Editorial Perspective

Should Microalbuminuria Ever Be Considered as a Renal Endpoint in Any Clinical Trial?

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The arguments made by each debater are clear. One of the major difficulties of using microalbuminuria as either a surrogate or an endpoint in a clinical trial is the fluctuation that occurs so commonly, particularly in the normo- and microalbuminuric range. Moreover, the lack of sensitivity of the older assays for microalbumin may also add to the difficulty in interpreting the results. Thus, one needs large observational cohorts and a long follow-up period to establish relationships between microalbuminuric and patient-centered events. Recent studies by Mauer et al. [1] and Steinke et al. [2] fail to show that changes in microalbuminuria predict nephropathy progression. If anything, their observations indicate that mesangial matrix expansion, the hallmark pathological finding of diabetic nephropathy, is evident in patients with type 1 diabetes who have normoalbuminuria and are normotensive, yet demonstrate progressive loss of GFR despite lack of progression to albuminuria.

These observations are not in conflict with the longitudinal observations of the Joslin Group [3]. What may be even more important is the competing hazard of cardiovascular events observed in patients with microalbuminuria regardless of diabetes status [4–7]. This observation may bias the results of observational studies, and explain why some patients with diabetes without microalbuminuria develop end-stage renal disease, as they have

fewer competing cardiovascular events. Thus, although data indicate that we can alter the progression of normo- to microalbuminuria, micro- to macroalbuminuria, and macroalbuminuria to end-stage renal disease/death, we still lack a prospective trial to test the hypothesis that medical management of microalbuminuria affects patient-centered events independent of blood pressure reduction. Lastly, recent guideline statements by groups such as NICE [8] and regulatory agencies such as the Food and Drug Administration [9] have failed to accept microalbuminuria change as a surrogate for nephropathy progression.

Taken together, the following perspectives on this question are proposed. Microalbuminuria should be assessed in all people who have cardiovascular risk factors including any factor contributing to the metabolic syndrome, evidence of kidney disease or a family history of kidney disease. The purpose of this assessment would be to identify those with a risk marker associated with vascular inflammation and higher cardiovascular risk. Often microalbuminuria levels will fall with blood pressure reduction to levels <140/90 mm Hg obtained with any

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antihypertensive agent. This albuminuria reduction is particularly true when blockers of the renin-angiotensin system are used or blood pressure levels are reduced to less <130/80 mm Hg. Microalbuminuria levels progressively increasing in spite of good blood pressure control, lipid and glycemia management, suggests underlying inflammation of the vasculature and signifies the potential

for either development of kidney disease if the level extends beyond 300 mg/day, or higher cardiovascular risk, analogous to elevated high-sensitivity C-reactive protein.

Please note, this discussion centers only on microalbuminuria, as the presence of macroalbuminuria clearly indicates kidney disease and has a different prognostic significance for kidney outcomes.

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