Reviewer’s report

Title: Patterns and characteristics of cognitive functioning in older patients approaching end stage kidney disease, the COPE-study

Version: 0 Date: 02 Nov 2019

Reviewer: Stephen Sozia

Reviewer's report:

I read with interest the manuscript by van Deudekom and colleagues. The authors explore the cross-sectional prevalence of cognitive impairment and several domains in patients with advanced kidney disease not yet on dialysis. They then explore risk factors associated with cognitive impairment, including MRI findings.

Among the strengths of this study:

1) Enrollment of patients with advanced CKD (eGFR<20), before they started renal replacement therapy. This is an understudied population.

2) Extensive battery of cognitive tests

3) Inclusion of MRI

I have several concerns, both major and minor.

Major:

Comment 1: The authors rightly identify that a limitation of this study is the cross-sectional nature of the study. While beyond the scope of the study as described, I wonder whether they could examine at least one longitudinal relationship. Since the study was conducted 2014-2017, perhaps they could look at whether cognitive impairment is associated with risk of RRT or death (either separate or combined)? This would strengthen the argument that it is important to measure cognitive function in patients with advanced kidney disease.

Comment 2: The authors state the study is in "older patients reaching ESRD." These patients are not yet on dialysis or with a transplant, so they did not reach ESRD. I would change throughout to either "approaching ESKD" or "with advanced kidney disease but not yet on renal replacement therapy." Likewise, "ESRD" should be changed to "end stage kidney disease (ESKD)."

Minor:
Comment 3: As a cross-sectional study, the authors cannot use the word "determinants." This needs to be changed to "associated factors" or something similar.

Comment 4: There are multiple grammatical mistakes. These need to be changed throughout, and due to the number of errors, a native English speaker may need to read the manuscript in detail. Here are just some:

- page 2, line 37: Change "the" to "The"
- RTT needs to be changed to RRT throughout
- page 4, line 71: change "developing the kidney disease" to "developing kidney disease"
- page 5, line 91: change to "outpatient CLINIC between"
- page 5, line 113: change to "consisted OF the following tests: in ASSESSING"
- page 6, line 117: delete "the"
- page 6, line 131: delete "with tested"
- page 6, line 134: change to "function WAS assessed"
- page 6, line 135: change to "switching WAS tested"
- page 7, line 142: change to "WERE used"
- page 8, line 172: change to "MODELS, we"
- page 9, line 182 and 183 and Table 1: add "/1.73 m2"
- page 12, line 266: change to "In other"
- page 13, line 287-288: change to, ", AND white matter hyperintensities ARE considered"
- page 13, line 303: change to "-making is NECESSARY in the process"

Comment 5: Page 13-14, lines 298-305 (clinical implications) is a main crux of "why this study matters." Yet, the authors do not list this in the conclusions in the manuscript or abstract. Many of the conclusions in the abstract are redundant of what is in the results, and the authors should therefore considering reorganizing.

Overall, an interesting study. Thank you for the contribution.

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