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OPEN PEER REVIEW

Demographics, Clinical Characteristics, Microbiological Findings, and Risk Factors of 66 Patients with Cardiac Implantable Electronic Devices Infection

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1 Original submission

3 comments · 17 Aug 2024 – 18 Sep 2024

Referee 1 Reviewer

MAJOR REVISION 17 Aug 2024

Dear Authors
Thank you for submitting your article to this journal.
Your manuscript needs major revisions as follows:
1- You should mention the total number of device implants during this time period so the incidence of device infection at your center can be determined.
2- You need a table that shows heart failure and other risk factors in the total implant population and in patients with infections so you can describe them as risk factors. For example, heart failure may be very common in the total implant population and not a real risk factor.
3- You should mention the final outcomes of the infections. How many deaths, how many surgeries, …

Associate Editor

MAJOR REVISION 18 Sep 2024

Needs major revision.

Editor-in-Chief

MAJOR REVISION 18 Sep 2024

Please do the revisions and resubmit the paper.

2

Revision 1

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Reviewer 1:

1- you should mention total device implants in this time period, so the incidence of device infection can be seen in your center

Unfortunately, the total implant population in this period is unavailable

2- you need a table that demonstrates heart failure and other risk factors in total implant population and infections, so you can mention them as risk factors. To exemplify; heart failure may be very popular in all device implants and not a real risk factor

Unfortunately, the total implant population and their information including risk factors are unavailable.

So, we change (predisposing factors or risk factors) to (comorbidities) in the article

3- you should mention the final destiny of infection. How many deaths, how many surgeries, ...

removal of the CIED system was performed in 58 patients (87.9%). No in-hospital mortality was observed among the patients.

Reviewer 2:
Abstract:
1. Add the objective in the introduction

We add the aim of the study to the introduction and abstract

In the present study, we aimed to determine demographic data, comorbidities, clinical presentations, and complications concerning CIED infections

2. Add the sample size, sampling method, and statistical methods.

It is done.
66 patients with confirmed CIED infections participated in the study.

Statistical Analysis

The mean ± standard deviation and frequencies (percentages) were used for descriptive analysis. The statistical analysis was performed with the SPSS software, version 18, for Windows (SPSS Inc., Chicago, Illinois, USA).

3. Add the SD to the mean.

It's done.

mean age of 59.67 +- 13.59 years.

2 Revision 1

3 comments · 21 Dec 2024 – 1 Jan 2025

Referee 2 Reviewer

MINOR REVISION 21 Dec 2024

Dear Editor in chief
Thanks for sharing the article.
Here are my comments:

Abstract:

1. Clarity on Study Objectives: The objective is mentioned, but consider making it slightly more concise to avoid repetition with the introduction.
2. Statistical Details: Add a brief mention of how findings like "91% with pocket site infection" were statistically significant, if applicable.

Introduction:

1. Literature Context: Expand slightly on why there is variability (0.13%–19.9%) in reported CIED infection rates, referencing geographical or methodological differences if possible.

Methods:

1. Exclusion Criteria: Mention if any patients were excluded from the study and why, as it helps in understanding the sample selection.
2. Definition of Terms: Clearly define "negative cultures" to avoid ambiguity, especially considering its significance in the results.

Results:

1. Comparative Findings: When presenting percentages, briefly compare these findings to established literature (e.g., is 91% pocket site infection high compared to other studies?).
2. Lab Findings Table: Add a short note about the clinical implications of elevated ESR and anemia observed in 36.4% and 34.8%, respectively.

Discussion:

1. Cultural Practices Impact: Address the potential role of local antibiotic use before cultures are taken, which could explain the high proportion of culture-negative results.
2. Future Research: Mention possible avenues for future studies, such as exploring newer diagnostic modalities in culture-negative cases.

Formatting:

1. Ensure uniformity in statistical reporting (e.g., "59.67 ± 13.59 years" should consistently include both mean and SD).
2. Use consistent terminology for CIED infection types throughout (e.g., "CIED-related endocarditis" vs. "CDRIE").

Tables:

1. Risk Factors Table: Clearly label comorbidities as "associated but not necessarily causal risk factors" to align with the discussion's nuance.

2. Microbiological Findings Table: Clarify how “Gram-negative bacteria” compare in significance to “Gram-positive bacteria” within the study cohort.

Ethical Statement:

1. Explicitly confirm if informed consent covered publication of anonymized patient data.

Associate Editor MINOR REVISION 1 Jan 2025

Needs minor revision.

Editor-in-Chief MINOR REVISION 1 Jan 2025

Please revise the paper based on the comments and resubmit it to the journal.

3

Revision 2

AUTHORS' RESPONSE TO REVIEWERS

Authors' reply to reviewers

The next pages contain the authors' point-by-point reply to the comments of this revision round, as submitted with the revised manuscript. It is published as the authors wrote it.

Abstract

1. **Clarity on Study Objectives**:
    - *Reviewer Comment:* The objective is mentioned, but consider making it slightly more concise to avoid repetition with the introduction.
    - *Response:* Thank you for this suggestion. We have revised the objective in the abstract as follows:
      "The study aims to analyze demographic data, comorbidities, clinical presentations, and complications related to CIED infections." This adjustment eliminates redundancy with the introduction.
2. **Statistical Details**:
    - *Reviewer Comment: Add a brief mention of how findings like "91% with pocket site infection" were statistically significant, if applicable.*
    - *Response: Thank you for this observation. We would like to clarify that 91% represents the percentage of patients who had signs of pocket site infection, and as it is a descriptive statistic without comparison to other groups or variables, no p-value is applicable. We have ensured that this is presented in the abstract to avoid any misinterpretation.*

Introduction

1. **Literature Context**:
    - *Reviewer Comment:* Expand slightly on why there is variability (0.13%–19.9%) in reported CIED infection rates, referencing geographical or methodological differences if possible.
    - *Response:* Additional explanation has been included in the introduction to address the variability in infection rates. Specifically, we noted:
      "The wide range in CIED infection rates (0.13%–19.9%) can be attributed to differences in healthcare practices, patient populations, and diagnostic methodologies across studies and regions. For instance, some regions may have stricter perioperative infection control measures or different criteria for diagnosing infections."

Methods

1. **Exclusion Criteria**:
    - *Reviewer Comment:* Mention if any patients were excluded from the study and why, as it helps in understanding the sample selection.
    - *Response:* The Methods section now specifies exclusion criteria as follows:
      "Patients were excluded if their medical records were incomplete or if the diagnosis of CIED infection was not confirmed based on clinical, microbiological, or imaging findings.
2. **Definition of Terms**:

- *Reviewer Comment:* Clearly define “negative cultures” to avoid ambiguity, especially considering its significance in the results.
- *Response:* A definition for “negative cultures” has been added to the Methods section: *"Negative cultures were defined as the absence of microbial growth in blood or wound cultures after a minimum incubation period of 5 days under standard laboratory conditions."*

Results

1. **Comparative Findings**:
    - *Reviewer Comment:* When presenting percentages, briefly compare these findings to established literature (e.g., is 91% pocket site infection high compared to other studies?).
2. *Response:* The Results section now includes a comparative analysis: *"The 91% prevalence of pocket site infection observed in this study is higher than the rates reported in some studies, such as 60%-75% (Bennett JE, 2019)*
3. **Lab Findings Table**:
    - *Reviewer Comment:* Add a short note about the clinical implications of elevated ESR and anemia observed in 36.4% and 34.8%, respectively.
    - *Response:* A note on clinical implications has been added: *"Elevated ESR (36.4%) and anemia (34.8%) were frequent among patients, suggesting systemic inflammation or chronic disease, which are known to be associated with CIED infections. These findings reinforce the need for thorough clinical evaluation in suspected cases."*

Discussion

1. **Cultural Practices Impact**:
    - *Reviewer Comment:* Address the potential role of local antibiotic use before cultures are taken, which could explain the high culture-negative results.
    - *Response:* The following explanation has been added to the Discussion: *"The high prevalence of culture-negative results (37.9%) in our study may be attributed to the widespread use of antibiotics before seeking medical care. This practice, which is common in our region, could suppress microbial growth, leading to false-negative culture results."*
2. **Future Research**:
    - *Reviewer Comment:* Mention possible avenues for future studies, such as exploring newer diagnostic modalities in culture-negative cases.
    - *Response:* Future research directions have been expanded upon: *"Further studies should focus on advanced diagnostic modalities, such as molecular techniques (e.g., PCR) and imaging technologies like FDG-PET/CT, to improve*

detection rates in culture-negative cases. These tools could provide a more accurate diagnosis, especially in complex cases where traditional methods fall short."

Formatting

1. **Statistical Reporting**:
    - *Reviewer Comment:* Ensure uniformity in statistical reporting (e.g., “59.67 ± 13.59 years” should consistently include both mean and SD).
    - *Response:* We have reviewed the manuscript to ensure consistency in reporting statistical data. All values now include both the mean and standard deviation, such as "59.67 ± 13.59 years."
2. **Consistent Terminology**:
    - *Reviewer Comment:* Use consistent terminology for CIED infection types throughout (e.g., “CIED-related endocarditis” vs. “CDRIE”).
    - *Response:* Terminology has been standardized throughout the manuscript. For example, the term “CIED-related endocarditis (CDRIE)” is used consistently in all sections.

Tables

1. **Risk Factors Table**:
    - *Reviewer Comment:* Clearly label comorbidities as “associated but not necessarily causal risk factors” to align with the discussion’s nuance.
    - *Response:* A clarifying note has been added to the Risk Factors Table:
      "The listed comorbidities are associated with CIED infections but should not be interpreted as causal risk factors."
2. **Microbiological Findings Table**:
    - *Reviewer Comment:* Clarify how “Gram-negative bacteria” compares in significance to “Gram-positive bacteria” within the study cohort.
    - *Response:* We have added a note in the Results section clarifying that Gram-positive bacteria, including coagulase-negative staphylococci (24.2%) and Staphylococcus aureus (21.2%), were the most commonly isolated pathogens in our cohort. Gram-negative bacteria, while less frequent (e.g., Klebsiella species at 4.5%), may hold clinical significance in specific patient subgroups and warrant further investigation.
    - **Ethical Statement**

1. **Informed Consent**:
    - *Reviewer Comment:* Explicitly confirm if informed consent covered publication of anonymized patient data.

- *Response:* The Ethical Statement now explicitly confirms:
  "Informed consent was obtained from all participants, and this included permission for the publication of anonymized data by institutional and ethical guidelines."

3 Revision 2

2 comments · 9 Feb 2025 – 9 Feb 2025

Associate Editor

ACCEPT 9 Feb 2025

accepted

Editor-in-Chief

ACCEPT 9 Feb 2025

accept