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Depression and clinical outcomes in CKD: do anti-depressants play a role? (EQUAL STUDY)

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We read with interest the impressive study “*Associations between depressive symptoms and disease progression in older patients with chronic kidney disease: results of the EQUAL study*” by Eveleens Maarse [1]. This study examined the association between depression symptoms and clinical outcomes in older people (aged ≥ 65 years) with chronic kidney disease (eGFR ≤ 20 mL/min/1.73m²) and considered sex differences. The study found no association between baseline depressive symptoms and decline in eGFR. Furthermore, there was no association between depressive symptoms and time to dialysis initiation, or a combined outcome (dialysis initiation and all-cause mortality). However, in men, there was a significant association between the presence of depressive symptoms (as defined by a score of ≤ 70 on the Mental Health Inventory; MHI-5) and all cause-mortality, compared to those with no symptoms (adjusted hazard ratio=1.41, 95% CI, 1.03-1.93). Whilst the study has several strengths, including the large sample size, comprehensive data defining the sample, and rigorous approach to data analysis, we would like to comment on two aspects of the study, 1) measurement of the depressive symptoms and 2) the role of anti-depressants.

Firstly, it is important to note that the MHI-5 was used to measure depressive symptoms. Whilst the authors recognise that the use of other validated depression tools may have improved the robustness of the findings, the MHI-5 is best conceptualised as measure of psychological distress, particularly as two of the items relate to anxiety. This is particularly problematic when considered together with how item-level missingness was addressed (“*the mental health score was calculated when minimal three of five questions were answered*”). In addition, there are unique features of depression in older age that have measurement implications. Therefore, it is likely that the MHI-5 is not the optimal measure given the focus and sample here.

Secondly in the discussion, we were interested to read the suggestion that in men antidepressants may improve survival given the association between depressive symptoms and mortality (“*might it is possible that at least in men, antidepressant treatment might not only improve HRQOL, but could potentially improve survival*”). We are not convinced by this interpretation, particularly as evidence for the efficacy and safety of antidepressants in people with kidney disease is inconclusive [2-4]. An additional point in relation to the interpretation offered for the association between depression and mortality in men, may be reduced help-seeking among men. It would be interesting to know whether the rates of past depression differed by sex (although we acknowledge numbers are relatively small).

We note that anti-depressant data was available in 1032 of the sample (77.9%). Whilst the analyses are suitably adjusted for confounders, we are intrigued by the lack of adjustment for use of anti-depressants. Whilst we recognise the authors comment regarding the challenges surrounding the number of confounders in survival models and the issues of overadjustment, it would be interesting to know the findings of an exploratory set of sub-analyses that adjust for anti-depressant use. Furthermore, it would be important to know the crude and adjusted effect of anti-depressant use on all-cause mortality.

Our reason for this interest stems from the retrospective analysis (albeit in hemodialysis patients and not CKD), which found that patients who initiated selective serotonin reuptake inhibitors (SSRIs) with higher QT-prolonging potential (citalopram, escitalopram) had a significantly increased risk of sudden cardiac death (adjusted hazard ratio=1.18, 95% CI, 1.05 to 1.31), compared with patients who initiated SSRIs with lower QT-prolonging potential (fluoxetine, fluvoxamine, paroxetine, sertraline) [4]. We have previously raised the *possibility* that in *some* kidney patients, anti-depressants may be doing more harm than good and suggest that trials evaluating the selective withdrawal of anti-depressants in suitable patients may be appropriate to undertake [5].

CONFLICT OF INTEREST STATEMENT

None to declare.

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