Regarding: “Management of Glomerular Proteinuria: A Commentary”

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We read with interest the comprehensive review of the management of glomerular proteinuria by Wilmer et al. (1). We found the commentary to be well organized and very informative, citing many relevant reports. We wish to take this opportunity to correct a statement regarding cardioprotection with angiotensin-converting enzyme inhibitors (ACEI) and angiotensin receptor blockers (ARB).

Under ACEI Therapy (Level 1), page 3223 of the commentary, it is stated: “In the captopril trial, the combined endpoint of death or ESRD was reduced significantly. By contrast, such benefit was not observed in RENAAAL or the IDNT study.” We would like to clarify that the RENAAAL trial (2) clearly demonstrated statistically significant risk reductions with losartan for the combined endpoint of ESRD or death (P = 0.01) and the single endpoint of ESRD (P = 0.002). Regarding the IDNT trial, our review of the relevant published reports (3,4) does not reveal that the combined endpoint of death or ESRD was ever reported, although the individual components did not attain statistical significance with irbesartan compared with placebo.

Diabetes is the most common glomerular disease contributing to the increasing number of patients with ESRD, yet to our knowledge, no studies have been conducted with ACEI examining cardiovascular outcomes in pre-ESRD patients with type 2 diabetes. In the same section of the commentary, the authors state that it is “unclear whether ARB are cardioprotective to the level of ACEI.” We would like to call attention to the recently published VALIANT study (5), the results of which were not available at the time the commentary was written. VALIANT, a large clinical trial in post-myocardial infarction patients, clearly demonstrated that an ARB was found to offer similar cardiac protection to an ACEI. In the placebo-controlled studies of CHARM (similar in design to older placebo-controlled trials demonstrating the efficacy of ACEI in heart failure), an ARB significantly reduced cardiovascular mortality and morbidity (6,7). In the CHARM “added” trial (8), an ARB offered statistically significant additional protection from cardiovascular death or heart failure hospitalization when added to routine therapy including ACEI.

The authors did point out in the commentary that, although the HOPE and LIFE trials showed significant risk reductions with ramipril and losartan, respectively, on similar composite endpoints, stroke was the only significantly reduced component of the composite endpoint in the LIFE study. In this regard, it is important to note that HOPE compared ramipril with placebo (9), whereas LIFE compared losartan with an active comparator, atenolol (10). As mentioned above, diabetesthe most common glomerular disease contributing to the increasing number of patients with ESRD; it is therefore important to focus on the diabetic subgroups of the HOPE and LIFE studies (11,12). In the diabetic subgroup of HOPE (n = 3577), a reduced risk in the primary composite cardiovascular outcome of 25% (P < 0.001) was observed. In the LIFE diabetic cohort (n = 1195), the risk reduction was 24.5% (P = 0.031) in the primary composite cardiovascular outcome with losartan, and the component of cardiovascular mortality was similarly reduced by 37% (P = 0.028).

Although ACEI have been considered the treatment of choice for cardioprotection, emerging data suggest that similar cardioprotection is achieved with ARB.

References


