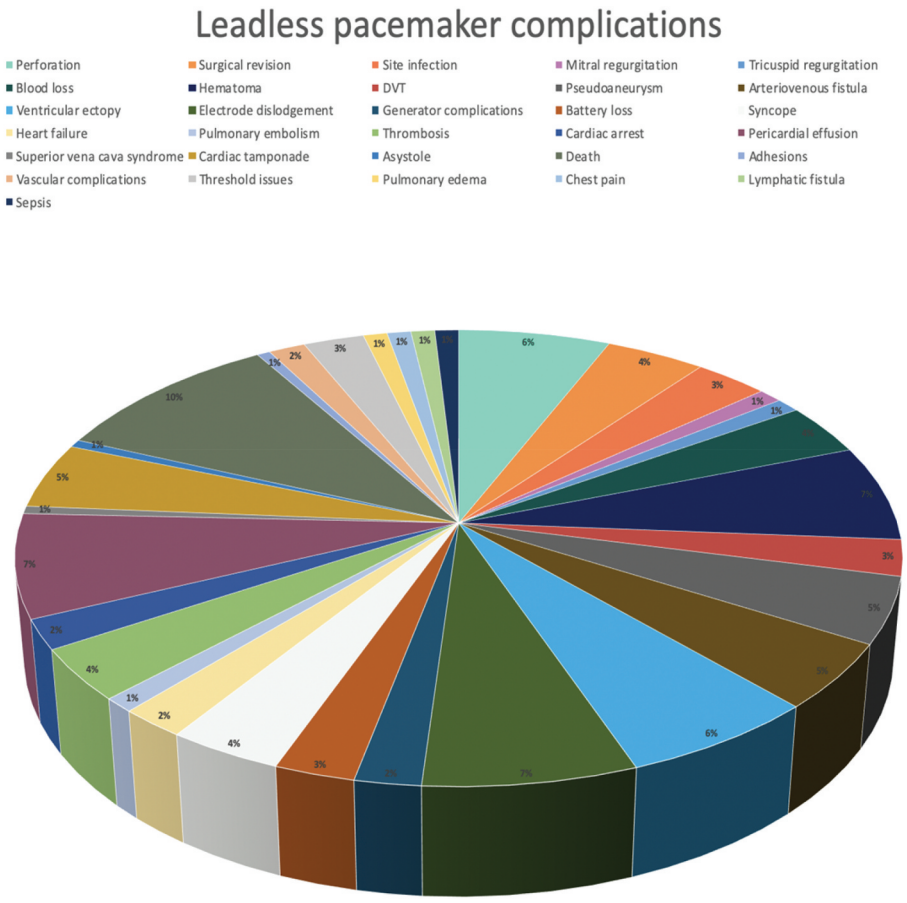

Figure 4. Pie chart showing percentage complications secondary to leadless pacemakers (LPM).

fistula, syncope, asystole, cardiac arrest, and death. None of these complications was statistically different between the two groups. Of note, the LPM group had a 1.2% lower death rate as compared to CPM ($P = 0.5$).

5. Conclusions

The goal of the study was to compare the difference of complications of CPM vs LPM by reviewing the relevant literature in available databases. Our results showed that LPM significantly reduces the risk of lead-associated complications, such as lead fracture, dislodgement, and infection. However, LPM can have a theoretically higher risk of pericardial effusion, cardiac tamponade, and thrombosis.

Author contribution

HR, MK, and MSA: Coordinated the data collection, did a literature review, and data collection;

WU and AA: Performed statistical analysis;

WU and YS: Wrote the manuscript, did search strategy, critical review, and proofread;

ZA, SR, and MCA: Did critical revisions of revised version, syntax check, and approved final version.

Disclosure statement

No potential conflict of interest was reported by the authors.

ORCID

Yasar Sattar http://orcid.org/0000-0002-1304-5748
Waqas Ullah http://orcid.org/0000-0002-4850-0309
Sohaib Roomi http://orcid.org/0000-0001-5998-9309
Maryam Mukhtar http://orcid.org/0000-0003-4870-3269
Asrar Ahmad http://orcid.org/0000-0002-6727-2591
M Chadi Alraies http://orcid.org/0000-0002-7874-4566

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