ARB therapy may have been stopped for safety reasons, for nonusers. For a proportion of these participants, ACEI/angiotensin-converting agent (ESA) prescription would have been classified as nonusers, which would have biased our results toward favoring angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) use in patients with predialysis advanced chronic kidney disease, hypertension, and anemia. We performed additional analyses to address the question raised in the letter. However, their speculation is not evidenced by the further analysis from our cohort.

In Reply We appreciate the comments of Tomlinson and Smeth concerning that the differential misclassification would tend to bias our results toward favoring angiotensin-converting enzyme inhibitor or angiotensin receptor blocker (ACEI/ARB) use in patients with predialysis advanced chronic kidney disease, hypertension, and anemia. We performed additional analyses to address the question raised in the letter. However, their speculation is not evidenced by the further analysis from our cohort.
To minimize the possibility of misclassification of those who had taken and then, for safety reasons, ceased ACEI/ARB therapy prior to the first erythropoiesis-stimulating agent (ESA) prescription as nonusers, we redefined the nonusers (the referent group) as those who have not ever been treated with an ACEI/ARB up to 3 months and 6 months before commencing ESA therapy, respectively. Our data showed that the adjusted hazard ratios (95% CIs) of chronic dialysis in ACEI/ARB users were 0.94 (0.91-0.97) and 0.95 (0.92-0.98), respectively, and of dialysis or death, 0.94 (0.91-0.96) and 0.95 (0.92-0.98), respectively. Similar results could also be observed in the multivariable models further adjusted for the propensity score. The serial sensitivity analyses suggest our previously published data1 that the hazard ratio of long-term dialysis or death for the ACEI or ARB users was 0.94 compared with nonusers was an unbiased estimate. We acknowledge the “new user” design2 is a good method for pharmaco-epidemiological research. However, it may not be applicable to our study. In fact, the number of new ACEI or ARB users who had never used an ACEI or ARB at least 6 months prior to the first ESA prescription was only 1159 (8.2% of total ACEI or ARB users3) in our cohort. The sample size was too small to secure a sufficient statistical power for the study. Few patients with advanced chronic kidney disease were also recognized to improve their renal function by stopping ACEI or ARB therapy in our study,1 and it has been mentioned in the small-scale observational study by Ahmed et al.3 However, our study and the study by Ahmed et al3 are not comparable and have differences in case number (28 497 vs 52), median follow-up period (7 vs 30 months) and study outcomes (70.7% dialysis and 20.0% death vs 9.6% dialysis and 9.6% death). Obviously, the medical conditions in our cohort were much more complex, indicating the beneficial impact of stopping ACEI/ARB therapy observed in the study by Ahmed et al3 is not generalizable to our study population.

In conclusion, we are confident in the validity of our study, and we also believe the observational study using a representative national database is one of the most feasible study designs for the predialysis hypertensive patients with advanced CKD. The implication of our study is to reassure that the renoprotective effect of ACEI/ARB therapy is unwarranted for patients with advanced chronic kidney disease. The implication of our study is to reassure that the renoprotective effect of ACEI/ARB therapy is unwarranted for patients with advanced chronic kidney disease and “withhold—not to start” ACEI/ARB therapy is unwarranted for patients with advanced chronic kidney disease.

Conflict of Interest Disclosures: None reported.

Letters

Improving Medication Adherence and Helping Patients Make Lifestyle Changes

To the Editor In the study by Cohen et al, the authors report no improvement in cardiovascular risk factors when dietician or nurse-led education was provided to patients following acute coronary syndrome (ACS) compared with usual care. This study represents an alternative approach to standard educational interventions that could be provided through clinic-based cardiac rehabilitation (CR) following ACS. Another major factor to consider when modifying CR services is medication adherence, as improvements in this behavior may predict further success with other, more complex lifestyle changes. In general, an adequate focus on medication adherence has only been achieved by more intense CR programs requiring a longer schedule of visits.1 The study by Cohen et al appeared to have a sufficient level of intensity and patient contact such that a pharmacist could have been included in order to assess and promote medication adherence. As reported by Cohen et al, it appears that medication adherence in the study was high; however, they did not report the percentage of patients stopping all guideline-recommended medications. Only percentages for individual medications are presented, and this is an unusual and inadequate measurement for reporting medication adherence. Ho et al demonstrated that patients who stop using all medications by 1 month after discharge are 10% more likely to have died during the 12 months following ACS. Given the 12-month time frame of the study by Cohen et al and the multiple visits required in the intervention, we would have been interested to see more emphasis placed on additional measures of medication adherence and interventions seeking to improve it. We are currently conducting a study investigating the impact on medication adherence from pharmacist home visits following ACS to help address this issue.

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