**RESPONSE TO LETTER** 

# Nerve Block Research in Diabetic Foot Ulcers: Concerns and Suggestions [Response to Letter]

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## Dear editor

We would like to thank Yaping Zhu and Weiling Song for their interest in our research and their valuable comments.<sup>1</sup>

As an anesthesiologist, I possess a profound comprehension of the significance and intricacy of nerve block anesthesia in the surgical treatment of diabetic foot ulcers. Factors like blood glucose regulation, the progression of diabetes, and the degree of neuropathy, as noted by Doctor Weiling Song, are critical for the efficacy of nerve block procedures. We have conducted a comparison and statistical analysis of blood glucose control in diabetes mellitus patients, specifically examining the presence of diabetic peripheral neuropathy, as presented in Table 1.

Furthermore, in the discussion part, we analyzed the possibility of processes influencing the elongation of nerve blocks in diabetes patients.<sup>2</sup> Research has revealed that the prevalence of peripheral neuropathy in diabetic foot patients was as high as 91.3%. The majority of patients were also diagnosed with poor blood glucose control (82.7%), anemia (86.7%), leukocytosis (84.6%), and malnutrition, which was defined by low fat (90.8%), and hypoalbuminemia (83.7%).<sup>3</sup> Diabetic peripheral neuropathy (DPN) is the predominant and devastating consequence of diabetes, significantly contributing to the formation of diabetic foot.<sup>4</sup> Long-term exposure to hyperglycemia can impact the microvascular system, ultimately resulting in various microvascular disorders, including diabetic nephropathy, retinopathy, neuropathy, and peripheral microvascular sclerosis or occlusion,<sup>5</sup> Furthermore, research has found that higher HbA1c levels resulting from chronic inadequate glycemic control can act as an independent risk factor for extended nerve block duration.<sup>6</sup>

In the patient follow-up, we observed that probable nerve injury was present in both diabetic and non-diabetic groups. In the diabetic foot cohort, all patients with suspected nerve damage reverted to their prior condition 72 hours following surgery. All patients were constantly monitored and recorded. In the non-diabetic group, one patient had complete sensory and motor recovery 36 hours after surgery, whereas the other had neurosensory numbness that lasted a week. All six patients with suspected nerve injury displayed numbress in the limbs after getting nerve block, and lower limb muscle strength of grade 2–3. Fortunately, all of the patients gradually returned to their pre-operation states. According to Hebl et al's retrospective study, patients with peripheral sensorimotor neuropathy or diabetic polyneuropathy prior to surgery had a 0.4% probability of having significant neurological impairment after getting nerve block anesthesia or analgesia.<sup>7</sup> In addition to the patient's clinical symptoms, the diagnosis of nerve injury can also be assessed by the following methods: Electrophysiological assessment of the nerve, nerve conduction studies, magnetic resonance neuroimaging (MRN),<sup>8</sup> neuro ultrasound<sup>9</sup> and nerve biopsy.<sup>10</sup> Electrophysiological examinations (EDX), including Electromyography (EMG) and Nerve Conduction examinations (NCS), are regarded as the gold standard for assessing nerve damage.<sup>11,12</sup> Electromyography (EMG) catches alterations in nerve resting and active potentials by inserting fine electrode needles into muscles, enabling the differentiation of lesions in nerves or muscles and the categorization of diseases into acute and chronic based on electrical data. TEDX offers valuable insights into neuroanatomical localization, nerve injury severity, and neurophysiology, as the amplitude of NCS is indicative of axon integrity. When the lesion affects nerve axons, the amplitude of the nerve response to electrical stimulation decreases or vanishes.<sup>13</sup> However, nerve

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variables	N-DM (n=48)	DM (n=83)	Р
Age (yr)	60(45,71)	65(55,69)	0.132
Man/women n,(%)	32 (66.7%)/16 (33.3%)	64 (77.1)/19 (22.9)	0.193
Body mass index, kg/m²	22(19.5,24.3)	22.1(20.55,25.1)	0.177
Smoking, n (%)	25 (52.1%)	48 (57.8%)	0.523
Dringking, n (%)	24 (50.0%)	49 (59.0%)	0.316
Education, n (%)			0.611
Junior high school	18 (37.5%)	30 (36.1%)	
Primary school	7 (14.6%)	8 (9.6%)	
High school or above	12 (25.0%)	29 (34.9%)	
Illiteracy	11 (22.9%)	16 (19.3%)	
Residence			0.138
City	14 (29.2%)	35 (42.2%)	
Rural	34 (70.8%)	48 (57.8%)	
Disabled	13 (27.1%)	61 (73.5%)*	0.001
ASA states (I/II/III/IV)	5/19/23/1	0/16/63*/4	<0.001
Diabetes duration (yr)	NA	11.(5.2, 15.7)	
Diabetes treatment Insulin/Oral	NA	27(32.5%)/12(14.4%)	
Not controlled	NA	44(53%)	
Comorbid disease by system			
Hypertension, n (%)	12 (25%)	42 (50.6%)*	0.04
Coronary disease, n (%)	6 (12.5%)	23 (27.7%)*	0.043
Coronary arteriosclerosis	17 (35.4%)	60 (72.3%)*	<0.001
Lung disease, n (%)	33 (68.8%)	71 (85.5%)*	0.022
Stroke, n (%)	0 (0.0%)	19 (22.9%)*	<0.001
Nephropathy	0 (0.0%)	83 (100%)*	<0.001
MNSI score	2 (1, 3)	5(4, 6)*	<0.001
TCSS score	4 (2, 5)	4 (  ,  5)*	<0.001
Tramadol	22 (45.8%)	24 (28.9%)	0.051
Nerve injury	I (2.1%)	4(4.8%)	0.971
Length of hospital stay(d)	8.5 (6, 11)	(7,  6)*	0.33
Hospital costs(US)	4541 (3697, 8071)	6166(4251, 9122)	0.125

**Table I** Patient Demographics and Baseline Variables, Data are Mean (SD), Median (25th–75th), or Number (%).\*P,0.05 Vs the N-DM Group

electrophysiological testing and nerve biopsy are invasive procedures that may induce distress in patients, as well as a sensation of pain that may result in intolerance in certain patients. We were unable to determine the type and extent of nerve damage since the patient declined to have a neurological function test conducted throughout the follow-up. The exact characteristics of the nerve injury's nature and severity were not elaborated upon; however, the recommendations are really helpful, and we will remain attentive to them in future studies. The potential of neurotoxicity is a major concern for us while executing nerve blocks, especially in diabetic patients. Diabetic patients who have neuropathy may have a lower nerve tolerance to local anesthetics and are more vulnerable to nerve injury. Our study showed that, while there were fewer occurrences of nerve damage, it also reminded us to be more cautious in clinical practice. We will enhance nerve damage monitoring and assessment, record the types, degree, and clinical signs of injury (eg, paresthesia, motor dysfunction), and explore its potential causes and mechanisms. The discussion portion of this article addressed the potential neurotoxicity of local anesthetics in diabetes patients. The mechanism behind the extended length of nerve block and the heightened risk of neurotoxicity in diabetes patients remains ambiguous, and we anticipate future highquality animal and clinical investigations to clarify this mechanism.

The addition of patient-reported outcome measures, such as pain levels, functional recovery, and quality of life, would allow us to better examine the effectiveness of nerve blocks in diabetic foot ulcer patients. These indicators not only reflect patients' subjective feelings and quality of life, but they also act as a significant reference for assessing the effectiveness of clinical treatments. Furthermore, long-term follow-up studies will allow us to better understand the longterm influence of nerve block on nerve function recovery and the development of chronic neuropathic pain in patients, providing a foundation for therapeutic treatment adjustments and optimization. While the VAS scores were not documented in this study, the administration of tramadol during the perioperative phase for both groups was noted, and tramadol analgesia can also indicate patients' postoperative pain levels and their need for pain treatment. Our team's study and tracking of surgical and anesthetic procedures for diabetic foot patients have remained continuous. Additionally, the ED-5Q Quality of Life Assessment Scale was utilized to assess the patient's quality of life during the follow-up period. The EQ-5D comprises mainly two parts: the Descriptive System and the EQ-5D Visual Analogue Scale. The EO-5D life scale has been widely utilized in clinical trials and demographic studies, and it has proven to have strong reliability, validity, and sensitivity in a number of illness sectors and populations.<sup>14</sup> However, we excluded the patient's postoperative recovery quality index from the data statistics because the primary outcomes of this paper are the duration of the nerve block and the onset of time. In future research, we will perform long-term follow-up and document relevant symbols.

General anesthesia is a prevalent alternative to nerve-block anesthesia and is one of the earliest kinds of anesthesia used in clinical practice. With the introduction of new medications and anesthetic monitor technology, general anesthesia is now commonly utilized in outpatient clinics, wards, operating rooms, and for a variety of examinations and operations. However, general anesthesia carries its own set of potential risks in addition to allowing comfortable medical progress. General anesthesia can increase the danger of hemodynamic variations, and the administration of excessive fluids to rectify these fluctuations may heighten the risk of postoperative pulmonary problems. Moreover, intraoperative hypotension correlated with postoperative acute kidney impairment (AKI).<sup>15</sup> General anesthetic agents are related to intraoperative hypotension due to their circulatory sedative effects.<sup>16</sup> Compared with general anesthesia, regional block anesthesia can minimize the prevalence of postoperative psychosis in the older population.<sup>17</sup>

Exploring alternate anesthetics and adjuvant therapies to reduce the risk of neurotoxicity is a noble goal that aligns with our mission of improving patient safety and anesthesia quality. In current research and clinical practice, achieving this goal may be challenging. The development of new narcotic drugs or the optimization of existing drugs requires indepth scientific research, including the safety, efficacy, pharmacokinetics, and pharmacodynamic properties of the drugs. New drugs or treatments need to go through rigorous clinical trials to verify their safety and effectiveness, which can take significant time and resources. In addition, developing new drugs or treatments can involve high costs, which may limit the feasibility of some alternatives. Despite these challenges, we remain open to your suggestions and will continue to explore and research new narcotic drugs and treatments to the extent possible. We believe that through continued research and innovation, we can gradually overcome these barriers and provide safer and more effective anesthesia and analgesia regimens for patients.

# Disclosure

The authors declare no conflicts of interest in this communication.

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