

## Peer Review File

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### ## Response to Reviewer A

#### General Comment

The article covers a wide range of themes, and I do hope it is published eventually. However, the manuscript appears unfinished, with an unclear aim, poor readability at times, and lacks proper citations. There are formal mistakes such as repeatedly defining terms and using abbreviations without prior definitions. I recommend major changes to the structure, with focus on removal of superfluous wording and content.

#### Major Specific Comments

##### Comment 1 (C1):

Readability of the abstract should be improved substantially.

The aim of the study is unclear, as it appears to support the authors' assumption rather than aligning with recommended research review guidelines (e.g., PRISMA). The stated aim of improving risk prediction does not align with the objectives of a systematic review. For instance, at the end of their introduction they write: "Therefore, we would like to emphasize the focus on improving risk prediction". This is not a fitting aim of a systematic review.

##### Reply 1 (R1):

Thank you for this great comment. We added the following lines to better describe the aim of the study (line 63) addressing PRISMA (PICO) guidelines:

*"..., in brief, frail cardiac surgery CS patients are exposed to pre-, peri, and post-interventional complications, most prominent naming atrial fibrillation AF, which is often subclinically appearing and overlooked. Continuous monitoring today through wearables (e.g. Apple-, Fitbit, Samsung-watch) can improve patient outcomes, as they already received CE-mark and FDA to report sinus rhythm, AF, and inconclusive (X). Moreover, Heart Rate Variability assessments via wearables could predict complications such as post-operative atrial fibrillation POAF or sudden cardiac death SCD. This systematic review aims to describe the current state of continuous monitoring through wearables in CS patients and outline an outlook of future potential highlighting AF detection and risk evaluation with HRV."*

##### Comment 2 (C2):

The paper is lacking citation for statements given (ex. Statement 44-46, 47-48, 175, 179, 185)

##### Reply 2 (R2):

Thanks you for this constructive comment. We have added the respective citations and adjusted

two sentences in line 175 and 178.

**C3:**

They do not state that the study has been preregistered, and with no protocol posted prior to study execution. This is of concern.

**R3:**

Since the review was an invited review we did not preregister the study.

**C4:**

It would have greatly added to the quality if the authors did a bias assessment of the included studies.

**R4:**

Thank you for this great comment. We have added a “study bias” paragraph to the methods section (Line 89), as shown below. Since this review put focus on technical limitations to describe the state of the art in continuous monitoring in CS patients, we assume an overview of most likely associated biases as best serving declaration.

“ ... 2.2 *Study Biases*

*Attrition-bias might have impact on the study outcomes since CS patients are often frail, elder, and undergo an emotionally arousing situation. Therefore, probands with a more deteriorated cardiovascular system and consequently a higher probability to develop arrhythmic events could be more likely to drop out of the studies or show incompliance wearing the wearable eventually impairing sufficient data collection. To mitigate attrition-bias, Intention-to-treat analysis that better preserves randomization than per-protocol-analysis was conducted in most included studies. When reported by these studies, intention-to-treat-analysis was often applied in wearables studies for cohorts obligated to wear the device, whereas per protocol analysis was conducted for patients that didn't undergo continuous monitoring in most cases.*

*There are other important biases of concern, such as the risk of response bias in cv symptom reports. Additionally, reporting bias may impact on the study that we could assess for this review, since positive results are more likely to be published than negative. This can substantially influence the findings of this systematic review.”*

**C5:**

The review is extensive, but content covered is at times also superfluous. I would recommend the authors to rework through the results section and substantially compress sections.

**R5:**

Thanks for this constructive comment. We have perused the whole manuscript and worked on the readability and comprehensiveness of the manuscript by consulting a native speaker. We do believe that the impression of superfluousness is rather due to language barriers than content.

## **Minor Specific Comments**

### **C6:**

POAF and CS is not defined prior to first use in abstract.

### **R6:**

We have defined now POAF and CS before the abbreviations occur in the review (line 20).

### **C7:**

The following sentences should be revised and shortened for easier communication: “Regarding the prognostic value of HRV in cardiac surgery patients, we were able to underline the predictive value of HRV in patients at risk for sudden cardiac death, after acute myocardial infarction, and POAF after CS.”, the same goes for the sentence after – and many sentences throughout the manuscript.

### **R7:**

We altered the mentioned sentence and the subsequent sentence with the following results (Line 18):

*“... Perusing these publications on HRV’s prognostic value, we could identify HRV as a predictor for sudden cardiac death SCD, mortality after acute myocardial infarction, and POAF. With regard to standard AF assessment, which typically includes extensive periods of unrecorded cardiac activity, we demonstrated that continuous monitoring via wearables recorded significant cardiac events that would otherwise have been missed.”*

### **C8:**

It is not clear from the abstract what methodology was used for the systematic review. I advise that the framework, search strategies, evaluations of studies, and statistics used should be clearly stated.

### **R8:**

We did mention the search strategy and evaluation in the abstract, with more details provided in the methods section. Since every study within the 33 results was considered and read to write the review, no additional statistical model has to be given.

### **C9:**

It is not clear from the abstract what the goal of the review is. In line 11 the goal of the study is stated to be “to highlight the untapped potential”. Do they mean “we review/summarize/describe the potential of...”? I advise the aim to be stated in a clearer manner. I advise the authors to provide some information on the field before they lead on to their aim of the study. The background given in the main text is informative and mostly well-written, so the authors do show that they know the background of their study.

### **R9:**

We specified now on the aim of the study as described above in the end of the introduction (Line 63). We summarized the background information in the 3.2 background information section. We assume that describing the aim of the review on the very top of the abstract provides a better orientation for the reader whether he/she is interested in reading the manuscript or not.

**C10:**

The abstract should be re-organized. I advise they include the following sections in this order: Background, objectives, methods, results, and discussion/conclusion. This will help readers understand the content of the research presented.

**R10:**

Since we have focused on HRV and AF screening, we decided to provide specific background order for each topic. That's why we provide background later in the review as reviewer A suggests.

A summary of background information and objective is stated within the introduction. Consequently, the order described above (explaining Background and objective first) is already established in the manuscript (following the PRISMA Checklist provided by M Health).

Moreover, Reviewer B appreciated the structure of the review, therefore we decided to keep the proposed order (reviewer B: "the structure of the paper is easy to follow").

**C11:**

I would like to be informed of the number of people this study might concern, meaning an estimate of prevalence of cardiac surgery where AF and HRV might be beneficial (percent-wise ex.)

**R11:**

Thanks for this great comment! We have inserted the following sentence at the end of the introduction:

*"... The number of conducted cardiac surgeries per year range from 0.5 per million in low- and lower-middle income countries (average  $107 \pm 113$  per million) to 500 in the upper-middle-income countries (average  $107 \pm 113$  per million). Outside the industrialized world cardiac surgery is insufficiently accessible for more than 6 billion people. Therefore, a population ranging from 1.6 billion to 500 billion per year would benefit from improved AF monitoring and HRV assessments. **Obviously, this benefiting population would further increase as worldwide access to CS improves, since low-income but also middle income countries are still on their way to meet needs (16).**"*

**C12:**

Line 54, remove the ":" before the in-text citation.

**C13:**

ECG is not defined prior to first use in text.

**R12+13:**

Thanks for the constructive feedback. We have undertaken the proposed adjustments.

**C14:**

In their first sentence under “search strategy” they write: “Photoplethysmography and single-lead ECG were identified as the most discussed and applied technical methods for continuous patient monitoring in commercial wearables”, this is unclear. Do they mean they did an informal review prior to the review?

**R14:**

We deleted this sentence since it was unclear and redundant.

**C15:**

The authors do not provide information on why the study removed prior to screening was removed.

**R15:**

We have added the following sentence (line 80):

*“...A single publication was removed even prior to screening, since the study didn’t focus on CS patients.”*

**C16:**

Line 92, they define a term that has already been defined.

**C17:**

This should be corrected. They do so again, with another term, in line 138 and 139. Then again for several other terms, ex. 310, 318.

**R16+17:**

Thanks for the constructive feedback. We have undertaken the proposed adjustments.

**C18:**

They do not reference the figure 2 close to where it is places (but much later) and they do not reference figure 3 at all in the text. This goes for several of the figures.

**R18:**

We referenced figure 2 (line 99), figure 3 (line 100 and 101), figure 6 and 7 (226), figure 5 (229), figure 8 (334), figure 9 (366), figure 10 (599);

**C19:**

Line 223, the number for the heading is missing (I assume it should be 3.3?)

**C20:**

Line 647: “is still questioned” should be corrected to “is still uncertain”.

**C21:**

665: “is not just a loose assumption”, I suggest this to be re-written.

**R19+20+21:**

Thanks for the constructive feedback. We have undertaken the proposed adjustments.

**C22:**

I suggest that the sections 3.1-3.4. are significantly comprised. If the sentences and superfluous information is removed, the article will become much improved. This advice can be applied in general to the paper, but particularly to these sections.

**R22:**

Thanks for this constructive comment. We have perused the whole manuscript and worked on the readability and comprehensiveness of the manuscript by consulting a native speaker. We do believe that the impression of superfluosness is rather due to language barriers than content.

**## Response to Reviewer B****Major Specific Comments****C23:**

PRISMA flow chart was correctly drawn and easy to understand. However, it would be nice if you could include the Fitbit Heart study paper around line 505. It was published last September. Seven months have passed since your literature search, so there must be some new papers that came out during this time.

**R23:**

Many thanks for this significant comment to improve the manuscript. We have added the following paragraph around line 505 summarizing the Fitbit Heart Study:

*“ ... Algorithn supported AF screening in a large population*

*Recently, the Fitbit Heart study, published in September 2022 by Lubnitz et. al., investigated on a novel PPG-based software algorithm aiming to detect irregular heart rhythms in the general population to identify undiagnosed AF. The Study population ( $\geq 22$  years) was monitored by using compatible wearable Fitbit devices and Android or iOS smartphones. In detail, 5-minute pulse windows (tachograms) were assessed, and subsequently participants revealing 11 consecutives irregular tachograms were identified as showing an irregular heart rhythm (IHR). These participants with an IHR were invited to a telehealth visit and received a 1-week ambulatory ECG patch monitor. Eventually, the first IHR detection with the ECG patch monitoring was assessed as a predictor for AF as the primary outcome. Results displayed 4728 IHR in a total of 455 699 enrolled participants representing 1% (4%, 2070 participants, in the  $\geq 65$ -year-olds). AF was present in 340 (32.2%) of the 1057 participants who received the ECG patch monitor and in 221 participants of the 225 participants with another IHR during ECG patch monitoring resulting in a positive predictive value of 98.2%. In conclusion, the combination of algorithm supported AF screening with fit bit wearables in a large population*

*exhibited a high positive predictive value and may be a strong tool for decreasing undiagnosed AF in the general population.”*

**C24:**

At line 326, I think the atrial fibrillation also has two other common types of “atrial fibrillation with slow ventricular response” (ventricular rate < 60 BPM) and “atrial fibrillation with moderate ventricular response” (ventricular rate between 60 and 100 BPM). It is not precise to say that AF has a clinical presentation with a HR of more than 175 BPM.

**R24:**

We have added the following explanation to the review:

*“... Besides AF is often associated with a ventricular rate of approximately 110 - 160 bpm, AF can be further distinguished between the two types of rapid ventricular response and slow ventricular response, constituting for a ventricular rate of > 100 bpm and < 60 bpm respectively.”*

**Minor Specific Comments**

**C25:**

1. Line 20, “POAF” and “CS” were used in the abstract without explaining the meaning. At line 159, “CS” occurred before explanation.

**C26:**

Line 32, typo “comprehensive.”

**C27:**

3. Line 72, typo: it should be “scopus,” not “sycopus.”

**C28:**

4. Line 83, typo “HVR.”

**C29:**

5. Line 331, “figure 10” should be “figure 8.” You have a figure numbering problem for figures 8, 9, and 10 throughout the paper. Line 304, it should be figures 7 and 8, not “figure 8 and 9).” Line 235, it should be figures 6 and 7, not “figure 8.”

**C30:**

6. Line 337, typo “healt.”

**C31:**

7. Line 379, reference was missing for the “Kim et al.” paper. I know this paper occurred several other places in the paper, but it is better to keep the reference everywhere it occurred.

Corrected

**C32:**

8. Line 408, missing period mark between “systems” and “Similarly.”

**C33:**

9. Line 475, typo “healzhcare.”

**R25-33:**

Thanks for the constructive feedback. We have undertaken the proposed adjustments.

*Again, thank you for your thorough review, which helped to improve the quality of the manuscript significantly! Please let us kindly know if you request further changes to be made to the manuscript.*