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Should Renal Function Become an Important Factor in Cognitive Impairment and Cognitive Decline?

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Dear Editor,

During the past decades, a strong body of evidence has demonstrated that the incidence of dementia is high in patients with diabetes or high glucose levels [1, 2]. Since the late 1980s, vascular risk factors have been the major focus of numerous etiological studies for dementia [3]. The associations of several vascular risk factors (such as smoking, obesity, and alcohol consumption) with dementia have been supported in systematic reviews and quantified in meta-analyses of prospective studies [4]. However, not all studies have shown that diabetes affects the risk for dementia [5], although previous meta-analyses have yielded consistent results that diabetes is a risk factor for developing dementia [including Alzheimer’s disease (AD), vascular dementia (VaD), and any dementia] [1, 6, 7].

Recently, Crane et al. [2] reported that higher glucose levels may be a risk factor for dementia, even among persons without diabetes. This finding is consistent with the Hisayama study of Ohara et al. [8]. They suggested that diabetes is a significant risk factor for all-cause dementia, AD, and probably VaD. Meanwhile, 2-hour postload glucose levels, but not fasting plasma glucose levels, are closely associated with an increased risk of all-cause dementia, AD, and VaD. However, a prospective study by Thambisetty et al. [9] found that measures of glucose and insulin homeostasis are not associated with AD pathology and likely play a small role in AD pathogenesis.

In view of these inconsistent findings, it is imperative to explore the variable methodological quality of longitudinal studies. After reviewing the previous observational studies [10, 11], all are limited by the fact that the established and readily available confounder of renal function was not accounted for. In the USA, there are an estimated 7.5 million individuals with moderate renal disease [12]. It has been shown to be associated with an excess risk of incident dementia among persons in good-to-excellent health. As reported by Fukunishi et al. [13], there is a 2.5% annual incidence

rate of dementia among elderly individuals on dialysis, which is more than double the rate reported in the Japanese general population. Thus, the change in renal function is related to the change observed in global cognitive ability. In addition, elevated albuminuria levels are also associated with a faster decline in cognitive function.

In conclusion, this evidence leads us to state that it is necessary to recognize renal function as an important factor in cognitive impairment and cognitive decline.

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