Author’s response to reviews

Title: Prevention of sudden cardiac death in patients with chronic kidney disease.

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Author’s response to reviews: see over
Responses to Reviewers:

Reviewer 1:

This manuscript is a review reporting about risk factors and potential treatments of sudden cardiac death in the general population and patients with chronic kidney disease. The topic is of interest and relevant to clinicians.

Thank you for your opinion.

I have some comments and suggestions:

Abstract: “Treatment of arrhythmias in CKD is much more difficult than in patients with preserved renal function” – the statement appears twice, i.e. redundant. Therefore the last sentence can be deleted.

Thank you. It has been deleted.

Introduction: “CV diseases are the cause of about 50% of deaths in Europe. “ The references provided fort his statement are confusing; the reader does not see how these references (Polish Lipid association; Hypertension) support the statement and may be citations from citations. Please provide the original sources. Similarly, references 4 and 5 are misleading. For the main causes of CKD, please provide original sources, for example the data from USRDS or the ERA-EDTA registry.

Thank you. The suitable references have been cited.

The reference confusion continues throughout the paper, please carefully revise to enable the reader to follow your statements directly.

Thank you. We have checked the references very carefully and have updated/corrected them.

„Mortality of patients with CKD is mainly associated with ischemic heart disease, MI and sudden cardiac death“. In fact, according to the USRDS, MI and ischemic heart disease account for a relatively small proportion of deaths, up to 11%. In contrast, non-cardiovascular causes account for a much higher proportion of deaths, e.g. infectious deaths! So please be carefully with this statement, potentially confusing the reader and more specifically provide the percentages of deaths attributed to specific causes, e.g. with data from USRDS.

Thank you. We have corrected the sentence accordingly.

Search strategy: In general, most dialysis patients are found dead in bed without a clear hint that a (relatively) sudden death was sudden CARDIAC death. So it would be helpful to include the term „sudden death“ in the search strategy. It is often very difficult to determine whether a sudden death was of cardiac origin as not all studies have regular ECG and cardiac enzyme assessments available; however the data about sudden deaths accounting for one quarter of all deaths in dialysis patients represent clinical practice and are important not to be missed in a review.
Main text: The structure of the main text may be improved to enable the reader a clear overview. Currently, data from the general population and CKD and dialysis are mixed throughout the text. However, data from the general population cannot be readily applied to CKD patients. I suggest restructuring the text to provide information more clearly:

1) general population
   a. risk factors and knowledge about SCD
   b. treatment of SCD in the general population
2) CKD
   a. Different risk factors: description of current knowledge
   b. Identification of patients at risk of SCD
   c. Treatment of SCD in patients with CKD
3) Dialysis
   a. Dialysis associated risk factors
   b. Treatment and specific considerations, caveats in patients on dialysis

Thank you for your valuable suggestion. However the structure of the text was designed in order to emphasize the risk of arrhythmias/SCD and methods of prevention/therapy in CKD/dialysis patients, therefore it has been presented from the side of arrhythmia’s problems rather than kidney aspects. It is important because the knowledge among physicians on the management of arrhythmias in CKD patients is often very limited. Therefore we have decided to keep the current structure of the paper.

Please revise references 19 about hypokalemia in the context of hypertension as the main player for ventricular arrhythmias; it is not obvious for the reader. Also, there are many references “in press” which are not visible for the reader. As long as there are enough published data (visible for the reader), please use the published data.

Thank you. The reference No. 19 has been revised. There are only 4 references in press, which are important for the current text. They all have already had DOI numbers and are available online in the full text.

The statement about the findings from the 4D study are misleading. It is an assumption that patients found dead in bed may have suffered from obstructive sleep apnea, but there are no measures or objective data available. Refs 55-56 do not refer to the 4D study. In contrast the 4D study investigated and found many potential risk markers including Vitamin D status, glycemic control, left ventricular hypertrophy, absence of sinus rhythm, wasting, BNP to affect the risk of sudden cardiac death. These data are published and helpful to identify patients at risk of SCD. The data can be used to support the authors overview of current knowledge concerning risk stratification for SCD in dialysis patients.

Thank you. We have completed the text accordingly.
Responses to Reviewers:

Reviewer 2:

This is an extensive review of cardiovascular disease, in particular sudden cardiac death in CKD. The authors have thoroughly and critically reviewed the literature. The conclusions are correct and this article provides insights and reviews the evidence in the field nicely. There are some phrases and sentences which should be changed.

Thank you for your opinion.

Minor essential revisions:
1. This sentence appears in the abstract and conclusion. I don't like the term stimulating system. This is unclear for the non-expert. ‘The decision concerning implantation of a stimulating system in patients with CKD should be made on the basis of individual assessment of the physical and mental condition of the patient, his prognosis as well as the ability to cooperate.’ I also think that this sentence needs revised something simpler, perhaps to ‘The decision concerning implantation of a pacing system in patients with CKD should be made on the basis of individual assessment of the patient.’

Thank you. We have corrected the sentence accordingly.

2. ‘disorders of carbohydrate’ - this should be diabetes or dysglycemia
3. ‘Cardiac arrhythmias deteriorate during dialysis’ should be cardiac arrhythmias are exacerbated by dialysis
4. the statement about iron overload is incorrect. Iron overload was associated with arrhythmia in the paper they refer to but did not ‘cause’ conduction abnormalities. This statement should be corrected
5. ‘guidelines considering the indications for ICD implantation were worked out’ should be defined rather than worked out

Thank you. We have corrected the sentences accordingly.

6. table 1. I would like to see a bit more detail here. please add a column for type of population (HD, CKD with eGFR range), type of study (RCT, retrospective etc), n of participants, results, ref and further comments (complications etc).

Thank you. We have completed the table accordingly.