Author’s response to reviews

Title: Cardiac valve calcification and risk of cardiovascular or all-cause mortality in dialysis patients: A meta-analysis

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Reviewer reports:
Mohan Palla (Reviewer 1):

Results and Statistics:

Author mentioned the following in results section. The confidence interval of outcome does not include 1, which suggest that there is significant difference between the two groups. However, the P-value is >0.05 which suggest there is no significant difference between the two groups.

CVC was related to a greater risk of all-cause mortality (HR: 1.73; 95% CI: 1.42-2.11; I2 = 24.6%; P = 0.242, Fig. 2) in a fixed-effect model.

Reply: P=0.242 is the P value of heterogeneity test. For the effects of CVC on the all-cause mortality, the P value of HR was less than 0.001.

CVC was associated with 1.81-fold greater risk of cardiovascular mortality (HR: 2.81; 95% CI: 1.92-4.10; I2 = 48.5%; P = 0.084, Fig. 2) in a random effect model.

Reply: P=0.084 is the P value of heterogeneity test. For the effects of CVC on the cardiovascular mortality, the P value of HR was less than 0.001.

Subgroup analysis for the study region demonstrated that Asian patients with CVC had greater cardiovascular (HR: 3.255; 95%CI: 2.428-4.363; I2=0.0%, P=0.492) and all-cause mortality (HR: 1.761; 95%CI: 1.380-2.246; I2=0.0%,P=0.45).
Subgroup analysis was performed with the number of physicians analyzing echocardiographic recordings serving as a variable, which revealed significant decrease in the heterogeneity (all-cause mortality: two physicians: HR: 1.386; 95% CI: 1.064-1.805; I² = 0.0%; P = 0.762; one physician: HR: 2.320; 95% CI: 1.714-3.140; I² = 0.0%; P = 0.778; cardiovascular mortality: two physicians: HR: 1.890; 95% CI: 1.256-2.845; I² = 9.0%; P = 0.333; one physician: HR: 3.718; 95% CI: 2.624-5.268; I² = 0.0%; P = 0.691) (Table 2). "

After reading the above mentioned result data and looking further results data of meta-regression analysis, which mentions only p-value and says no significance is seen because P>0.1. Reader will be skeptical to trust this study whether the statistics were performed correctly.

In the Meta-regression analysis, region, follow up duration, dialysis modality, being a multicenter study or not, a randomized study or not, a blinded follow up or not served as variables to investigate the effects of CVC on the cardiovascular or all-cause mortality. No statistical differences were noticed (all P>0.1).

Reply: After checking with care, in the meta-analysis focusing on the effects of CVC on the cardiovascular mortality, region was a variable (P=0.064). However, as the sample size was small, region may be a source for the inter-study heterogeneity. The other data are OK.

In addition, Meta-regression analysis showed that there was a trend towards the number of physicians analyzing echocardiographic recordings being correlated to study outcomes (all-cause mortality: P=0.054; cardiovascular mortality: P=0.061).

Finally, with the help above mentioned points regarding the review of this manuscript, I would not accept this manuscript for publication.

Emmanuel Akintoye (Reviewer 2):

1. Since you approximated the HR from the data presented in the Varma R et al., this need to be stated in your stat section and the method used for approximation also needs to be cited in the manuscript

Reply: We have added the following information in the manuscript:

We approximated the HR from the data presented in the Varma R et al according to the method by Chen et al.

2. Decrease in interstudy heterogeneity after subgrouping is not a valid way of testing for sources of heterogeneity. Since your metaregression does not reveal any significant source of heterogeneity, the author should refrain from claiming that they found the source of heterogeneity throughout the manuscript. The authors should just report and discuss the report of the overall meta-analysis result and mention that there was no statistically significant difference between subgroups that were explored.
Reply: We have revised the manuscript as follows:

For the analysis of all-cause mortality, Meta-regression analysis revealed region, follow up duration, dialysis modality, being a multicenter study or not, a randomized study or not, a blinded follow up or not were not the major sources for the inter-study heterogeneity (all P>0.1). Besides, the number of physicians analyzing echocardiographic recordings may be a source for the heterogeneity (P=0.054). Single physician may increase the bias, which overestimated the effects of cardiac valve calcification on the all-cause mortality.

For the analysis of cardiovascular mortality, Meta-regression analysis revealed that region may be a source for the inter-study heterogeneity (P=0.064), however, follow up duration, dialysis modality, being a multicenter study or not, a randomized study or not, a blinded follow up or not were not the major sources for the inter-study heterogeneity (all P>0.1). Besides, the number of physicians analyzing echocardiographic recordings may be a source for the heterogeneity (P=0.061). Single physician may increase the bias, which overestimated the effects of cardiac valve calcification on the cardiovascular mortality.