Diabetes, Metabolic Syndrome and Obesity

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CLINICAL TRIAL REPORT

Comparison of the Effects of Combined Femoral and Sciatic Nerves Block versus General Anesthesia on Hemodynamic Stability and Postoperative Complication in Patients with Diabetic Foot: A Prospective, Double-Blind and Randomized Controlled Trial

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Background: Perioperative anesthetic management of patients with diabetic foot undergoing surgical treatment is challenging due to their poor cardiovascular health status. According to previous literature, general anesthesia and peripheral nerve block have their own advantages and disadvantages for such patients. We reported the effect of these two anesthesia techniques on perioperative hemodynamics and prognosis in these patients.
Methods: This study employed a prospective randomized controlled design, where patients meeting the inclusion criteria were assigned to two groups: the general anesthesia group (GA group) and the peripheral nerve block group (PNB group). The primary outcomes were the differences in intraoperative hemodynamic stability and the incidence of postoperative complications between the two groups. The second outcomes were postoperative numerical rating scale scores, analgesic drug remedies, postoperative sleep conditions monitored by sleep bracelets and health status assessed by EQ-5D-5 L scores.
Results: One hundred and nine subjects were enrolled in this study, including 54 in the GA group and 55 in the PNB group. The baseline parameters of the two groups were comparable. The GA group exhibited a significantly higher incidence of hypotension, and Colloid intake and total fluid intake were significantly higher in the GA group than in the PNB group. Additionally, a larger proportion of patients in the GA group. The scores of postoperative pain during the 48 hours after surgery were significantly higher, and more patients needed tramadol for postoperative analgesia during the 24 h after surgery in the GA group than in the PNB group. Patients in the PNB group slept better, first feeding time, earlier out-of-bed activity and earlier discharge from the hospital, compared to the GA group. However, there was no obvious difference in postoperative complications between the two groups except pharyngeal pain.
Conclusion: Peripheral nerve block is a better option in patients with diabetes undergoing elective below-knee surgery than general anesthesia.
Keywords: diabetic foot, general anesthesia, peripheral nerve block, hemodynamic, postoperative pain, postoperative complication

Introduction

Diabetes affects half a billion people worldwide, and the global incidence has risen rapidly over the past 20 years, with studies suggesting that the number is projected to increase by 25% in 2030 and 51% in 2045.[1] Diabetic foot (DF), one of

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the clinical manifestations of diabetic neuropathy, and diabetic neuropathy, peripheral vascular disease and other complex pathological processes may evolve into diabetic foot complications such as DF ulcer, Charcot osteoarthropathy and subsequent ulceration and amputation.[2] Diabetic foot complications are the leading cause of hospitalization and amputation in patients with diabetes, with a prevalence of up to 25%.[3] Patients with DF complicated with gangrene and infection may need surgeries to control the further spread of infection. Common intervention measures include wound incision and debridement, wound debridement combined with vacuum sealing drainage (VSD) negative pressure attraction, transverse tibial bone transport or amputation.[4–6] However, most of these patients are elderly and often suffer from other systemic diseases, such as ischemic heart disease, renal insufficiency, and hypoxemia.[7–10] In addition, approximately 30 to 40% of DF patients undergo a second operation after one debridement or amputation. Therefore, maintaining the hemodynamic stability of patients during the perioperative period and ensuring a smooth operation while also ensuring adequate anesthetic and analgesic effects is a great challenge for anesthesiologists.

Peripheral nerve block can not only provide a good anesthetic effect as a simple anesthesia method but can also be combined with other anesthesia methods to reduce postoperative pain.[11–13] The noninvasive, real-time visualization and reproducibility of ultrasound provide accurate data and abundant means for clinical preanesthesia evaluation, intraoperative monitoring and pain treatment. With ultrasound guidance, the efficacy and safety of nerve block have been greatly improved.[14–16] Ultrasound-guided femoral nerve block combined with sciatic nerve block offers a new anesthetic option for lower extremity surgery, which is suitable for patients with poor general condition. It can not only provide effective surgical anesthesia and ensure adequate postoperative pain control but also have less influence on hemodynamic stability, minimizing the risk for urinary retention in these studies.[13,17] In cases where the surgical intervention extends beyond the midfoot or involves the use of a thigh tourniquet, the utilization of general or spinal anesthesia becomes essential, and ultrasound-guided femoral nerve block also has the risk of local anesthetic poisoning and nerve damage.

General anesthesia has the advantages of safety, reliability and controllability and is the most widely used in clinical practice. Nevertheless, general anesthesia may affect the physiological function and internal environment of patients and is more likely to cause complications such as circulatory fluctuations, delayed postoperative recovery, cognitive dysfunction and pneumonia during the perioperative period.[18–20] In addition, there are many adverse reactions caused by general anesthetics, especially nausea and vomiting, constipation, hypotension, respiratory depression and hyperalgesia caused by opioids.[21–24]

There are few data currently available from published studies that compared peripheral nerve blocks with general anesthesia for patients who underwent DF surgery. To compare the effects of the above two different anesthesia methods on the perioperative physiological function of patients, this study intends to prospectively analyze the impact of general anesthesia versus peripheral nerve block anesthesia on perioperative hemodynamic changes and the prognosis of diabetic patients to evaluate the beneficial and detrimental effects of the two different anesthesia methods on patients.

Materials and Methods

Study Population

This was a prospective, double-blind and randomized controlled trial. This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Identifier: 2020-015). This study was registered in the Chinese Clinical Trial Registry on June 7, 2020 (ChiCTR2000033621) and and with the Helsinki Declaration of 1964 and later versions.

We analyzed a total of 109 patients with diabetes treated with elective below-knee surgery in the First Affiliated Hospital of Guangxi Medical University from May 2020 to January 2022. After obtaining consent from eligible patients, individuals who fulfilled the predetermined selection criteria were recruited. The inclusion criteria were as follows: (1) patients with diabetes who were scheduled for elective below-knee surgery, such as tibial transverse bone transfer (TTT), debridement and toe amputation; (2) age >18 years; (3) American Society of Anesthesiologists (ASA) grade II–IV; (4) no paralysis or lower limb nerve injury before operation; (5) no previous history of local anesthetic drug allergy; and (6) patients who had not participated in other clinical trials in the last 4 weeks. The exclusion criteria were as follows: (1) patients who explicitly refused to participate in the experiment before surgery or were asked to quit during the experiment; (2) patients who withdrew from the study; (3) patients who experienced severe anaphylaxis or excessive blood loss during the perioperative period; (4) emergency patients; (5) patients who had lower extremity surgery within a month; (6) patients requiring a second operation 3 days after surgery; and (7) persistent hypoxemia during the operation (SpO_2<90% longer than 5 minutes) and serious cardiovascular events (malignant arrhythmias, acute myocardial ischemia, etc).

Criteria of Diabetic Foot Surgery

Infection: If there is an uncontrolled or deep-seated infection in the foot that does not respond to antibiotic therapy and wound care, surgical debridement (removal of infected tissue) or even amputation might be necessary to prevent the spread of infection.

Non-healing Ulcers: Diabetic foot ulcers that do not show signs of healing after several weeks of appropriate wound care, offloading pressure, and management of underlying factors (like blood sugar control) may require surgical intervention. Surgery could involve debridement, skin or tissue grafts, or revascularization procedures to improve blood flow.

Peripheral Artery Disease (PAD): Poor blood flow to the feet due to PAD can impede healing and increase the risk of amputation. Revascularization procedures like angioplasty or bypass surgery might be recommended to restore blood flow before or in conjunction with other foot surgeries.

Neuropathic Deformities: Neuropathy, or nerve damage, can lead to foot deformities such as Charcot foot, hammer-toes, or bunions. If these deformities cause persistent pain, difficulty wearing shoes, or lead to ulcer formation, corrective surgery may be necessary.

Osteomyelitis: Infection of the bone (osteomyelitis) is a serious complication in diabetic patients and often necessitates surgical intervention, including debridement or even partial bone resection, followed by appropriate antibiotics.

Risk Assessment: Surgeons will evaluate the patient's overall health status, including their cardiovascular health, kidney function, and ability to heal, to determine if they can tolerate surgery and minimize postoperative risks.

Patient Compliance: The patient's willingness and ability to comply with post-operative care instructions, wound care, and diabetes management are crucial factors. Non-compliance can lead to surgery failure and recurrent problems.

Quality of Life Considerations: The impact of the foot condition on the patient's daily activities and mental well-being is also taken into account. Surgery may be recommended to alleviate chronic pain or improve mobility.

It's important to note that surgery is a last resort and every effort should be made to manage diabetic foot complications conservatively first. A multidisciplinary team approach involving endocrinologists, podiatrists, vascular surgeons, and wound care specialists is essential in determining the best course of action for each individual case.

Study Design

All 120 patients were randomly divided into the GA group and the PNB group according to a 1:1 (n=60 in each group) allocation by a random number table. In the GA group, target-controlled infusion (TCI) of remifentanil and propofol was performed. The initial target concentrations of propofol and remifentanil were set to 2.0 μg/mL and 2.0 ng/mL, respectively, and were fine-tuned according to the change in bispectral index (BIS). A single injection of cis-atracurium and fentanyl on demand. To maintain the pressure of end-tidal carbon dioxide ($P_{ET}CO_2$) at 35–45 mmHg, the patients received mechanical ventilation with an inspired oxygen concentration (F_IO2) of 60%. The ventilation was administered at a respiratory rate of 10–15 breaths per minute, using a tidal volume of 6–8 mL/kg of the ideal body weight. Additionally, a positive end-expiratory pressure (PEEP) of 5–10 cm H_2O was applied, along with an inspiratory-to-expiratory time ratio of 1:2. All patients received conventional inhalation anesthesia using sevoflurane at a dosage adjusted to 0.6–1.0 minimal alveolar concentration according to their age. Patients were also administered remifentanil at a concentration of 1–4 ng/mL. Throughout the procedure, the BIS monitor (Aspect A-2000 model, Aspect Medical System Inc., USA) was used to maintain a targeted value between 40 and 60.

An experienced anesthesiologist conducted femoral combined sciatic nerve block in the PNB group. All patients were fixed in a supine position and fully exposed to the intended operation area. A Sonosite M-Turbo ultrasound unit with an 80-mm, 22-gauge block needle and a 7.5-MHz linear probe was employed, combined with a Belan plexus stimulator used for nerve localization. Wear sterile gloves after ultrasonic localization of the nerve and routine disinfection towel. The neurostimulator was connected and opened, the ultrasonic probe was fixed on the predetermined plane, and the injection site was subjected to local infiltration anesthesia with 2 mL of 2% lidocaine. After the local anesthetic took effect, an 80 mm gauge nerve stimulation needle was used to perform in-plane injection technology. The stimulation current intensity of the initial neural stimulator was 1.0 mA, the pulse duration was 0.1 ms, and the frequency was 2 Hz. When the nerve stimulation needle is close to the nerve, it will induce contraction of the relevant muscle and then reduce the current of the nerve stimulation instrument to 0.3~0.5 mA. If convulsions of the target muscle can still be seen and there is no intranerve or intravascular injection of the stimulation needle observed under ultrasound, the injection depth is appropriate. After determining the location of the needle tip, the assistant was asked to slowly inject 20 mL of local 0.5% ropivacaine and draw back before injecting the local anesthetic to ensure that the needle tip was not in the blood vessel again to prevent intravascular local anesthetic injection. Following the completion of the procedure, the sensory and motor blocks were evaluated. Sensory function was examined by testing the patient's response to a pinprick stimulus on both the plantar and dorsum surfaces of the foot. Motor function was evaluated by measuring the power of ankle movement. Surgery commenced only after confirming the presence of complete sensory and motor blocks, ensuring adequate anesthesia for the intended surgical intervention.

Data Collection

The following preoperative data were recorded and analyzed: demographic information and preexisting conditions such as hypertension, chronic kidney disease, diabetic neuropathy (DNP), diabetic retinopathy (DR), cerebrovascular accident, or coronary artery occlusive disease. Preoperative laboratory data, including hemoglobin and albumin levels, indicators of renal function, fasting blood glucose (FBG) and 2 hours postmeal blood glucose (PBG), were recorded. The Frail Scale assesses the patient's preoperative state and degree of weakness, the EQ-5D-5 L score assesses patients' quality of life, and self-rated data provided by each respondent can be applied to quantitatively assess health outcomes. The Huawei 4e Standard sports bracelet was used to monitor patients' sleep conditions. Moreover, the use of hypoglycemic drugs before surgery was recorded. The intraoperative data were the operation duration; data on diastolic blood pressure (DBP), systolic blood pressure (SBP), heart rate (HR), and mean blood pressure (MBP) were recorded at five time points. The five time points were at the moment of patient arrival in the operating room (T_0), at the time of induction intubation/nerve block puncture (T_1), at the beginning of the operation (T_2), 10 min after the operation (T_3), and at the end of the operation (T_4). During the surgical procedure, several parameters were documented, including the intraoperative fluid administered, volume of blood loss, dose of ephedrine administered, and the need for blood transfusion. Postoperatively, pain levels were assessed using the numeric rating scale (NRS), where a score of 0 indicated no pain at all, and a score of 10 represented the worst imaginable pain. Patients were informed to request additional analgesics if their pain score reached or exceeded 4, ensuring appropriate pain management and intervention based on individual pain levels. Tramadol was administered intravenously in 50 mg increments if the pain score exceeded 4 or the patient requested additional analgesics, and tramadol dosage was evaluated 48 hours following surgery in the two groups. The following post-operative information was analyzed: the first time to eat and get out of bed, duration of postoperative hospitalization, number of patients admitted to the intensive care unit (ICU), and postoperative complications such as sore throat, bleeding, nausea and vomiting, pneumonia, delirium, heart failure, and nerve damage. Furthermore, we assessed the in-hospital mortality rate after surgery.

Statistical Analysis and Sample Size Calculation

R 4.1.2 software was used for data analysis, in which the mice package was used for missing value interpolation and the remaining statistical analysis was performed using the stats package. Continuous variables are presented as the means ± standard deviations or median and interquartile range values, while dichotomous variables are presented as the number of patients (percentage). The analysis of parametric data was performed using the independent *t*-test, and dichotomous variables were analyzed using the chi-square test. For the comparison of repeated measurements such as EQ-5D-5 L score and sleep status between the two groups, the generalized estimation equation was used to calculate the time and main effect between the two groups. A P value of <0.05 was deemed significant. GraphPad Prism 7 software was used for statistical mapping. It has been reported[25] that 26% of diabetic patients were transferred to the ICU for lower extremity surgery under general anesthesia, and 4% were transferred to peripheral nerve blocks. The alpha level was predetermined as 0.05, the confidence interval used was two-sided, and the beta level was set at 0.10. At least 47 patients were needed in each group. Taking into account the possible loss of follow-up during the study, a total of 120 cases were selected as the designated sample size.

Result

We prospectively studied data from 120 patients who underwent elective below-knee surgery in the First Affiliated Hospital of Guangxi Medical University between May 2020 and January 2022. There were 3 patients who abandoned surgical treatment, 2 patients who refused to continue to participate in the experiment, 3 patients who needed a second operation 3 days after surgery, and 3 patients who had serious cardiovascular events. The remaining 109 patients were included in the final analysis (Figure 1). There were no obvious differences in preoperative baseline features between the two groups (Table 1).

Hemodynamic Variables

The intraoperative variables are listed in Table 2. The GA group exhibited a higher incidence of hypotension, with 29 patients experiencing hypotension compared to only 5 patients in the PNB group ($p<0.001$). Moreover, the GA group also had a significantly greater number of patients who necessitated ephedrine administration, with 29 patients requiring it compared to

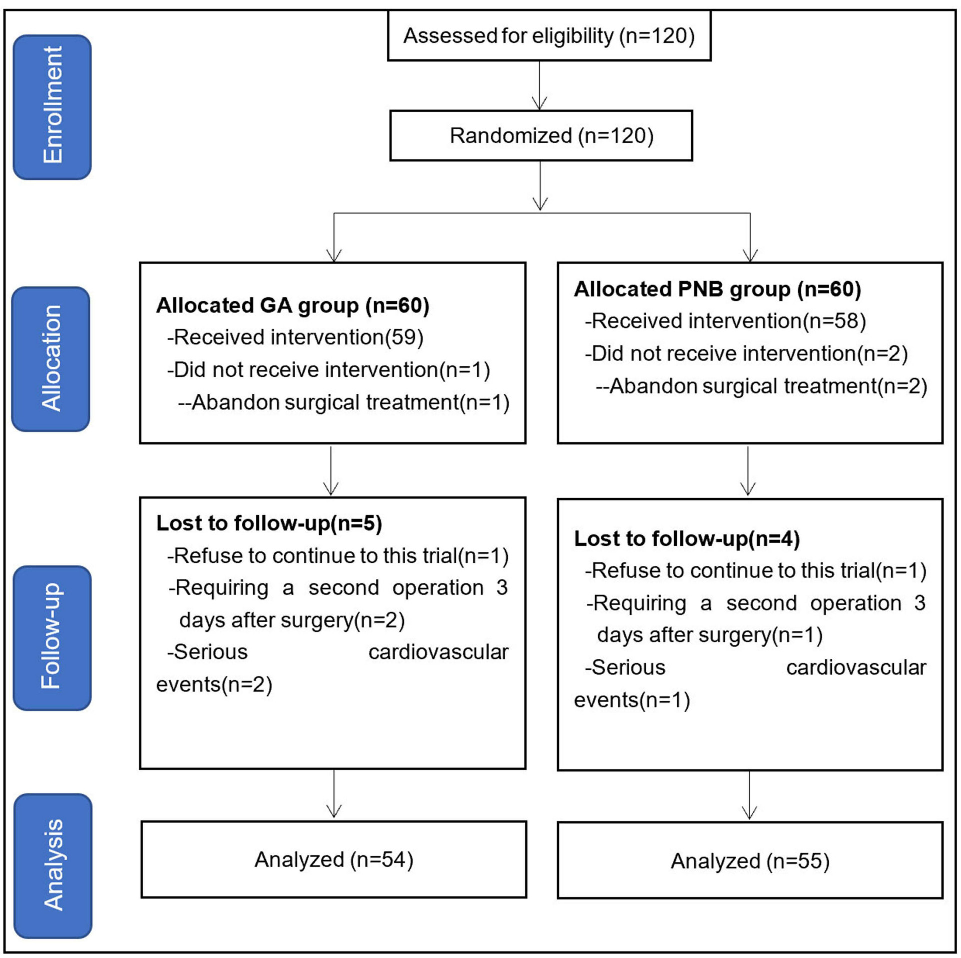

Figure 1 Consort flow of clinical procedures.
Abbreviations: GA, general anesthesia; PNB, peripheral nerve block.

Table 1 Characteristics of Patients in Each Group

	GA (n=54)	PNB (n=55)	*P value*
Age	59.87±9.14	61.32±10.23	0.745
Gender (M/F)	43/11	45/10	0.768
BMI	22.74±3.19	22.81±3.37	0.935
Smoking (Y/N)	24/30	26/29	0.231
Drinking (Y/N)	23/31	25/30	0.118
Disabled (Y/N)	42/12	44/11	0.368
Loss of labor (Y/N)	45/9	43/12	0.343
ASA-PS			0.571
II	7 (12.9%)	8 (14.5%)	
III	44 (81.5%)	43 (78.2%)	
IV	3 (5.5%)	4 (7.3%)	
Hypertension	23 (42.6%)	26 (47.3%)	0.547
IHD	15 (27.8%)	13 (23.6%)	0.458
CI	11 (20.4%)	10 (18.2%)	0.601
DN	23 (42.6%)	26 (47.3%)	0.269
Uremia	4 (7.4%)	6 (10.9%)	0.271
DR	14 (25.9%)	16 (29.1%)	0.303
DNP	52 (96.3%)	53 (96.4%)	0.741
DMAP	32 (59.3%)	35 (63.6%)	0.425
Chronic pain	13 (24.1%)	12 (21.8%)	0.432
Hypoglycemic therapy			0.249
Yes (Oral drug)	8 (14.8%)	9 (16.4%)	
Yes (Insuin)	10 (18.5%)	12 (21.8%)	
Preoperative laboratory data			
Hb, g/L	97.03±21.88	101.51±23.67	0.131
WBC, $*10^9$/L	11.37±4.69	11.21±5.03	0.674
Albumin, g/dL	32.34±6.77	33.19±5.89	0.224
A/G ratio	0.88±0.26	0.86±0.24	0.437
FBG, mmol/L	9.76±4.38	9.33±3.87	0.273
PBG, mmol/L	11.35±4.01	11.49±3.86	0.761
HbA1C, %	8.49±2.63	8.63±2.35	0.565
APAIS score	15.96±4.93	15.37±4.64	0.501
FRAIL Scale score	3.69±1.21	3.48±1.28	0.283

(*Continued*)

Table 1 (Continued).

	GA (n=54)	PNB (n=55)	*P value*
Type of operation			0.183
TTT & Debridement	48 (88.9%)	49 (89.1%)	
Toe amputation	6 (11.1%)	6 (10.9%)	

Note: Values are presented as the median (range), mean ± SD or number of patients (%).
Abbreviations: ASA-PS, American Society of Anesthesiologists (ASA) Physical Status; HD=ischemic heart disease; CI, cerebral infarction; DN, diabetic nephropathy; DR, diabetic retinopathy; DNP, diabetic neuropathy; DMAP, diabetic microangiopathy; Hb, hemoglobin; A/G, albumin/globulin; FBG, fasting blood glucose; PBG, postprandial blood glucose; HbA1C, glycated hemoglobin; TTT, tibial transverse transport.

Table 2 Intraoperative Variables

	GA (n=54)	PNB (n=55)	*P value*
Duration of anesthesia, min	131.7 ± 8.9	129.629 ± 11.4	0.147
Duration of surgery, min	89.7 ± 11.4	92.4 ± 9.5	0.154
Colloid intake, mL	270 ± 24	80 ± 18	<0.001
Total fluid intake, mL	1100 ± 80	600.0 ± 70	<0.001
Intraoperative blood loss, mL	50 ± 13	53 ± 11	0.112
Perioperative blood transfusion	26 (48.1%)	12 (21.8%)	<0.001
Hypotension	29 (53.7%)	5 (9.1%)	<0.001
Number of patients using vasopressor			
Ephedrine	29 (53.7%)	5 (9.1%)	<0.001
Norepinephrine	3 (5.5%)	1 (1.8%)	0.093
Phenylephrine hydrochloride	2 (3.7%)	0 (0.0%)	0.153

Note: Values are presented as the median (range) or number of patients (%).
Abbreviations: GA, general anesthesia; PNB, peripheral nerve block; SD, standard deviation.

only 5 patients in the PNB group (p <0.001). The colloid input and total liquid intake were higher in the GA group than in the PNB group. Similarly, the number of blood transfusions in the GA group was markedly greater than that in the PNB group (p <0.05), but SBP, DBP and mean arterial pressure (MAP) in the GA group were markedly lower than those in the PNB group at $T_{1–3}$ (p <0.05). There was no obvious difference in the perioperative heart rate between the two groups (p>0.05, Figure 2).

Prognosis During Hospitalization

NRS pain rating scores in the GA group at the postanesthetic care unit (PACU) and 2 h, 6 h, 12 h and 24 h after surgery were dramatically lower than those in the PNB group, and there was no significant difference in NRS scores between the two groups at 48 h (Figure 3). In addition, a larger proportion of patients in the GA group needed tramadol for postoperative analgesia within 24 h after surgery, and the number of patients requiring remedial medication (tramadol) was comparable between 24 h and 48 h after surgery (Table 3).

The PNB group exhibited longer total sleep time, deep sleep time, and light sleep time on both the first and second postoperative days in comparison to the GA group. Additionally, the PNB group experienced fewer instances of night wakefulness than the GA group (Table 4). We compared the overall health status of all patients by EQ-5D-5 L scores. The health status of patients in both groups improved on the first, second and third days after surgery, but it was not

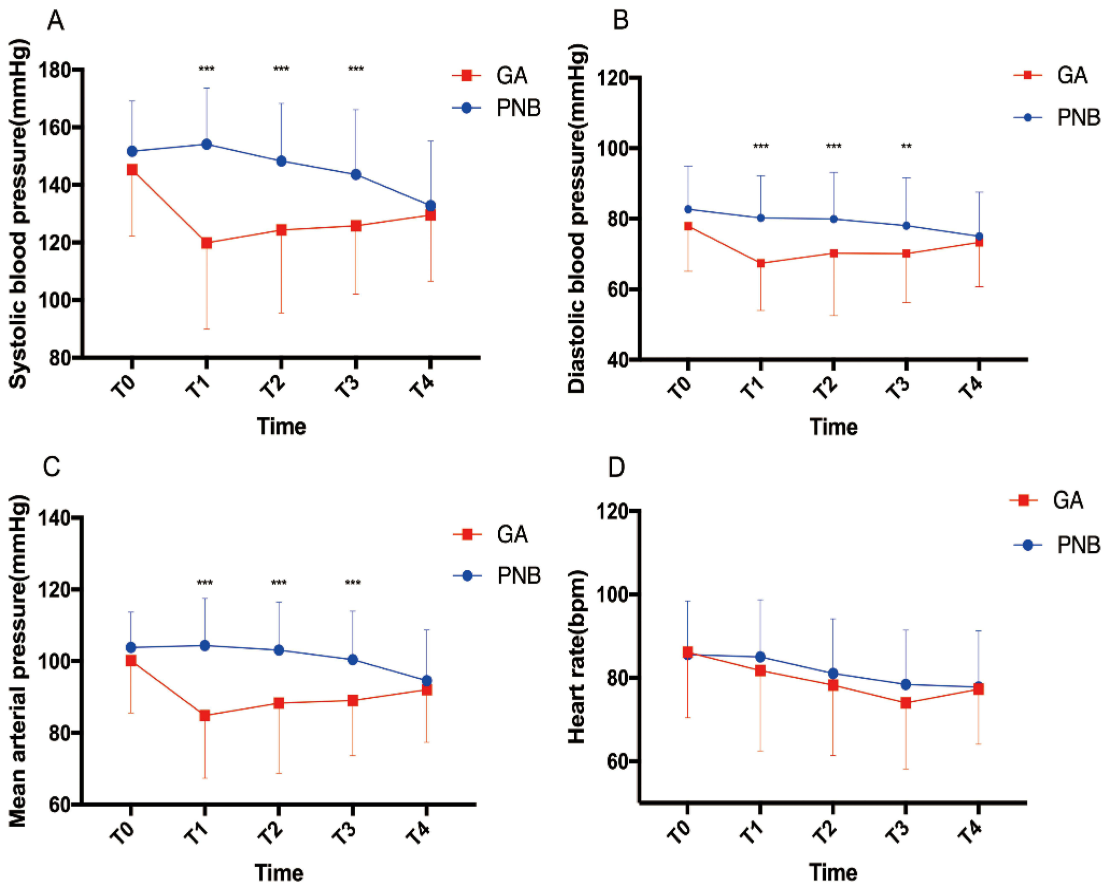

Figure 2 Comparison of systolic blood pressure, diastolic blood pressure, mean arterial pressure and HR between the two groups at five time points.
Notes: (**A**) The systolic blood pressure between the two groups at five time points. (**B**) The diastolic blood pressure between the two groups at five time points. (**C**) The mean arterial pressure between the two groups at five time points. (**D**) The heart rate between the two groups at five time points. Values are presented as the means ± SDs. **P<0.01, ***P<0.001 versus the GA group.
Abbreviations: GA, general anesthesia; PNB, peripheral nerve block.

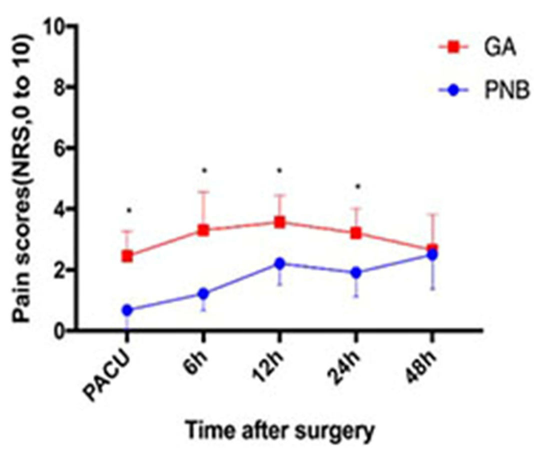

Figure 3 Postoperative pain scores during 48 hours after surgery. Values are presented as the means ± SDs. (*) p<0.05, versus the GA group.
Abbreviations: GA, general anesthesia; PNB, peripheral nerve block; NRS, numeric rating scale; PACU, postanesthetic care unit; SD, standard deviation.

related to the anesthesia method (Table 5). Patients in the PNB group ate food earlier after surgery than those in the GA group (P<0.05). When comparing the incidence of postoperative complications between the two groups, it was observed that there were no cases of pharyngeal pain in the PNB group, while the GA group reported 8 cases of

Table 3 Comparison of Postoperative Rescue Analgesics Between the Two Groups

Tramadol Dosage	GA (n=54)	PNB (n=55)	*P* value
0–24 h	23 (42.6%)	10 (18.2%)	<0.001
50 (mg)	0 (0.0%)	1 (1.8%)	
100 (mg)	18 (33.3%)	9 (16.4%)	
200 (mg)	5 (9.3%)	0 (0.0%)	
24–48 h	15 (27.8%)	18 (32.7%)	0.593
50 (mg)	0 (0.0%)	1 (1.8%)	
100 (mg)	6 (11.1%)	9 (16.4%)	
200 (mg)	9 (16.7%)	7 (12.7%)	
300 (mg)	0 (0.0%)	1 (1.8%)	

Note: Values are presented as the number of patients (%).
Abbreviations: GA, general anesthesia; PNB, peripheral nerve block.

Table 4 Comparison of Sleep Quality Between the Two Groups

	GA (n=54)	PNB (n=55)	*t* value	*P* value
Total sleep time (min)				
Day-1	390.43±132.17	421.89±136.89	−1.374	0.171
POD1	304.53±147.29	422.47±128.67	−5.312	<0.001
POD2	334.81±141.38	422.51±158.69	−3.354	0.001
Deep sleep time (min)				
Day-1	136.59±62.74	165.07±78.61	−2.331	0.022
POD1	108.35±61.29	175.49±63.47	−6.193	<0.001
POD2	122.43±62.93	168.58±77.49	−3.985	<0.001
Light sleep time (min)				
Day-1	251.49±97.61	262.23±87.29	−0.585	0.561
POD1	194.53±94.14	251.88±82.73	−3.878	<0.001
POD2	218.73±94.02	254.24±100.07	−2.161	0.031
Number of nightly awakenings				
Day-1	3.68±1.35	3.74±1.49	0.043	0.964
POD1	5.05±1.47	3.68±1.34	5.462	<0.001
POD2	4.73±1.44	4.11±1.59	2.696	0.007

Note: Values are presented as the mean ± SD, Day-1=1 day before surgery.
Abbreviations: POD, postoperative; GA, general anesthesia; PNB, peripheral nerve block; SD, standard deviation.

Table 5 EQ-5D-5 L Score

	Regression Coefficient	Standard Error	Score	*P* value
Time				
Day-1	Baseline			
POD1	1.287	0.472	7.436	0.006
POD2	3.222	0.616	27.415	<0.001
POD3	3.724	0.654	32.227	<0.001
Methods of anesthesia				
GA	Baseline			
PNB	2.298	2.157	1.134	0.286

Abbreviations: Day-1, 1 day before surgery; POD, postoperative; GA, general anesthesia; PNB, peripheral nerve block.

Table 6 Postoperative Outcomes Between the Two Groups

	GA (n=54)	PNB (n=55)	*P* value
First feeding time, h	3.12±1.08	1.09±0.76	<0.001
Out-of-bed activity-POD1	13 (24.1%)	26 (47.3%)	0.004
Sore throat	8 (14.8%)	0 (0.0%)	<0.001
Nausea/vomiting	2 (3.7%)	1 (1.8%)	0.765
Pneumonia	2 (3.7%)	0 (0.0%)	0.138
Heart failure	1 (1.9%)	1 (1.8%)	0.512
ARDS	1 (1.9%)	0 (0.0%)	0.415
Delirium	1 (1.9%)	0 (0.0%)	0.415
Nerve injury	0 (0.0%)	2 (3.6%)	0.512
Postoperative ICU admission	2 (3.7%)	1 (1.8%)	0.765
Postoperative hospital stay, d	14.81±9.17	12.68±7.73	0.342
Mortality in hospital	1 (1.9%)	1 (1.8%)	0.512

Note: Values are presented as the mean ± SD or number of patients (%).
Abbreviations: POD, postoperative; ARDS, acute respiratory distress syndrome; ICU, intensive care unit; GA, general anesthesia; PNB, peripheral nerve block; SD, standard deviation.

pharyngeal pain as the chief complaint. This difference between the two groups was found to be statistically significant ($P<0.05$, Table 6).

Discussion

Patients with diabetes are of particular concern to anesthesiologists because diabetes often affects multiple organ systems, such as in patients with diabetic nephropathy and diabetic microangiopathy.

This study comprised 109 patients, including patients with diabetic nephropathy 44.9%, diabetic microangiopathy 27.5%, ischemic heart disease and cerebral ischemia 25.7% and 19.3%, respectively. In a systematic review of 4,549,481 patients with type 2 diabetes, the authors demonstrated that the overall incidence of macrovascular complications was 32.2%, with coronary heart disease being the most commonly reported form of cardiovascular disease (21.2%).[25] Follow-up studies have reached similar conclusions: T2 DM has an "equivalent" relationship with coronary heart disease, and diabetes mellitus is a potential risk factor for coronary heart disease.[26,27] Intraoperative hypotension is associated with cardiac ischemia, renal injury, acute tubular necrosis, and cerebral hypoperfusion. Monk and coworkers found a correlation between intraoperative hypotension and an elevated 30-day surgical mortality rate.[28] Consequently, it is prudent to exercise caution regarding intraoperative hypotension, particularly in patients with diabetes who are susceptible to multiorgan complications.

For these high-risk patients, perioperative hemodynamic stability is critical. Hou Yee Lai[29] found that peripheral nerve block provided more stable hemodynamics for patients undergoing unilateral diabetic foot surgery below the knee compared to lumbar anesthesia. Hye Jin Kim[30] reviewed 320 patients with diabetes treated with lower limb amputation under nerve block anesthesia or general anesthesia and found that the general anesthesia group had a higher crystal infusion volume and a higher frequency of vasopressors, especially norepinephrine. This is consistent with our findings. We found that total liquid input and colloid input were markedly higher in the general anesthesia group than in the peripheral nerve block group, and the number of patients using vasopressors was markedly higher than that in the peripheral nerve block group, while the systolic blood pressure, diastolic blood pressure and mean arterial pressure in the general anesthesia group were significantly lower than those in the nerve block group during anesthesia induction and surgery.

Diabetic foot is the disease of blood vessels and nerves in the foot far from the ankle joint of patients with diabetes, resulting in insufficient blood supply to the foot, paresthesia, ulceration and infection symptoms. In severe cases, muscle and bone can be affected, leading to necrosis and even amputation, and it is associated with a variety of complications and disabilities.[31] In addition, the pain, weakness, loss of labor force, frequent hospitalization, reduced social and family interaction and economic burden caused by diabetic foot can affect the psychological state of patients and, in severe cases, can produce anxiety and depression. In this study, anxiety status was assessed by the Amsterdam Anxiety Rating Scale (APAIS) before surgery, and it was found that the APAIS scores were high in both groups, but no statistical significance was observed.

Qing Liu[32] analyzed the relationship between preoperative depression and postoperative pain in 120 patients over 65 years old with gastrointestinal tumors and found that high preoperative anxiety was moderately positively correlated with high postoperative pain (p<0.001, r = 0.410). Studies have shown that approximately twenty percent of patients with type 2 diabetes have neuropathic pain,[33] and diabetic peripheral neuropathy is the leading cause of neuropathic pain in the population.[34] Herein, 22.9% of the 109 patients had chronic pain, while 97.2% of diabetic peripheral neuropathy was detected by Michigan Neuropathy Screening (MNSI) before surgery. Postoperative pain management of these patients is a great challenge for anesthesiologists. Rune Sort[35] found that peripheral nerve block anesthesia had a significant benefit for postoperative pain in surgery for acute ankle fractures, despite significant rebound pain after the effect of nerve block anesthesia subsided. Patients receiving peripheral nerve block anesthesia had significantly lower postoperative NRS scores and morphine dosages than those in the general anesthesia group. In addition, patients receiving peripheral nerve block anesthesia were more likely to choose the same type of anesthesia again, and older patients benefited more from peripheral nerve block anesthesia. Na Young Kim retrospectively analyzed pain scores and analgesic remedies 24 hours after amputation in 59 diabetic foot patients who underwent general anesthesia and nerve block anesthesia, respectively. The results showed that the NRS of patients who underwent peripheral nerve block anesthesia was lower than that of patients who underwent general anesthesia, and within 6 hours after surgery, patients receiving peripheral nerve block anesthesia needed lower doses of analgesic remedies.[25] Our findings demonstrated that the NRS scores of the peripheral nerve block group in the PACU and at 6 h, 12 h, and 24 h after surgery were markedly reduced compared to those of the general anesthesia group. However, no obvious difference was found between the two groups at 48 h after surgery. We speculated that postoperative pain would affect patients' sleep, so we further studied the difference in postoperative sleep between the two groups. On the first and second days after surgery, the total sleep duration and deep sleep duration of patients in the PNB group were dramatically higher than those in the GA group. In addition, on the first day after surgery, patients in the GA group were awake more often at night than those in the PNB group, suggesting that the sleep quality of patients was better in the PNB group than in the GA group, and the effective postoperative analgesic effect of nerve block anesthesia had a positive effect on patients' sleep. Nicholas A. Giordano[36] studied the correlation between peripheral nerve block, postoperative pain, and sleep disorders in the first and second weeks after surgery in patients who underwent lower limb joint replacement. At the three postoperative time points, the intensity of pain at each time point was positively correlated with sleep disorders at the same time point. The mediating analysis revealed that the effect of PNB on 1-week sleep disturbance was indirectly affected through its impact on 1-week pain intensity. Furthermore, it was observed that peripheral nerve block had an indirect association with 2-week sleep disturbances mediated by its effects on 1-week pain intensity and 1-week sleep disturbances. In short, receiving a peripheral nerve block during lower limb joint replacement was associated with an improvement in pain intensity one week after surgery and reduced the incidence of sleep disturbances the first and second weeks after surgery.[36] During hospitalization, we used the EQ-5D-5 L scores to evaluate the recovery of patients on the first, second and third days after surgery. The median EQ-5D-5 L score in the two groups was approximately forty points, and most patients showed a negative attitude toward their own quality of life evaluation. Studies have shown that the ED-5D self-rating scale of patients with diabetes usually presents a low score, and patients feel that their quality of life is poor.[37] We found that the quality of life scale of patients in the two groups improved with the passage of time after surgery, but it was not related to the anesthesia method received by patients during surgery, which may be related to the scale being susceptible to multiple influencing factors, including gender, occupation, course of disease, education level, preoperative flimsy state, surgical method and postoperative complications by generalized estimation equation.

The proportion of patients in the PNB group who were physically active on the first day after surgery was markedly increased compared with that in the general anesthesia group, and early getting out of bed was more conducive to the recovery of various physiological functions, promoting the blood circulation of the affected limb, and relieving wound swelling. In terms of other outcomes and prognosis, none of the patients in the PNB group had pharyngeal pain, while 8 patients in the GA group had pharyngeal pain, which may be related to the need for tracheal intubation under general anesthesia. Pulmonary complications occurred in 2 patients in the GA group but not in the PNB group, although the difference was not significant. Peripheral nerve blocks have shown lower rates of postoperative lung complications than general anesthesia.[29,35] It is worth noting that there were 2 cases suspected of nerve injury in the PNB group, and the patients did not complain that the skin sensory and motor functions of the affected limb were restored to the same state as before until the 4th day after the operation. Regarding the occurrence of nerve injury, the possible influencing factors include neurotoxic injury caused by local anesthetic drugs, aggravation of patients' original peripheral neuropathy, and ischemic nerve injury caused by tourniquet compression during surgery.[38,39] High-quality and large-sample prospective studies are warranted to confirm the occurrence of nerve damage after nerve block in patients with diabetes. The relationship between the mode of anesthesia and ICU transfer rate and mortality remains controversial. In this study, general anesthesia did not increase the ICU transfer rate or inpatient mortality.

This research had many limitations. In this study, peripheral nerve block anesthesia had no advantage in terms of ICU transfer rate and mortality. First, we only followed up patients for ICU transfer rate and mortality in this hospitalization, which may be related to the insufficient follow-up time, and we failed to find the long-term prognosis of patients. Second, the possible association between the observed results and the insufficient sample size of this study highlights the need for a larger sample in future investigations. Further controlled studies are warranted to comprehensively assess the impact of anesthesia on patients with diabetic foot following surgical treatment.

Conclusion

In conclusion, when compared to general anesthesia, nerve block anesthesia demonstrates several advantages in patients with diabetic foot. It offers more stable intraoperative hemodynamics, improves postoperative analgesia, and enhances postoperative sleep quality. These findings suggest that nerve block anesthesia may be a preferable choice for surgical procedures in patients with diabetic foot. However, there were no significant differences in patients' quality of life during hospitalization, ICU transfer rate or death rate between the two types of anesthetic techniques. In the upcoming study design, we will be integrating a number of parameters, such as cardiac output, beat-to-beat variability index, central venous pressure, and mixed venous oxygen saturation, aiming to achieve a more thorough and multidimensional monitoring of cardiovascular function in our subjects.

Abbreviations

GA, general anesthesia; PNB, peripheral nerve block; DF, diabetic foot; VSD, vacuum sealing drainage; TTT, tibial transverse bone transfer; ASA, American Society of anesthesiologists; TCI, target-controlled infusion; BIS, bispectral index; PEEP, positive end-expiratory pressure; DNP, diabetic neuropathy; DR, diabetic retinopathy; FBG, fasting blood glucose; PBG, postmeal blood glucose; DBP, diastolic blood pressure; SBP, systolic blood pressure; HR, heart rate; MBP, mean blood pressure; MAP, mean arterial pressure; NRS, numeric rating scale; ICU, intensive care unit; PACU, postanesthetic care unit; APAIS, Amsterdam anxiety rating scale; MNSI, Michigan neuropathy screening.

Data Sharing Statement

The data that support the findings of this study will be available from the corresponding author, Yubo Xie, upon reasonable request. All of the individual participant data collected during the trial will be available after deidentification. The data will be made available immediately following article publication, with no end date.

Ethics Declarations

This study was approved by the Medical Ethics Committee of the First Affiliated Hospital of Guangxi Medical University (Identifier: 2020-015). This study was registered in the Chinese Clinical Trial Registry on June 7, 2020 (ChiCTR2000033621) and with the Helsinki Declaration of 1964 and later versions. Informed consent for it was obtained from all patients for being included in the study.

Consent for Publication

The research article is original, has not already been published in any other journal (medical, or otherwise) or is not currently under consideration for publication by another journal, and does not infringe any existing copyright or any other rights prescribed by law.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no competing interests in this work.

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