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Letter to the Editor

Before Vagus Nerve Stimulation is Recommended for the Treatment of Disorders of Consciousness, Evidence of its Efficacy is Required

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Letter to the Editor

We read with interest the article by Zuo *et al*. regarding a retrospective study on recovery from disorders of consciousness (DoC) in epilepsy patients treated with vagus nerve stimulation (VNS) using propensity score matching (PSM) [1]. The study found that the VNS group exhibited a greater increase in "Coma Recovery Scale-Revised" (CRS-R) scores compared to the control group and that responder status was associated with a baseline state of minimally conscious state and better seizure control [1]. The conclusion was that, compared to conservative treatment for DoC, VNS was associated with greater clinically significant improvement after one year and a larger longitudinal increase in CRS-R scores [1]. While the study is noteworthy, certain aspects warrant discussion.

A first point concerns the retrospective study design [1]. Retrospective designs have various drawbacks, such as lower data quality, missing data, the inability to establish causality (only associations can be identified), susceptibility to recall and selection bias, difficulties in controlling for confounding factors, and a generally lower level of evidence compared to prospective studies [2].

A second point is that PM) was employed [1]. PSM has several disadvantages [3]. Its primary drawback is that it balances only observed characteristics. If a hidden or unmeasured factor influences both treatment selection and the final outcome, bias (systematic error) persists [3]. Furthermore, the matching process may exclude subjects from the treatment or control groups for whom no suitable counterpart is found, thereby reducing statistical power [3]. Excluding unmatched subjects means the results may not be generalizable to the original total population [1]. If unsuitable variables are selected, non-linear relationships may be overlooked. Using an inappropriate functional form can actually increase bias and model dependence rather than reduce them [3]. Since PSM mimics a randomized trial rather than a fully blocked study design, random matching errors can occur, exacerbating covariate imbalance [3].

A third point is that the CRS-R scale has various disadvantages [4]. Its main drawback is that it relies exclusively on physical actions and behavior, potentially causing signs of consciousness to be missed. Additionally, patients with severe motor or communication impairments may perform poorly on physical tests even if they are mentally alert. Moreover, a single test may fail to detect signs of consciousness, leading to false-negative results. The score provides no information regarding the cause of the DoC or the prognosis for recovery, and it is also dependent on body position [4].

A fourth point is that the effect of VNS can depend heavily on the severity of the DoC. Therefore, it is important to know how many patients were in a coma, a vegetative state (unresponsive wakefulness syndrome), or a minimally conscious state, and how many suffered from post-traumatic confusion. Evidently, patients in a coma were not included. What was the reason for this?

After all, recovery from a DoC can depend heavily on the cause of the DoC [5]. The more severe the brain injury, the less likely it is that a DoC can be improved through therapy, including VNS. The causes of the DoC should be included in the analysis.

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