

# Is cobalamin deficiency associated with increased risk of all subtypes of postoperative delirium?

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## Dear editor

In a recent paper, Sevk et al used the single-hospital-based database to investigate whether cobalamin (vitamin B12) deficiency increased the risk of postoperative delirium in patients aged >60 years undergoing cardiac surgery with cardiopulmonary bypass.<sup>1</sup> In this retrospective study, the incidence of postoperative delirium in 100 patients with cobalamin deficiency was compared to 100 controls without cobalamin deficiency. Because the incidence of postoperative delirium in patients with cobalamin deficiency was significantly higher than that in the control group ( $P=0.017$ ), the authors concluded that cobalamin deficiency may be associated with increased risk of delirium in elderly patients undergoing cardiac surgery. This article has drawn the attention of anesthesiologists who are involved in prevention and treatment of postoperative delirium.

Apparently, the conclusion raises a plausible defect when all patients developing delirium were considered as one group. Delirium is a clinical diagnosis with a wide range of neuropsychiatric manifestations. The pathophysiology of delirium is not fully understood. Delirium is classified as hyperactive, hypoactive, or mixed forms.<sup>2</sup> Etiologic diagnosis of the hyperactive and hypoactive subtypes of delirium may be different.<sup>3</sup> Nutritional status has been suggested to play a role in predisposing or directly causing this acute cerebral dysfunction.<sup>4</sup> A previous study reported that vitamin B12 supplementation for 40 weeks reduced delirium in demented patients aged over 60 years with low serum vitamin B12 (<200 pmol/L).<sup>5</sup> In the model, a reasonable result was demonstrated because delirium is often reversible when the underlying cause of delirium is treated.<sup>4</sup> It is well-known that patients with cobalamin deficiency may develop a wide range of neuropsychiatric manifestations such as restless, aggressiveness, delirium, cognitive impairment, depression, hallucination, and mania. Based on the literal reports, agitated manifestations seem to be more likely.<sup>6-8</sup> Subtypes of delirium may be explained by different pathophysiologic mechanisms. Subgroup analysis by classifying delirious patients into hyperactive and hypoactive subtypes may be conducted to give the readers more information.

The cause of delirium is often multifactorial.<sup>4</sup> In patients with cobalamin deficiency, differences between delirium and nondelirium patients should be compared to identify additional risk factors such as chronic obstructive pulmonary disease and diabetes mellitus to help patients.<sup>9,10</sup> Furthermore, a binary or trinary model in patients with cobalamin deficiency<sup>11</sup> may be performed to assess the association between serum cobalamin levels and the incidence of delirium to support the conclusion with biological plausibility.<sup>4</sup>

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## Disclosure

The authors report no conflicts of interest in this communication.

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## Authors' reply

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## Dear editor

We read with great interest the letter to the editor written regarding our article 'Relationship between cobalamin deficiency and delirium in elderly patients undergoing cardiac surgery', and appreciate the opportunity to respond to the letter.<sup>1</sup>

In our study, we examined the relationship between cobalamin deficiency and delirium in elderly (>65 years old) patients undergoing coronary artery bypass grafting surgery. Multivariate analysis demonstrated that cobalamin deficiency

was independently associated with postoperative delirium in patients undergoing coronary artery bypass grafting. We agree that subgroup analysis regarding the types of delirium would give more information to the readers. Although, subgroup analysis by classifying delirious patients into hyperactive and hypoactive subtypes could be conducted in our study, this analysis would have a lower statistical power. Based on previous reports, hyperactive delirium rate is higher in patients with cobalamin deficiency.<sup>2-4</sup> However, delirium after cardiac surgery with cardiopulmonary bypass may be explained by different pathophysiologic mechanisms.

We believe that the association between cobalamin deficiency and the type of delirium can be examined in another study with a larger sample size.

## Disclosure

The authors report no conflicts of interest in this communication.

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