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LETTER

Critical appraisal concerning "Wearable cardioverter defibrillators for the prevention of sudden cardiac arrest: a health technology assessment and patient focus group study"

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Dear editor

We read with great interest the article "Wearable cardioverter defibrillators for the prevention of sudden cardiac arrest: a health technology assessment and patient focus group study" by Ettinger et al.[1] The authors conclude that wearable cardioverter defibrillators (WCDs) seem to be fairly safe in the short-to-medium term, but the quality of the available evidence is low. They also state that – according to their study inclusion criteria – they were not able to identify studies to assess the clinical effectiveness of the WCD. Given the importance of WCD for its target population and considering our clinical expertise, we see a particular need to clarify some points of this article.

The authors consider an implantable cardioverter defibrillator (ICD) as a WCD comparator. However, it is important to clarify that a WCD is not a substitute for an ICD, since it will only be temporarily worn. Treatment with a WCD may be considered for patients with a high risk of sudden cardiac death who are currently not candidates for an ICD.

Health Technology Assessments systematically aim to evaluate the effects of a technology on different health aspects, by collecting as much evidence as possible. This includes not only randomized controlled studies, but also studies with "weaker" designs should be considered and results should be discussed, taking into consideration their hierarchical importance in terms of internal validity.[2] Ettinger et al[1] decided to exclude retrospective studies, but this type of study design is not only the most often applied to evaluate the WCD's effects, it is also the one that embodies by far the largest number of patients, such as that of Epstein et al,[3] (N=8,678), Zishiri et al,[4] (N=4,149), and Chung et al,[5] (N=3,569). Simultaneously, the authors included case series involving very few patients (Duncker et al[6] [n=7 of N=12 with WCD] and Kondo et al[7] [N=24]), making it questionable why small one-armed case series are preferred to large retrospective studies with several thousand patients. The narrow inclusion criteria led to the nonidentification of publications for efficacy studies on the WCD.

The authors did not account for the heterogeneity in study designs (interventional single-arm study, prospective case series, and prospective registry studies), when

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reporting the research results: findings were summarized for N=2,000 (Kutyifa et al[8]) patients together with a case series including only N=12 patients (Duncker et al[6]). We suggest that the study results are presented in a way that takes into account differing study methodologies as well as differing study populations.

The authors claim to have conducted a focus group, although the requirements are not fulfilled. Only 5 participants, who had all undergone heart transplantation, were included, none with practical experience in using the WCD, none with an indication for a WCD, and none with knowledge regarding its technology. Thus, participants could not meaningfully comment on the possible use of the WCD. It is highly questionable how accurately the focus group participants were informed about the devices' functionalities: participants seem concerned that patients must decide when to receive a shock by pressing the WCD response buttons. This suggests a serious misunderstanding. It is crucial to highlight that patients can neither prevent an appropriate therapy nor trigger inappropriate shocks by pressing the WCD response buttons. Shocks must only be triggered when patients are in an unconscious state. We find it rather misleading that findings of what was apparently a single-group interview have been reported as if they were results of a qualitative study.

In our opinion, it is of high relevance to make the reader aware of the aforementioned limitations and how they influence the conclusions of the publication.

Disclosure

Ana Sofia Oliveira Gonçalves, Hanna Sydow, Tonio Schoenfelder, and Volker Eric Amelung received financial support from Zoll GmbH for the submitted work. The authors report no other conflicts of interest in this communication.

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Authors' reply

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Dear editor

We read the letter to the editor with regard to our published paper on "Wearable cardioverter defibrillators for the prevention of sudden cardiac arrest: a health technology assessment and patient focus group study" and gladly take the opportunity to appropriately address and clarify the issues that were raised.

Following the processes and procedures established by the European network for Health Technology Assessment (EUnetHTA), this HTA is a result of a cooperation between a wide range of European HTA institutes, experienced cardiologists, and methodological experts.

We would like to clarify that it is not the case that the wearable cardioverter defibrillator (WCD) is only to be used in situations when the use of an implantable cardioverter defibrillator (ICD) is not possible or as a bridge to an ICD, but it may also be used in situations where the two can be compared (ie, post myocardial infarction [MI]). MADIT II and VALIANT trials suggest that there is no mortality benefit from an ICD implantation immediately post MI. However, to prove a mortality benefit from WCD in that time period, a controlled trial needs to be conducted. It needs to be established and proven that WCD has an added therapeutic benefit (including clinical as well as quality of life benefits).[1] In addition, currently there is an ongoing, controlled, Zoll Medical Corporation-funded, VEST trial comparing WCD and conventional treatment immediately post MI; this can be interpreted as Zoll considering this patient group as potential candidates for the use of WCD. WCD is also used in patients who refuse ICD therapy, so it is important to see the relative effectiveness of a WCD in comparison to an ICD. This is appropriately defined in the Population–Intervention–Comparison–Outcome study design in our paper.

We recognize that the assessment of medical devices might be subject to specific challenges in comparison to pharmaceutical technologies. Randomized controlled trials (RCTs) are nonetheless the preferred study design for evaluation of effectiveness since they provide the most robust evidence. Nonrandomized intervention studies or observational studies might be included in the evaluation of effectiveness under certain conditions: no RCT was performed, no RCT was yet published, no RCT was feasible, or the observational data complemented RCTs.[2] In the case of WCD, we concluded that an RCT is possible (one is already ongoing), and the lack of required controlled trials was previously also acknowledged by other organizations eg, the American Heart Association[3] and the BlueCross BlueShield Association.[4] We also allowed for inclusion of nonrandomized controlled studies in the effectiveness domain in the attempt of providing the "best guess," rather than having no answer at all, for the relatively new technology of WCD.[5] For the evaluation of safety, we also took account of prospective observational studies since they could help identify other or less frequent types of risks.

It is important to state that the goal of HTA is not to collect as much evidence as possible but to collect as much high-quality evidence as possible for making a valid conclusion. The hierarchy of evidence shows systematic reviews and meta-analysis at the top, followed by RCTs, quasi-experimental studies (like nonrandomized controlled trials), observational studies (prospective, retrospective), and expert opinion at the bottom. Study designs at the bottom of the hierarchy are often more prone to various different kinds of bias (eg, selection bias, information bias, etc.) than the ones at the top. The Grading of Recommendations, Assessment, Development and Evaluation – GRADE – methodology shows that the quality of evidence from observational studies (especially retrospective studies) is usually low to very low.[6,7] As stated in our paper, we excluded retrospective studies since only prospective evidence can provide robust and reliable data in both effectiveness and safety domains. Moreover, we did not find any reason to go further down the hierarchy of the evidence. Furthermore, the inclusion of other study designs may mislead manufacturers into the false belief that RCTs and controlled studies are not required and,

therefore, not worthwhile to perform.[5] After consultation with a statistician, we decided to also include studies with a small sample size, in order to present all the existing prospective research on WCD.

We recognize the issue of heterogeneity in the studies that we have included in our assessment. Due to the great variety of indications, there also exists a wide range of study populations that are included in different study designs. We have presented the results in an extensive extraction table within our paper, which should enable the reader to differentiate the results of the different study designs appropriately.

The focus group participants definitely fulfilled our criteria to comment on the possible use of WCD since all patients who were selected would have qualified for the use of a WCD at one point in their disease history. As described in our paper, our intention was to evaluate perspectives of patients on areas of their cardiac disease and on the possible use of WCD therapy. We highly valued the questions from the patients with regard to device functionalities, which showed the importance of patient information and training in order to enable patient compliance. We used the terminology "qualitative study" since we followed the steps that are conducted in qualitative research: we framed the research question and the research design including a data collection method. The questions to the focus group participants were prepared based on available literature (as explained in our paper), and the results of the focus group were appropriately recorded, transcribed, and analyzed.[8]

We appreciate the critical review of our paper and hope to have clarified the issues raised for your readers.

Disclosure

The authors report no conflicts of interest in this communication.

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