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The authors' reply

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We appreciate the interest of Dr. Bolasco in our recent publication "Very low protein diet plus ketoacid analogs of essential amino acids supplement to retard chronic kidney disease progression" [1].

First, Dr. Bolasco has commented on "how we have calculated the glomerular filtration rate (GFR)." In the Materials and Methods section of our study, we indicated that all routine laboratory tests including assays for plasma levels of hemoglobin, albumin, potassium, creatinine, calcium, and phosphate and estimated GFR using the 2009 CKD-EPI creatinine equation and staging according to The Kidney Disease: Improving Global Outcomes (KDIGO) 2012 at baseline and at the end of the study were performed. However, there are limitations of using creatinine to estimate GFR, i.e., variations in creatinine production and secretion. Dietary changes or dietary supplements can alter creatinine production [2,3].

The second comment was "The assessment of residual renal function outcome and evaluate the patient's adherence to a high dose of ketoanalog plus very low protein diet (VLPD) for a long period of time by a strict education program and expert nutritionist should be documented." Ensuring compliance is a main target for effective nutritional intervention [4]. Several studies have indicated that about 40% to 50% of CKD patients follow a VLPD diet [5,6]. As a retrospective study using medical electronic databases, our study could have involved selection bias including compliance to diet and other nephroprotective therapies. Moreover, dietary protein intake was assessed

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using a three-day food diary, so we cannot exclude the possibility of erroneous reported intake. We have mentioned this in the limitation part of the Discussion.

The third comment addressed omission of the prescribed and introduced kilocalories power energy amount by a skilled renal dietician. We noted our study design as a retrospective study using an electronic medical database. All patients with CKD received standard care team treatment according to the medical history records and were followed in clinical practice in nephrology clinics every three months.

The fourth comment noted that exclusion of all patients suffering from acute, subacute, or chronic intestinal diseases would exacerbate the microbiota already severely hit by the uremic milieu and amino acids adsorption. Our study comprised only patients who participated in regular follow-up based on medical reports in our hospital electronic data base. We excluded patients with active malignancy; severe heart, lung, or liver disease; stroke; chronic infection; protein-energy wasting based on anthropometric data and laboratory data especially serum albumin less than 3.5 g/dL; pregnancy; or any immunological or inflammatory disorders.

Finally, assessment of the urea nitrogen appearance is easy and allows derivation of the protein catabolic rate to provide accurate information corresponding to true protein intake. Thank you for the suggestion on this point, but dietary protein intake was assessed using a three-day food diary in our retrospective study. We have indicated this point as a limitation of the study.

Further research to investigate VLPD plus ketoacidic analogs of essential amino acids supplementation with CKD progression is needed using larger randomized control trials and longer treatment periods.

Conflicts of interest

All authors have no conflicts of interest to declare.

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