COMMENTS AND RESPONSES

Comment on: Singer et al. Adiponectin and All-Cause Mortality in Elderly People With Type 2 Diabetes. Diabetes Care 2012; 35:1858–1863

JIAN-JUN LIU, MBBS, PHD[1]
SUBRAMANIA TAVINTHARAN, MBBS MRCP[2,3]
CHEE FANG SUM, MBBS, MRCP[2,3]
SU CHI LIM, MBBS, MRCP, PHD[2,3]

From the [1]Clinical Research Unit, Khoo Teck Puat Hospital, Republic of Singapore; the [2]Diabetes Centre, Khoo Teck Puat Hospital, Republic of Singapore; and the [3]Department of Medicine, Khoo Teck Puat Hospital, Republic of Singapore.
Corresponding author: Su Chi Lim, lim.su.chi@alexandrahealth.com.sg.
DOI: 10.2337/dc12-1814

The article in *Diabetes Care* by Singer et al. (1) elegantly showed that higher adiponectin was independently associated with increased all-cause mortality in elderly subjects with type 2 diabetes mellitus (T2DM). This was in contrary to the authors' hypothesis that higher adiponectin level would be associated with lower all-cause mortality given the anti-inflammation, antiatherogenic, and insulin-sensitizing properties of adiponectin. The authors alluded to the important association between elevated adiponectin and chronic kidney disease, which could have contributed to increased mortality. However, they conceded that the lack of direct measure of renal function was a limitation in their study (1).

In support of the observation of Singer et al., we would like to highlight two previous studies on both type 1 diabetes and T2DM that reported positive association between adiponectin, degree of albuminuria, and elevated serum creatinine. Looker et al. (2) demonstrated that in 1,069 Pima Indians T2DM, urinary albumin-to-creatinine ratio, and serum creatinine were positively correlated with adiponectin (Spearman $r = 0.43$, $P < 0.0001$ and $r = 0.37$, $P < 0.0001$, respectively). Saraheimo et al. (3) extended similar observation to 189 type 1 diabetic patients from the Finnish Diabetic Nephropathy Study. Adiponectin concentrations were higher in patients with macroalbuminuria (19.8 ± 12.0 mg/L) than in patients with microalbuminuria (13.1 ± 4.8 mg/L) or normoalbuminuria (11.8 ± 4.2 mg/L) ($P < 0.001$). The association was unaffected by adjustment for multiple confounders. Even though Singer et al. did not measure renal filtration function directly, subjects with higher mortality showed higher adiponectin and greater degree of albuminuria (Table 1 in ref. 1). The latter was expected to be positively associated with serum creatinine. Hence, it was conceivable that renal impairment (manifesting as albuminuria or the closely associated impaired renal filtration function, albeit unobserved in Singer et al.) might have contributed meaningfully to the increased mortality.

Notably, several large prospective studies also validated the positive relationship between adiponectin and mortality (4). Proposed mechanisms to explain elevated adiponectin in chronic kidney disease included resistance to adiponectin action, reduced renal clearance of adiponectin and compensatory increase in adiponectin as a "response to metabolic injury." Taken together, evolving body of evidence suggested that adiponectin might be a biomarker potentially useful in clinical practice to identify diabetic individuals at risk for adverse outcome.

Acknowledgments—No potential conflicts of interest relevant to this article were reported.

References

1. Singer JR, Palmas W, Teresi J, Weinstock R, Shea S, Luchsinger JA. Adiponectin and all-cause mortality in elderly people with type 2 diabetes. Diabetes Care 2012;35:1858–1863
2. Looker HC, Krakoff J, Funahashi T, et al. Adiponectin concentrations are influenced by renal function and diabetes duration in Pima Indians with type 2 diabetes. J Clin Endocrinol Metab 2004;89:4010–4017
3. Saraheimo M, Forsblom C, Fagerudd J, et al.; FinnDiane study group. Serum adiponectin is increased in type 1 diabetic patients with nephropathy. Diabetes Care 2005;28:1410–1414
4. Kronenberg F. Emerging risk factors and markers of chronic kidney disease progression. Nat Rev Nephrol 2009;5:677–689