Response to Letter Regarding Article, “Serum Alkaline Phosphatase and Phosphate in Cerebral Atherosclerosis and Functional Outcomes After Cerebral Infarction”

We appreciate the interest of Dr Tsuda in our recently published article.1 In our study, we showed that higher levels of alkaline phosphatase (ALP) were associated with a poor functional outcome after acute stroke, but phosphate was not. Dr Tsuda wanted to know whether the levels of ALP/phosphate were correlated with changes in bone mineral density (BMD) and serum vitamin D levels. Dr Tsuda’s questions were based on evidence that (1) there was an association between BMD and stroke; (2) lower serum 25-hydroxyvitamin D levels were associated with carotid atherosclerosis and fatal stroke; and (3) both ALP and phosphate might be related to calcium and bone metabolism. As Dr Tsuda has suggested, low BMD or vitamin D deficiency could be a link for poor clinical outcome in stroke patients with higher ALP.2,3 Bone tissue is a major source of ALP, and the level of ALP increases in osteoporosis or vitamin D deficiency. A growing number of epidemiological studies have demonstrated increased morbidity and mortality among patients who have low levels of vitamin D, which plays an essential role in bone mineralization.4 Recent studies suggested that parathyroid hormone, another important mediator for bone metabolism, also plays a role in cardiovascular disease.

Unfortunately, we do not have data for BMD and level of vitamin D in our study patients because of the limitation of the retrospective design. Although epidemiological studies suggested the presence of significant association between low vitamin D levels and cardiovascular diseases, a causal relationship has not been established. The low level of vitamin D may be a result of cardiovascular disease rather than the cause.4 Many clinical trials with vitamin D supplements failed to show significant beneficial effects.1 Furthermore, the administration of vitamin D plus calcium supplement might be harmful.5 In our study, the levels of serum phosphate, which might be another marker of vitamin D or parathyroid hormone, were associated neither with cerebral atherosclerosis nor with functional outcome. It should be emphasized that the beneficial effect of vitamin D supplement for stroke prevention has not been proven.

In this regard, there still exist issues to be resolved in this field. Serum ALP includes several isoenzymes derived from bone, liver, intestine, and so on. The measurement of bone-specific ALP will help to elucidate the association of vitamin D and BMD with ALP in stroke outcomes. There is a need for further studies to know what the exact mechanism of poor outcome in stroke patients with higher ALP or in those with vitamin D deficiency is, and who would be benefitted from vitamin D supplement.

Disclosures

None.

References

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