Jerzy Tadeusz Chudek, Professor

Editor-in-Chief

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Dear Dr. Chudek,

We thank you for this opportunity to resubmit a revised version of our manuscript now entitled '**Bow-and-arrow sign on point-of-care ultrasound for diagnosis of pacemaker lead-induced heart perforation: A case report and literature review'.** We also thank the reviewers for their helpful comments. We have revised the manuscript based on these comments and provide point-to-point responses on the appended pages. In the manuscript, these revisions are underlined for convenience.

Issues and responses

Reviewer #1:

1. **Issue:** Comments: (1) The case is interested and well described.

   (2) Are there other clinical conditions which mimicking archery sing, if this is the case you are better to add this issue to your article (not obligation).

   (3) The case needs minor language polishing.

Response： Thank you for these helpful comments. So far as we know, no "archery" or "bow and arrow" sign on ultrasound has been reported for other clinical conditions. We have polished the language, including changing the term "archery" sign to "bow and arrow" sign.

Reviewer #2:

1. **Issue:** Page 5 Line 12 This is not grammatically correct. Change "we presents with" to "we present" or reword the entire sentence. If I may editorialize, I'm curious if "bow-and-arrow" sign is more colloquial than

"archery" sign. Much like the "sea-and-sand" sign assessing for pneumothorax. I agree with the scientific contribution of the paper. Perhaps as a reader, I think including the "archery sign" or "bow-and-arrow sign" in the title would emphasize this tool as to me it is the take-home point.

Response： We have revised the sentence on Page 5 Line 12 accordingly. We agree and have changed "archery" to "bow-and-arrow" throughout the revised manuscript as indicated above.

Revision：

We also describe a step-wise POCUS-based approach for diagnosis of RV apex perforation, (Page 5 Line 12)

Bow-and-arrow sign on point-of-care ultrasound for diagnosis of pacemaker lead-induced heart perforation: A case report and literature review (Title of the case report)

Reviewer #3:

Overall Comments:

1. **Issue:** Overall, this is not a new concept. There was a fairly similar recent POCUS cardiac perforation case report published (https://www.jmuonline.org/article.asp?issn=0929-6441;year=2022;volume=30;issue=3;spage=221;epage=222;aulast=Chen).

   If anything is a new concept, potentially your 'archery' sign but these diagnostic features are described elsewhere as well. Additionally, without being able to see your images, pictures, or tables I again am unsure of what this case report adds to the current knowledge regarding cardiac perforation following pacemaker placement (specifically figures 3 and 5).

   Response： Thank you for your careful review and helpful critique. A number of case reports have been published showing the use of POCUS for the diagnosis of lead perforation, but this is the first study reporting a

unique "bow-and-arrow" sign on POCUS for rapid diagnosis. According to our literature review, 22 case studies have reported the sonographic features of the right ventricular (RV) apex perforation by lead using POCUS. Overall, these studies present a very wide range of imaging variations such as the lead mimicking a "spear", the lead entering and retracting from the RV with each cardiac movement, and discontinuation of RV free wall. Our report highlights the unique nature of this "bow and arrow" sign and emphasis the utility of POCUS for diagnosis of lead perforation. Knowledge of these representative imaging features as well as the "bow-and-arrow" sign in our report can help clinicians rapidly reach a diagnosis of lead perforation.

We regret that we are unable to upload the figures and tables. We have resubmitted the manuscript with figures and tables correctly.

Revision： We include the "bow-and-arrow" sign in our title to emphasize the take-home point of this study.

Bow-and-arrow sign on point-of-care ultrasound for diagnosis of pacemaker lead-induced heart perforation: A case report and literature review (Title of the case report)

2. **Issue:** One thing I did find interesting about this case was the presentation. In this ICU patient post-surgery I would not have had cardiac tamponade due to pacemaker lead perforation first on my differential (in my mind I would have considered sepsis, PE, bowel ischemia, bowel perforation). This is not discussed much but to me that is truly the use of POCUS in this situation is that you have a critically ill patient who decompensated from an unknown etiology and now your POCUS exam is there to help you find out why. The way you present this case, it seems like you already 'knew' it was cardiac tamponade?

Response： We have reviewed the medical records of this patient carefully and revised the manuscript to highlight the differential diagnosis of acute

abdomen in light of recent abdominal surgery. We have changed the wording to avoid ambiguity.

Revision： In the setting of recent abdominal surgery 6 d prior, acute abdomen, such as gut perforation and necrosis, and septic shock were initially suspected. However, there was no distension and tenderness with rebound on abdominal examination.

3. **Issue:** Additionally, you advertise this as a literature review but give no detail about the case reports you looked at, how they were selected, how the literature was reviewed, etc. This is not a literature review.

   Response： We present a protocol describing how the review was performed, including the search strategy and inclusion criteria. We have reviewed the literature once again and 22 case reports with sonographic features of RV apex perforation by lead are included in our review.

   Revision： A systematic English language literature search of PubMed and China National Knowledge Infrastructure (CNKI) was conducted for the period 2002–2022 using key words “heart perforation”, “cardiac perforation”, “pacemaker lead”, and “ultrasound” with reasonable Boolean connectors to identify previous cases of RV apex perforation by lead diagnosed using ultrasound. Eventually a total of 22 cases [18,22-42] diagnosed by ultrasound with definite imaging information were identified. These cases are summarized in Table 2.

4. **Issue:** There were many word choice/grammatical errors throughout (some of these are listed below). The check list and line specific comments are listed below.

   Response： We have polished the language accordingly.

Check List:

1. **Issue: 11 References.** I would cut down the number of references (not all

your stated references add to your paper). 63 references for a case report is entirely too many.

Response： We have reduced the number of references to 46.

2. **Issue: 13 Research methods and reporting.** Yes, except: Informed consent: In the document it states that informed written consent was obtained from the patient. It seems that the patient was critically ill and died 24 hours post operatively. In that this is a case report, it seems unlikely that this patient herself gave written consent for this publication. Please clarify.

   Response： We apologize for this mistake. Written consent was provided by the patient's son rather than the patient herself. We have revised the manuscript accordingly.

   Revision：Informed consent statement: Informed written consent was obtained from the patient's son for publication of this report and any accompanying images.

Line Specific Comments:

1. **Issue: Page 3: Line 12-13:** CT scan was 'not applicable' this does not make sense. If it was that patient was too unstable then that should be what is said. Or if a CT scanner was not available then that should be said.

   Response： We have clarified the reason in the revised manuscript.

   Revision： Computed tomography (CT) was not available due to unstable hemodynamic status in the patient.

2. **Issue: Page 3：Line 15-19:** redundant

   Response： We have revised the manuscript accordingly.

   Revision： Further POCUS by an ultrasonographist revealed a unique "bow-and-arrow" sign indicating right ventricular (RV) apex perforation by the pacemaker lead which facilitated the rapid diagnosis.

3. **Issue: Page 6：Line 16:** Was the blood pressure via a NIBP cuff or arterial line?

   Response：Blood pressure was measured using an arterial catheter. This is now specified in the revised manuscript.

   Revision：Examination of vital signs revealed hypotension (88/60 mmHg) with infusion of noradrenaline (1.4 µg/kg × min) as measured by an arterial catheter,

4. **Issue: Page 6：Line 21-22:** Distant heart sounds alone do not make me think tamponade. If anything, the JVD, hypotension would make that story more probably. Also in the setting of the lead placement 26 days prior and recent operation 6 days ago, was tamponade due to lead perforation the highest thing on your differential at this point? To me it seems like sepsis, bowel perforation, others should also have been considered.

   Response： This is answered in the previous section.

5. **Issue: Page 6：Line 25-26:** I would just change to say that 'Laboratory studies were obtained and are summarized in Table 1.' For the laboratory studies in this critically ill patient I think it would be beneficial to include the labs prior to this acute episode so that the reader can see any sudden changes that coincide with this new clinical presentation.

   Response： We have included laboratory values prior to and after symptom onset in the revised text and Table 1.

   Revision：Laboratory studies prior to and after the onset of chest pain and dyspnea were obtained and are summarized in Table 1.

6. **Issue: Page 7：Line 12-13:** Again, I would not use the phrase 'not applicable' to describe why the CT scan was not obtained; can just use 'not

obtained due to the critical status of the patient.'

Response： We now specify the reason in the revised manuscript.

Revision： CT scan was not obtained due to the critical status of the patient.

7. **Issue: Page 7：Line 12-15:** Cardiac tamponade is a clinical diagnosis not an ultrasound diagnosis thus saying that the pericardial effusion was associated with cardiac tamponade is not correct. You could say that this supported the diagnosis of cardiac tamponade but you need to delineate what ultrasonographic features support that (the size of the pericardial effusion has nothing to do with whether there is tamponade physiology it has to do with chamber collapse during particular phases of the cardiac cycle).

   Response： The POCUS findings supporting cardiac tamponade are now included in the revised manuscript.

   Revision： Urgent POCUS using a portable machine (Mindray M9, Shenzhen, China) to assess hemodynamic status at the bedside revealed a large volume of pericardial effusion associated with diastolic collapse of the RV free wall, supporting a diagnosis of cardiac tamponade.

8. **Issue: Page 7：Line 16-19:** Amount of blood has nothing to do with ongoing life-threatening bleeding. Due to this one exam as a snapshot in time you have no idea how fast this fluid accumulated. This should be further specified. Additionally, I would comment on the hemodynamic response to pericardial drainage (i.e. if hemodynamics improved that would support tamponade physiology).

   Response： We describe the drainage method and findings, including the evidence for sustained bleeding into the pericardial cavity, in the revised manuscript.

   Revision： Briefly, a pig-tail catheter was successfully implanted into the pericardial sac at the cardiac apex and drainage yielded a large amount

(600 mL) of bloody pericardial effusion within half an hour. Drainage markedly improved the dyspnea and increased blood pressure (140/71 mmHg) with decreased infusion of noradrenaline (1.1 μg/kg × min). However, there was still ongoing pericardial bleeding with an accumulative total of 970 mL within 7 h after the initial drainage, strongly suggesting life-threatening active bleeding in the pericardial cavity.

9. **Issue: Page 8：Line 11-13:** final diagnosis section does not add anything to case report, would suggest removal.

   Response： The final diagnosis section is required for case reports in WJCC.

10. **Issue: Page 8：Line 15-28:** I assume that TEE was performed during the case. I would add TEE findings, specifically any changes in RV function pre and post repair.

    Response： We regret that the TEE was not performed for this patient.

11. **Issue: Page 8：Line 24-28:** You state the patient 'presented' with refractory circulatory shock… I would specific if this was during the case, after repair, ongoing process, or after certain period in the ICU.

    Response： We have included a description of refractory shock in the revised manuscript.

    Revision： During the operation, blood pressure fluctuated between 128/85 and 108/65 mmHg with infusion of norepinephrine (1.3–2.0 μg/kg × min). After the operation, the patient presented with refractory circulatory shock as evidenced by decreased blood pressure (75/41 mmHg) during infusion of high-dose norepinephrine (2.2 μg/kg × min), as well as hypothermia (35.5 °C), coma, and anuria. The patient received blood transfusion, fluid resuscitation, continuous renal replacement therapy (CRRT), and advanced life support treatment including invasive

mechanical ventilation and cardiac inotropic support with venous pumped milrinone (0.5 μg/kg × min).

On the second postoperative day, the patient developed recurrent ventricular tachycardia, fibrillation, and cardiac arrest. Cardiac pulmonary resuscitation (CPR) was attempted and both intravenous epinephrine and an antiarrhythmic drug (lidocaine) were administered; however, the patient died from shock and multiple organ failure syndrome (MODS).

12. Issue: Page 9： Line 1: Remove word 'however'

Line 3-4: Remove last sentence.

Line 9: I would give data as to what percent of serious complications are lead induced cardiac perforation.

Response： We have revised the manuscript accordingly.

Revision： On the second postoperative day, the patient developed recurrent ventricular tachycardia, fibrillation, and cardiac arrest. Cardiac pulmonary resuscitation (CPR) was attempted and both intravenous epinephrine and an antiarrhythmic drug (lidocaine) were administered; however, the patient died from shock and multiple organ failure syndrome (MODS).

More than one million permanent pacemaker implantation procedures are performed annually across the globe, of which approximately 1% result in lead-induced heart perforation[8].

13. Issue: Page 10： Line 28: Replace phrase 'not applicable'

Response： We have specified the reason in the revised manuscript.

Revision： In our case, CT scan was not obtained due to unstable hemodynamic status.

14. Issue: Page 11： Line 16-31: You need to include some rationale for what cases you reviewed, how you selected them, etc. A literature review as you are implying needs to be done in a standardized fashion or you can

just self select for what cases you want. You need a protocol or diagram for how this review was conducted.

Response： This is answered in the previous section.

15. Issue: Page 12：Line 14: change exaction to extraction

Line 27-29: 'was' required in this case

Response： We have revised the manuscript accordingly.

Revision： However, an expert consensus statement recommends that lead extraction should be performed in cases with significant manifestations such as pericardial bleeding, chest pain, and device malfunction[43].

Nevertheless, the case patient required thoracotomy to repair the heart perforation given the severe pericardial bleeding.

16. Issue: Page 13：Line 12: You say delayed but do not define what delayed is (earlier in paper you use acute, subacute, and chronic). Consider using consistent terminology.

Line 16-18: This is the first mention of your archery sign thus you cannot say it is indicative. Additionally this sentence should be rephrased to be more clear.

Response： We have revised the manuscript accordingly.

Revision： (1) we present the complete clinical course of subacute lead perforation rapidly diagnosed by POCUS

An "archery" sign on POCUS can be easily recognized that facilitates the rapid diagnosis of lead perforation.

Best regards
Dr. Xing