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## **25-Hydroxyvitamin D and Risk of Stroke: Possible Mediation by Statin Therapy?**

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## 25-Hydroxyvitamin D and Risk of Stroke: Possible Mediation by Statin Therapy?

To the Editor:

We read with interest a recent study by Pilz et al, which reported an association between low levels of 25-hydroxyvitamin D (25-OH D) and an increased risk of fatal stroke.<sup>1</sup> In their study, low circulating 25-OH D levels predicted fatal stroke, independent of traditional cerebrovascular risk factors, including age, sex, body mass index, lipid levels, smoking, hypertension and diabetes mellitus. Despite adjustment for low-density lipoprotein (LDL) and high-density lipoprotein (HDL) cholesterol levels, the prevalence of statin use is not reported. This is an important covariate to consider, because adjustment for lipid levels may not fully exclude residual confounding by differences between the groups in statin use. Because the subjects came from a cohort study comprised of patients referred to coronary angiography, statin use is likely to be prevalent among subjects.

As the authors discuss, various mechanisms have been proposed to explain the association between vitamin D deficiency and stroke. Vitamin D has been increasingly recognized for its pleiotropic effects, playing an important role in immunomodulation, cell proliferation, insulin action and calcium homeostasis.<sup>2</sup> Such pleiotropism is reminiscent of HMG CoA reductase (hydroxymethylglutaryl CoA reductase) inhibitors or statin medications. Statins have emerged in recent years as an important therapy in the primary and secondary prevention of stroke and cardiovascular diseases. However, similar to vitamin D, statin therapy may also have benefits in the management of diabetes mellitus, cancer and osteoporosis.<sup>3</sup> This raises an interesting question as to whether the 2 therapies are related mechanistically.

There is recent evidence that by inhibiting HMG-CoA reductase, statins can increase circulating 25-OH vitamin D levels.<sup>4</sup> Although the significance of such observation requires further

study, one may speculate that the beneficial therapeutic effects of statins may at least be partly related to an increase in circulating 25-OH D levels. As with statin use in ischemic heart disease,<sup>5</sup> the benefits of statins in stroke prevention are not completely explained by lipid-lowering alone.

In summary, it would be informative to examine the prevalence of statin use in this cohort of patients, because it may provide a possible explanation for the association between vitamin D deficiency and increased risk of fatal stroke. Future studies are required to investigate the significance and potential therapeutic benefits of increased circulating 25-OH D levels after statin therapy.

## Disclosures

None.

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