Title: A commentary on the use of accelerometers to improve clinical outcomes in patients with implantable cardioverter-defibrillators

Commentary on: Kolk MZH, Frodi DM, Andersen TO, Langford J, Diederichsen SZ, Svendsen JH, Tan HL, Knops RE, Tjong FVY. Accelerometer-assessed physical behavior and the association with clinical outcomes in implantable cardioverter-defibrillator recipients: A systematic review. Cardiovasc Digit Health J. 2021 Nov 24;3(1):46-55. doi: 10.1016/j.cvdhj.2021.11.006. PMID: 35265934; PMCID: PMC8890329.

Abstract

The Implantable Cardioverter-Defibrillator (ICD) is pivotal in preventing sudden cardiac death, monitoring cardiac activity, and restoring normal sinus rhythm with electrical shocks. With sudden cardiac death accounting for half of cardiac-related fatalities, ICD significantly reduces mortality in high-risk patients. Integrated with accelerometers, ICDs track physical activity (PA), which helps predict cardiac support needs and hospitalisation. Enhanced PA post-ICD implantation is also associated with improved outcomes. Wearable accelerometers hold promise in assessing individual physical behaviour (PB), potentially serving as prognostic predictors of future events. This commentary critically evaluates a recent systematic review by Kolk et al. (2022), which examines the association between PB and key clinical outcomes in patients with ICD or at risk of sudden cardiac death.

Key Points

- Declining physical activity for individuals with implantable cardioverter-defibrillator may be associated with increased risk of mortality and hospitalisation.
- Individuals with implantable cardioverter-defibrillator and low physical activity may be at increased risk of mortality and hospitalisation.
- Future primary research should focus on standardisation of time of outcome reporting and outcomes assessed.

Introduction

Implantable cardioverter-defibrillator (ICD) is a battery-powered device implanted under the skin for continuous cardiac monitoring, detecting any life-threatening arrhythmias, and prompt restoration of normal sinus rhythm via electrical shocks when necessary (Mirowski 1985). Sudden cardiac death accounts for approximately half of all cardiac-related deaths (Wong et al. 2019) therefore, ICD represents a significant preventative measure that reduces cardiac mortality among survivors of sudden cardiac death and patients at high risk for ventricular arrhythmias (Friedman et al. 2022).

Currently, ICDs are designed to include a device-embedded accelerometer, which facilitates in detecting physical activity (PA) changes (Kolk et al. 2022). It has been suggested that increased PA, often achieved through cardiac rehabilitation, is associated with a reduced risk of further cardiac complications and improved outcomes in patients with heart failure (Atwater et al. 2021). Conversely, low PA following implantation of ICD has been shown to increase the risk of mortality, ICD shock, and hospitalisation (Zhao et al. 2017).

Therefore, it is possibly valuable to explore the potential of accelerometer-based methods, which could provide detailed insights into individual physical behaviour (PB) and serve as a more precise indicator of clinical deterioration in cardiac health (Kolk et al. 2022). PB encompasses various dimensions, including PA, sleep patterns, daily activities, postures and sedentary behaviours (Bussmann and van den Berg-Emons 2013). A previous systematic review by Kolk et al. (2022) assessed the association of PB with clinical deterioration leading to implantable cardioverter-defibrillator therapy, heart failure hospitalization, and mortality (Kolk et al. 2022).

Aim of commentary

This commentary aims to critically appraise the methods used within the systematic review by Kolk et al. (2022) and expand upon the findings in the context of clinical practice.

Critical appraisal and methods of the review by Kolk et al. (2022)

Using the Joanna Briggs Institute (2017) critical appraisal tool for systematic reviews, three out of nine criteria were judged to be satisfactory for this review (Aromataris et al. 2015). See Table 1 for full critical appraisal. Firstly, from a methodological standpoint there was a non-specific question proposed. When designing a systematic review, it is helpful to structure your question around one of the standardised systematic review types (Munn et al. 2018). Based upon the reviews question and the results presented in the review it appears that this review aims to assess both prognostic and diagnostic test accuracy simultaneously (Campbell et al. 2015; O'KeeffeGreene and Kearney 2014). Due to this lack of clarity, it makes it difficult to appraise certain methodological processes within the systematic review as most methods are critically appraised in context to the aims of the review. Due to this mixture of methodological designs, it brings into question the use of the Quality in Prognosis Studies tool to assess the risk of bias as this tool is not designed to additionally assess test accuracy studies (Hayden et al. 2013). Consequently, the accuracy outcomes of device-embedded accelerometers, in comparison to validated wearable accelerometers, have not been adequately assessed in the context of potential bias.

The third area of concern was related to the search strategy and the number of databases searches. Within the search strategy there was no clear rationale why the review only searched from 2000 onwards. Where this may be justified based upon certain technologies only being introduced at this time point this was not stipulated within the paper. Due to potential indexing bias in the resources used for searching, it is possible that important papers may have been missed. Previous recommendations for healthcare-related subjects suggest that, at a minimum, Embase, MEDLINE, Web of Science, and Google Scholar should be included as essential databases for comprehensive searches (Bramer et al. 2017).

The fourth area of concern was regarding data extraction, the review did indicate that two reviewers did undertake the data extraction process however there was lack of clarity regarding this process being undertaken independently. The current gold standard for this process is that two reviewers undertake data extraction independently (Higgins et al. 2021). Thus, it is possible that errors may have occurred within these processes.

The final areas of concern pertained to the methods of synthesis and the assessment of publication bias. Concerning the synthesis methods, the effect estimates for directional association were not always presented as ratios. This omission made it challenging to ascertain whether the directional association was representative of all the studies assessed, rather than only those studies that demonstrated that specific direction of association. Additionally, there appeared to be consistency regarding the reporting of hazard ratios for a range of outcomes, but no attempt of meta-analysis was undertaken. With no explanation of any breaches of assumptions needed to carry out this procedure.

Table 1 Critical appraisal using the Joanna Briggs Institute (JBI) critical appraisal checklist for systematic reviews and research syntheses (delete the tool which is not relevant)

JBI critical appraisal checklist items	**Responses**
1. Is the review question clearly and explicitly stated?	No - The review presents a broad clinical question that does not specifically focus on diagnostic test accuracy or prognosis studies. With the review stating that the question of interest is "what is the clinical value of PB for identification of clinical deterioration
2. Were the inclusion criteria appropriate for the review question?	Yes - The inclusion criteria are appropriate. Patients with an Implantable cardioverter-defibrillator, regardless of the use of cardiac resynchronisation therapy or wearable cardioverter-defibrillator, were all included. Patients who are at high risk of developing sudden cardiac death without Implantable cardioverter-defibrillator were included. Eligible accelerometer-based methods included wearable or device-embedded accelerometry, with outcomes of interest being ICD therapy for ventricular arrhythmias, heart failure hospitalization, mortality, functional status (e.g., NYHA class), and quality of life. The included population allows the review to have a detailed comparison between Implantable cardioverter-defibrillator and wearable accelerometer.
3. Was the search strategy appropriate?	Yes- The review used 2 electronic data bases MEDLINE and EMBASE to identify studies published between Jan 2000 and Aug 2020. Relevant keywords and terms were used to search papers, together with the use of reference lists of relevant papers to identify potentially missed papers.
4. Were the sources and resources used to search for studies adequate?	No - This review only covers 2 electronic data bases. This review should ideally cover multiple electronic databases, as well as trial registries to minimise publication bias.

5. Were the criteria for appraising studies appropriate?	No - QUIPS (Quality in Prognosis Studies) tool was used in the review to appraise the included studies. However as indicated in the results three studies explored validation of wearable and device-embedded accelerometry based upon the studies the validation studies should be assessed accordingly.
6. Was critical appraisal conducted by two or more reviewers independently?	Yes - The review stated that 2 independent reviewers conducted the appraisal. If there were any disagreement, a third reviewer will be consulted.
7. Were there methods to minimize errors in data extraction?	No - Data extraction was completed by two reviewers; however, it was not specifically stated whether the screening process was undertaken independently.
8. Were the methods used to combine studies appropriate?	No - Within the method section there is no specific indication of exactly how the descriptive analysis was undertaken. It appears that a vote counting method has been used however study direction was not presented as a ratio making it difficult to assess the degree of association for all outcomes. Similarly, within the results there appears to be consistency in regard to hazard ratios presented within the studies although there was no explanation why a meta-analysis was performed.
9. Was the likelihood of publication bias assessed?	No - There was no specific reference used to assess publication bias.

Results of the review by Kolk, et al. (2022)

After duplicate removal 4222 studies were identified of which after screening 52 studies were included in the systematic review. Of these studies, 22 were identified as having a low risk of bias, 19 as having a moderate risk, and 8 as having a high risk of bias.

Among the studies which measured device-embedded accelerometery there was an association between low PA following device implantation and increased risk of mortality (5 studies, n = 101,617, 12–31 months), hospitalization (3 studies, n = 1,715, 15–36 months), combined hospitalization or mortality (3 studies, n = 1,715, 15–36 months) atrial arrhythmias (1 study, n = 770, 25 months) and ICD shock (1 study, n = 4,057, 1 months). A similar association was observed between low PA, measured using wearable accelerometery, and an increased risk of hospitalization and mortality (3 studies, n = 286, 12–36 months).

Similarly declining PA was associated with increased risk of mortality (4 studies, n = 126,234, 26–28 months), hospitalization (5 studies, n = 3,522, 11.7–17 months), combined hospitalization or mortality (3 studies, n = 1,715, 15–36 months) atrial arrhythmias (1 study, n = 770, 25 months) and ICD shock (1 study, n = 4,057, 1 months).

In the studies that utilized device-embedded accelerometery, several factors were identified as reducing PA. These included seasonal variation (1 study, n = 102, 12 months) and pandemic lockdown (1 study, n = 24, 80 days), both of which were associated with decreased PA. Additionally, implantable cardioverter-defibrillator placement (2 studies, n = 2,944, 12–22 months) and onset of atrial fibrillation (1 study, n = 266, 51.6 months) were associated with a decreased risk of PA reduction. In the studies that utilized wearable accelerometer, several factors were identified as associated with PA. Ischaemic heart failure patients had a lower mean activity level compared to healthy adults (1 study, n = not reported in the systematic review [N/R], N/R months).

Unfortunately, other outcomes related to wearable devices were reported, but there were significant inconsistencies and a lack of data concerning important variables. For instance, although it was mentioned that ischemic heart failure patients spent more time engaging in vigorous activities, there was no clarification regarding what this was compared to or the specific period during which this observation was made. Similarly, it was noted that sleep behaviour and physical activity were linked to patient-reported physical function, quality of life, and cognitive function. However, details such as the number of studies and participants for each specific association, the observation period, and the type of sleep behaviour observed remained unclear.

Commentary

Overall, it was deemed that this systematic review is likely to provide an accurate and comprehensive summary of the results of the available studies that address the question of interest. However, more research needs to be done to provide a more detailed and holistic review of this subject.

This review highlights the promising potential of using accelerometer-based methods, (implantable) in identifying the potential risks of patients with an ICD. Based on the current evidence in the review, there is not enough evidence to indicate that accelerometers should be used as a stand-alone detection method for increased risk of negative clinical outcomes (e.g., mortality and heart failure). However, it can possibly act as a moderating factor in a multifactorial assessment in identifying clinical deterioration. It is challenging to determine the precise impact that low or declining PAwould have within a predictive model based on this systematic review. As no single estimate of association was generated within the review for any outcome. Therefore, to generate an accurate weighted model, a weighted assessment of association (meta-analysis) for both low and declining PA across the outcomes assessed in this review is required. The individual estimates could then be incorporated into multifactorial predictive models, alongside other key prognostic factors identified in previous systematic reviews. Previous studies in this area have identified that other such factors such as anxiety and depression (Lindekilde et al. 2022), dialysis, chronic renal disease, cancer, advanced age (Alhakak et al. 2022) and ICD shocks (Qian et al. 2016) are also associated with increased risk of mortality. Accelerometer data on PA, if available, could enhance clinical risk stratification by serving as an additional indicator of potential clinical deterioration. This data can be combined with other key risk factors, such as anxiety, depression, and comorbidities, to provide a more comprehensive assessment of a patient's overall risk profile. Due to the significant inconsistency across studies and insufficient reporting within the review, it is challenging to draw any clear recommendations or conclusions regarding the findings on wearable accelerometry based upon this review.

Primary research in this area should aim to standardize both the exposed and unexposed groups, as well as establish consistent outcomes measured at multiple time points. Given the perceived but untested heterogeneity identified in this review, further investigation into potential moderating factors is recommended. Future systematic reviews in this area should aim to focus on a single type of study—either aetiology or test accuracy. While combining these two assessments in one review is possible, it requires two separate methodologies for critical appraisal and evidence synthesis. Separating them may also enhance the search strategy by allowing for more specific term sets tailored to the review being conducted. Future systematic reviews in this area should aim for a more comprehensive search strategy, as this review's focus on only two databases may have led to the omission of relevant studies. To

improve data synthesis, future studies should attempt a meta-analysis when there is sufficient data commonality. If the data proves too heterogeneous for meta-analysis, alternative methods such as vote counting based on the direction of association, reporting medians and quartile ranges, or using visualization techniques like Harvest Plots, Albatross Plots, or Strip Charts should be employed. Given the methodological limitations of these approaches, findings should be interpreted with caution unless more robust synthesis methods are feasible. Additionally, future research must emphasize the complete and consistent reporting of all key variables to allow for more accurate interpretation of the results.

CPD reflective questions

1. What are the key limitations of the systematic review presented in this commentary?
2. What advice can be given on lifestyle modifications and adherence to cardiac rehabilitation post-surgery to improve prognosis?
3. What are the other moderating factors of sudden cardiac death that should be considered in future research?

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