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Motor and Somato Sensory Evoked Potentials During Intraoperative Surveillance Testing in Patients with Diabetes

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Abstract

Cerebral vascular surgery can damage patients' motor and sensory nerves; therefore, neuromonitoring is performed intraoperatively. Patients with diabetes often have peripheral neuropathy and may be prone to nerve damage during surgery. This study aimed to identify factors that should be considered when diabetic patients undergo intraoperative neuromonitoring during brain vascular surgery and to present new criteria. Methods: In patients with and without diabetes who underwent cerebrovascular surgery (n = 30/group), we compared the intraoperative stimulation intensity, postoperative motor power and sensory, glycated hemoglobin (HbA1c) and glucose levels, and imaging findings. Results: Fasting glucose, blood glucose, and HbA1c levels were 10%, 12.1%, and 9.7%, respectively; they were higher in patients with than in patients without diabetes. Two patients with diabetes had weakness, and 10 required increased Somato sensory evoked potential (SSEP) stimulation, while in 16, motor power recovered over time rather than immediately. The non-diabetic group had no weakness after surgery, but 10 patients required more increased SSEP stimulation. The diabetic group showed significantly more abnormal test results than the non-diabetic group. Conclusion: For patients with diabetes undergoing surgery with intraoperative neuromonitoring, whether diabetic peripheral neuropathy is present, their blood glucose level and the anesthetic used should be considered.

Keywords: *Aneurysm, Diabetes, Somato Sensory Evoked Potential, Motor Evoked Potential*

1. INTRODUCTION

Intraoperative neuromonitoring (IONM) is a neurophysiologic test conducted to prevent nerve damage during nervous system surgery. During brain vascular surgery, ischemic neuropathy caused by blood circulatory dysfunction, the patient's neurological condition, changes in anesthesia, and neurological damage due to body position, can be detected by IONM. Electrophysiological tests can be affected by the anesthetic used during surgery, in addition to the drugs used to treat diabetes. In particular, anesthesia can affect the

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results of neuromonitoring tests during surgery [1]. Furthermore, long term hyperglycemia can lead to diabetic peripheral neuropathy [2], and patients with diabetic polyneuropathy require changes in the intensity of the stimuli and parameters used for electrophysiological diagnostic examinations [3]. Therefore, if patients with diabetes undergo brain vascular surgery, many variables must be considered.

The reason for the selection of patients with cerebral aneurysm in this study was that these cases accounted for the largest number of operations in such patients in our institute. Additionally, diabetic patients were chosen because they were very likely to suffer from diabetic neuropathy; therefore, the neuromonitoring test was likely to show abnormal symptoms [4]. Cerebral aneurysm occurs in about 1 in 50 adults [5], and is closely associated with diabetes mellitus; high blood sugar levels (126 mg/dl) can be a direct causal factor in cerebral aneurysm [6]. Most individuals with diabetes have also been diagnosed with hyperlipidemia and high blood pressure, and thus, their risk of having a ruptured cerebral aneurysm is markedly higher than that of healthy adults [7].

Surgical treatment, such as clipping and intravenous coil embolism, is used for cerebral aneurysms that cannot be treated with drugs. Clipping surgery can result in a blood circulation disorder, caused by brain tissue retraction and temporary clipping during surgery [8]. Various risk factors can affect the prognosis of surgery, such as hemorrhage during surgery and ischemic complications caused by inappropriate clip location [9]. In addition, for a malformed cerebral aneurysm that cannot be treated with a normal clipping procedure, superficial temporal artery–middle cerebral artery anastomosis (bypass) is performed, which blocks blood flow of the proximal vessel for a long time [10]. This causes infarction due to blood flow disorder during surgery. Bypass is usually performed for surgery of posterior internal carotid artery aneurysms, giant aneurysms, and patients with Moyamoya [11, 12]. Furthermore, when bypass is performed, more retraction is needed than for normal clipping, which can cause damage to the corticospinal tract [13]. During surgery, the presence or absence of the infarction can be assessed by conducting IONM, which can help the surgeon to assess the situation of the operation [14].

This study aimed to identify factors that should be considered when diabetic patients undergo IONM during brain vascular surgery and to present new criteria.

2. MATERIALS AND METHODS

2.1 Study Subjects

This study was approved by Dankook University's Institutional Bioethics Committee (institutional review board number: 2019-04-017). This retrospective study included patients who underwent IONM during brain vascular surgery in Seoul National University Bundang Hospital from October 2018 to December 2019. Patients with diabetes (n = 30; subject) were selected if they were diagnosed with diabetes or if their glucose test results exceeded 126 mg/dl. Patients without diabetes (n = 30; subject) were patients without diabetes and other underlying neurological diseases. 56 patients who underwent surgery for aneurysm and 4 patients who underwent surgery for aneurysm with bypass were among the enrolled patients. No tests were conducted on patients who had electrical equipments, such as pacemakers, implanted.

Fasting glucose level (126 mg/dl), serum calcium level (8.5−11.8 mg/dl), blood sugar test result (24 hour glucose test, 140−200 mg/dl), glycated hemoglobin (HbA1c) level (6.5%), urinary glucose level (+), and radiologic findings were compared between the non-diabetic and diabetic groups. The values in parentheses are within the normal range of the corresponding test items set by Bundang Seoul National University Hospital. Fasting glucose levels were measured after collecting blood upon waking, while blood sugar tests were determined every two hours, from waking, for 1 day.

2.2 Motor and Somato Sensory Evoked Potential Test

We used the Xtek Protector (Natus Medical Inc., ExcelTech Ltd., Oakville, Ontario, Canada) as test equipment. In accordance with the International 10-20 Electrode system, motor evoked potential (MEP) stimulation needles were inserted into the positive and the negative stimulation needles at C2, C4 and C1, C3 for stimulation of the right cerebral hemisphere, and at C1, C3 and C2, C4 for stimulation of the left cerebral hemisphere. The following stimulus parameters were used: biphasic polarity, continuative 5 pulse stimuli, 500 Hz of stimulation rate, 0.05 ms of stimulus duration, 150–300 Voltage for MEP. MEP stimulation power was recorded in the abductor pollicis brevis and the adductor digiti minimi, and in the tibialis anterior and abductor hallucis of the lower limbs. The upper Somato sensory evoked potentials (SSEPs) were recorded at C3, C4, by stimulating the median nerve (Stimulation power : 15 mA)., while the lower SSEPs were recorded at Cz, by stimulating the post tibia nerve (Stimulation power : 20 mA).

2.3 Statistical Analysis

In order to test the factors affecting the state of patients' physiology, data are presented as a frequency, percentage, mean and standard deviation. Data analysis was performed using SPSS Statistics version 22 program (SPSS Inc., Chicago, IL, USA), and the significance level was set to $P < 0.05$.

3. RESULTS

3.1 Characteristics of Overall Patients

Of the 60 participants in this study, the average age was 57.5 years. There were 16 men and 44 women. Overall, average values were as follows: fasting glucose, 113.3 mg/dl; blood sugar, 135.6 mg/dl; calcium, 9.0 mg/dl; and HbA1c, 6.04%.

3.2 Non-diabetic Group

The characteristics of the non-diabetic group are described in Table 1.

Table 1. Characteristics of the patients by group

	Diabetic group		Non-diabetic group	
Characteristic	Variable	Value	Variable	Value
Sex	Male	5	Male	11
	Female	25	Female	19
Age (Mean, Min-Max)		57.5 (33-65)		62.2 (49-79)
Vessel	ICA	2	ICA	1
	MCA	35	MCA	14
	ACA	5	ACA	3
	Acom	9	Acom	3
	AchoA	10	AchoA	7
	Pcom	4	Pcom	4
	PCA	1	PCA	1
	PICA	1	PICA	1

Glucose level (mg/dl, Min-Max)	113.3 (86.7-120.1)	124 (75-220)
BST result (mg/dl, Min-Max)	135.6 (94-160.1)	152.1 (80-360)
Calcium level (mg/dl, Min-Max)	9.1 (8.3-9.9)	8.9 (8-9.6)
HbA1c level (%, Min-Max)	6.04 (4.7-5.8)	6.63 (5.3-9.65)

ICA: internal carotid artery, AchoA: anterior choroidal artery, ACA: anterior cerebral artery, ACom: anterior communicating artery, MCA: middle cerebral artery, PCom: posterior communicating artery, PCA: posterior cerebral artery, PICA: posterior internal carotid artery, HbA1c: glycated hemoglobin, BST: blood sugar test.

3.2.1 IONM Test Results in Non-diabetic Patients

None of the 30 patients in the non-diabetic groups showed abnormal IONM test results.

3.2.2 SSEPs and Patients' Weakness

Ten non-diabetic patients had a baseline stimulus value stronger than the standard stimuli of 15 mA (median nerve) and 20 mA (post-tibia nerve) in SSEP tests. Additionally, 2 cases in the non-diabetic group had postoperative weakness and needed more than the standard stimulation during the SSEP test; these patients are described further in section 2.3.

3.2.3 Patients with Postoperative Weakness

Two non-diabetic patients failed to recover motor function immediately after surgery, but recovered over time. One of these patients recovered motor function on the first day after surgery, and the other recovered motor function on the second day after surgery. Their grade was reduced to 4 after surgery, but returned to normal within 2 days. One of the non-diabetic patient's radiologic finding was a small subarachnoid hemorrhage after surgery, but this disappeared by postoperative day (POD) 5. The radiologic finding in the other patient was a hematoma, which disappeared before discharge; it was concluded that the muscle function in this patient decreased because of pain and anesthetic use. The indicators of diabetes for these 2 patients are shown in Table 2.

Table 2. Comparison of indicators of diabetes between the diabetic and non-diabetes patients, with and without weakness

	Diabetic group		Non-diabetic group	
	With muscle weakness	Without muscle weakness	With muscle weakness	Without muscle weakness
BST result (mg/dl)	153.1 (86.2-174.1)	110.9 (88.2-154.2)	126.8 (83.2-138.2)	113.7 (84.5-151.8)
Glucose level (mg/dl)	128.0 (92.1-156.1)	105.7 (91.2-167.2)	104.1 (90.1-119.2)	106.7 (90.2-118.3)
HbA1c level (%)	6.8(4.9-5.8)	5.9 (4.7-5.2)	5.4 (4.8-9.65)	5.75 (4.9-5.7)
Calcium level (mg/dl)	9.2(8.3-9.4)	8.6 (8-9.3)	9.1 (8.2-9.5)	8.9 (8.2-9.6)

BST: blood sugar test, HbA1c: glycated hemoglobin

3.3 Diabetic Group

The characteristics of the diabetic group are described in Table 1.

3.3.1 Abnormal IONM Test Results

In 1 case in the diabetic group, the waveform on IONM changed during surgery. In this patient, amplitude reduction and loss of the left upper SSEP were observed after using a temporary clip for 7 minutes. At 1 minute after removal of the temporary clip, all evoked potential waveforms returned to normal; however, amplitude reduction and loss of the left upper SSEP were observed again at 5 minutes after using the temporary clip but recovered within 1 minute after removing the temporary clip, and then those waveforms recovered. The patient was reduced to grade 3 immediately after surgery and recovered to grade 4 on the POD 1 when she was discharged from the hospital; she recovered all her muscle power. According to computed tomography imaging, a 2 cm hematoma appeared in the right hemisphere immediately after surgery, and was reduced by about 1 cm by POD 2. By the time the patient was discharged from hospital, the hematoma had not disappeared. Her glucose level was 117 mg/dl and BST result was 129 mg/dl.

3.3.2 Somato Sensory Evoked Potential and Patients' Weakness

Ten patients in the diabetic group had postoperative weakness and needed more than the standard stimulation during the SSEP test (median: 15 mA, posterior tibia: 20 mA). Among these, 7 patients showed postoperative weakness; and among patients with increased stimulus strength, 3 patients showed a significant decrease in motor power ($P < 0.05$). In case 3 (Table 3), postoperative motor function was grade 4 immediately after surgery, but on the afternoon of POD 4, he improved to grade 5. However, he had sensory aphasia, such as showing his right hand when asked to show his thumb.

Table 3. Characteristics of patients with increased stimuli for the baseline setting and postoperative weakness

No.	Sex/Age (years)	Vessel	Stimulation	Day of recovery	Glu level	BST result	HbA1c level	Ca. level
1	F/69	Lt. MCA	PT 25–30 mA	POD 1	145.7	156.1	-	9.3
2	F/62	Lt. MCA	MN 15–20mA	POD 2	145.6	145.6	-	9.2
3	F/54	Rt. Pcom	PT 20–25 mA	POD 1	91.8	135	-	9
4	M/63	Acom	PT 20–25 mA	POD 1	166.8	171.8	6.5	9.3
5	M/72	Lt. MCA	MN15–20, PT20–25	Immediately	111.5	157.9	7	9
6	F/61	Lt. MCA	MN 15–25, PT20–25	Immediately	113.5	148.4	-	8.4
7	F/62	Lt. AchoA	MN 10–20, PT20–30	Immediately	165.6	191.3	Urine 3+	8.5
8	F/62	Lt. MCA	PT 20–25 mA	POD 6	116.5	149.2	5.7	8.6
9	F/62	Lt. MCA	PT 20–25 mA	POD 6	116.5	149.2	5.7	8.6
10	F/54	Rt. MCA	MN 15–20 mA	POD 1	106.6	143	Urine 3+	8.8

No.: number, POD: Postoperative day, Lt.: left, Rt.: right, M: male, F: female, ACom: anterior communicating artery, MCA: middle cerebral artery, PCom: posterior communicating artery, AchoA: anterior choroidal artery, Glu: glucose, BST: blood sugar test, HbA1c: glycated hemoglobin, Ca.: calcium

3.3.3 Patients with Postoperative Weakness

Among 30 patients with diabetes, 14 patients had no weakness and 16 patients had postoperative muscle weakness (Table 4). Among those with weakness, 1 patient recovered motor function on the day of surgery, 8 patients recovered motor function after 1 day, 2 patients recovered after 2 days, 2 patients recovered after 3 days, and 3 patients did not recover by the time they were discharged. Among the patients with muscle weakness, 4 patients had hemorrhagic fluid caused by bleeding from capillaries around the cerebral aneurysm during surgery, and 2 patients had infarction. Patients with muscle weakness had higher blood sugar, fasting glucose, and HbA1c levels than those without muscle weakness ($P < 0.05$, Table 2; Figure 1).

Table 4. Characteristics of patients with muscle weakness and diabetes

Case no.	Sex/Age (years)	Vessel	Day of recovery	Glu level	BST result	HbA1c level	Ca. level
1	F/61	Rt, MCA	POD 3	106	145.4		9.1
2	F/66	Rt. MCA	POD 3	117	129	-	8.6
3	F/66	both A2-3	POD 2	120.7	129.7	5.7	8.8
4	F/54	Lt. AchoA, A1	After discharge	145	221.8	6.8	9.3
5	F/65	MCA	POD 1	110	132.3	-	9.5
6	M58	Acom	POD 1	125.1	162.2	7.2	9.5
7	F/69	Lt. MCA	POD 1	147.5	156.1	-	9.3
8	F/62	Lt. MCA	POD 2	145.6	145.6	-	9.2
9	M/49	AchoA	POD 1	148.7	149.8	7.9	9.4
10	F/54	Rt. Pcom	POD 0	91.8	135	-	9
11	M/63	Acom	POD 1	166.8	171.8	6.5	9.3
12	M/72	MCA	POD 1	111.5	157.9	7	9
13	M/60	Lt. PCA	After discharge	130	159	9.65	8.4
14	M/49	Lt. AchoA	POD 1	148.8	150	7.9	9.6
15	F/62	Lt. MCA	After discharge	116.5	149.2	5.7	8.6
16	F/54	Rt. MCA	POD 1	106.6	143	5.8	8.8

No.: number, POD: Postoperative day, Lt.: left, Rt.: right, M: male, F: female, ACom: anterior communicating artery, MCA: middle cerebral artery, PCom: posterior communicating artery, AchoA: anterior choroidal artery, PCA: posterior cerebral artery, Glu: glucose, BST: blood sugar test, HbA1c: glycated hemoglobin, Ca.: calcium

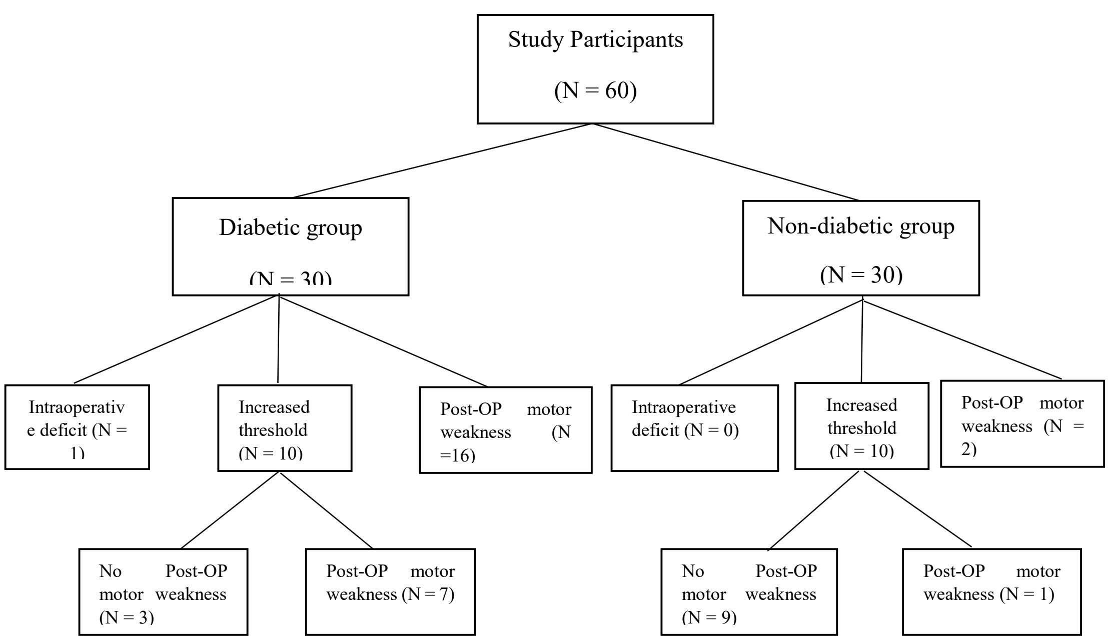

Figure 1. Study participants' inspection patterns of evoked potential. Post-OP: postoperative

4. DISCUSSION

This study investigated the correlation between diabetic patients and the results of IONM during surgery in order to identify factors that should be carefully considered. We found that patients with diabetes had a higher threshold for SSEPs than patients without diabetes, and that they took longer to recover their motor power after surgery [15]. Patients with diabetes feel postoperative pain but have slightly decreased sensory function as compared to patients without diabetes. In addition, magnetic resonance imaging and computed tomography findings also suggested that abnormalities are more prevalent in patients with than in those without diabetes. These abnormalities are more likely to result in cerebral infarction and cerebral hemorrhage [16]. In particular, if subdural or subarachnoid cerebral hemorrhage after surgery is severe, the patient's neurological defects may appear after surgery due to the physical pressure caused by the hematoma [17]; these symptoms are difficult to observe during the surgery. This may lead to false negative results between intraoperative monitoring and neurosurgery. According to Vinik [18], the prevalence of neurological disease in patients with diabetes was higher than that of patients without diabetes, suggesting that peripheral blood circulation may be due to disorders and metabolic dysfunctions and that postoperative recovery may be delayed due to neuropathic pain. In addition, hyperglycemia causes not only cerebral blood circulation disorder, but also cardiovascular problems, and is accompanied by autonomic nervous system disorder, which can delay recovery of overall physical function. According to the results of this study, the diabetic group had more peripheral neuropathy than the non-diabetic group. Calcium is useful as a pathological indicator of diabetes [19, 20] . Calcium affects the antagonism of pancreatic beta cells, which regulates blood sugar, thereby controlling progression of diabetes. In this study, diabetic patients also had hypocalcemia. Abnormalities in the calcium channel in muscles have a significant effect on evoked potential tests [21]. In this study, we evaluated the relationship between hypocalcemia, typical of diabetes, and evoked potentials. The mean blood calcium level in patients with diabetes was 8.9 mg/dl, compared to 9. 1 mg/dl in patients without diabetes ($P < 0.05$) Calcium levels have been associated with the prognosis and neuropathy of patients with diabetes; in these patients, calcium levels are decreased because of the abnormal function of pancreatic β cells [22]. However, the present study had a small sample size and the disease duration could not be investigated. If calcium levels in patients with diabetes are below normal levels, abnormality of calcium channels due to calcium deficiency can explain the high SSEP threshold in these patients [23]. Therefore, diabetic patients are more likely to have a higher threshold and baseline abnormalities in the evoked potential test than non-diabetic patients, due to blood circulation and ion balance disorders. High baseline thresholds may result in false positives due to distortion of the waveform. In diabetic patients, atherosclerosis due to hyperlipidemia is more likely to develop in the cerebrovascular system [24], resulting in infarction and postoperative motor dysfunction. In this study, there were 2 patients with infarction, who had higher HbA1c levels than those in the non-diabetic group ($P < 0.05$). Therefore, in patients with diabetes, blood glucose control may affect the postoperative outcome [25]. In these patients, the responsiveness of blood vessels during cerebral ischemia is reduced as compared to patients without diabetes, which suggests that the vessel's elasticity and dilatability is reduced. This may result in the delayed recovery noted in these patients in the present study. Impaired blood flow increases the cell density around the site, which can lead to bleeding during surgery and can lead to kidney failure or encephalopathy; thus, vital signs should be carefully monitored [24]. In the study, we found that diabetics were more likely to have hyperlipidemia [26], which can lead to atherosclerosis and result in cerebral aneurysm. In other words, the blood flow of cerebrovascular blood in diabetics does not maintain normal blood flow for external reasons such as atherosclerosis [24]. If blood flow is not influenced by any other detrimental factors, the lateral circulation supplies blood to the brain when a temporary clip is used [27]. However, in diabetic patients, changes in blood flow due to atherosclerosis lead to deterioration of brain function, which can result in abnormal IONM signals [28]. In this study, there was a decrease in SSEP during surgery in 1 case. The SSEP warning criteria used in this study were based on a >50% amplitude reduction and 1 ms latency delay [29]; however, there were more cases with a slight decrease (10−50%) in amplitude after temporary clipping in the diabetic group than in the non-diabetic group. In order to assess patients' recovery, other criteria, such as a 0.7–0.8 ms delay or 30–40% decreased amplitude, can be used, which may be more appropriate to prevent surgery related neurophysiological deficits in patients with diabetes.

To date, no previous study has investigated factors influencing IONM during surgery in patients with diabetes. The present study was limited by the small sample size; inclusion of more patients may result in different findings. In addition, the warning criteria presented here should be verified in further studies. Further detailed studies should consider the duration of the patient's disease. This is because the longer the disease is, the greater the effect on nerve damage and blood disorders.[30] This study examined only the duration of the patient's discharge from surgery; longer term follow up of 3–6 months would be valuable.

5. CONCLUSION

This study was conducted to identify factors that should be considered in neuro-monitoring tests during brain vascular surgery in patients with diabetes. We found that patients with diabetes have higher thresholds in SSEP and MEP than patients without diabetes. We also found that recovery time after surgery was longer in patients with than in those without diabetes. This suggests the need to apply slightly different warning criteria to patients with than in patients without diabetes during surgery, more sensitive and faster warning. Importantly, the monitoring technician should consider the patient's diabetes status, fasting glucose, HbA1c, blood glucose, and calcium levels, etc., prior to surgery, and should work closely with anesthesiologists to monitor anesthesia and drugs, vital signs, and clinical changes during surgery to ensure quality IONM.

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