Intracerebral Hemorrhage and Venous Infarction after Deep Brain Stimulation Lead Placement

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To the Editor: Cerebral vascular events (intracerebral hemorrhage [ICH] or venous infarction) are the most feared complications of deep brain stimulation (DBS) surgery. The estimated risk of ICH in DBS surgery reportedly varies from 0.2% to 5.6%.[1-3] ICH may develop at one of two sites depending on the puncture tract: (1) in the basal ganglia or target area or (2) in the puncture channel or cortex area. However, venous infarction in association with DBS surgery has rarely been described.[4-6]

Whether factors such as age, sex, hypertension, anatomic target, or use of microelectrodes affect the risk of cerebral vascular events during the DBS surgery remains controversial.[2,7,8] In this study, the authors retrospectively investigated factors possibly affecting the risk of cerebral vascular events (ICH or venous infarction) during DBS surgery in 268 patients (518 DBS electrodes), including patient age, sex, anatomic target, use or nonuse of microelectrode recording (MER), number of MERs performed, number of channels used in MER, and other parameters. The study was approved by the Ethics Committee of Chinese People's Liberation Army General Hospital and the requirement for informed consent was waived because of the retrospective design.

From July 2008 to December 2015, 268 patients (187 males and 81 females) with movement disorders underwent DBS (518 electrodes) at People's Liberation Army General Hospital. Twelve patients (8 males and 4 females) developed cerebral vascular events (ICH in 10, venous infarction in two). They ranged in age from 19 to 72 years with a mean of 59.3 ± 15.0 years. The mean disease course was 3.7 ± 6.2 years (range, 2–13 years). Eight patients had Parkinson's disease, one had essential tremor, two had spasmodic torticollis, and one had Tourette syndrome. None of the patients with cerebral vascular events had hypertension. The electrodes were implanted in the subthalamic nucleus in eight patients, in the globus pallidus internus in three, and in the ventral intermediate nucleus in one. Ten patients underwent single-channel MER and two underwent multi-channel MER.

Patients who met the following criteria were diagnosed with venous infarction. First, the intraoperative magnetic resonance imaging (MRI) or early postoperative computed tomography (CT) scan (within 24 h after surgery) showed no hemorrhage around the lead. Second, the second imaging examination, which always involved a CT scan on the postoperative day 2–7 (routine cerebral CT scan before discharge or CT scan due to symptoms), showed low-density lesions (cerebral edema) surrounding the superficial aspect of the implanted lead. We also referred to the report by Morishita *et al*.[5] regarding the diagnosis of postoperative venous infarction after DBS.

All patients underwent intraoperative or postoperative imaging examinations. Patients who underwent local anesthesia after intracranial electrode implantation underwent intraoperative MRI examination if they were able to tolerate it. Patients who could not tolerate MRI because of drug withdrawal effects or general anesthesia underwent CT, usually 6–24 h postoperatively. The second imaging examination involved a CT scan on the postoperative day 2–7 (routine cerebral CT scan before discharge or CT scan due to symptoms).

Statistical analysis was performed using SPSS 18.0 for Windows, version 18 (IBM Corp., Armonk, NY, USA). Variables were expressed as the mean ± standard deviation (SD) or number (%) of patients. Categorical variables were analyzed by the Chi-square test and Fisher's exact test. Statistical significance was defined as $P < 0.05$.

Twelve (4.48%) of 268 patients developed a cerebral vascular event (ICH in 10 [3.73%] and venous infarction in 2 [0.75%]). Ten cases of ICH were unilateral, accounting for 1.93% per electrode. Two patients showed complication with venous infarction on CT.

Eight patients with ICH showed clinical manifestations and five showed physical signs (e.g., agitation, hemiplegia, and high blood pressure) during the operation. One patient developed a large amount of bleeding (about 20 ml) and underwent immediate intraoperative hematoma aspiration. A drainage tube was placed,

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and the hematoma was completely drained without displacement of the electrode. The other patients underwent conservative treatment. Two patients showed psychiatric symptoms (such as hallucinations and cognitive dysfunction) during the first 3 days postoperatively, and one patient developed severe headaches, nausea, and vomiting. Another two patients with no clinical symptoms or signs of change exhibited a small amount of ICH on a routine postoperative CT scan. Two patients with venous infarction had minor psychiatric symptoms that were difficult to distinguish from the side effects of drug withdrawal. Four patients developed long-term postoperative mild hemiparesis.

Among the 10 sites of ICH, five were deep ICH (basal ganglia or target) and five were located in the frontal cortex and puncture channel. Venous infarction occurred in two patients, and both were located in the frontal lobes surrounding the lead.

Patients aged ≥60 years were more likely to develop vascular events ($\chi^2 = 4.361$, $P = 0.039$), intraoperative bleeding ($\chi^2 = 4.495$, $P = 0.046$), and vascular events in the cortex or puncture channel ($\chi^2 = 5.831$, $P = 0.016$). However, deep ICH ($\chi^2 = 0.000$, $P = 1.000$) and infarction ($\chi^2 = 0.053$, $P = 0.527$) showed no association with age. The application of intraoperative MER significantly increased the risk of vascular events; vascular accidents occurred in all patients who underwent MER ($\chi^2 = 12.408$, $P = 0.000$), especially those with ICH ($\chi^2 = 9.761$, $P = 0.002$).

Vascular injury was unrelated to sex, the implant target location, and the number of MERs performed ($\chi^2 = 0.058$, $P = 0.758$; $\chi^2 = 0.021$, $P = 0.989$; and $\chi^2 = 0.970$, $P = 0.335$, respectively). Ten (8.62%) patients who underwent single-channel MER and two (22.22%) who underwent multi-channel MER developed vascular accidents. There was a higher proportion of bleeding in those who underwent multi-channel MER, but without a significant difference ($\chi^2 = 0.558$, $P = 0.455$). However, among patients with deep ICH (3 [2.59%] of 116 patients who underwent single-channel MER and 2 [22.22%] of 9 patients who underwent multi-channel MER), our comparison showed that multi-channel MER increased the risk of deep ICH ($\chi^2 = 4.052$, $P = 0.044$).

With respect to the association between cerebral vascular injury and age, the present study showed a significant correlation between age and cerebral vascular events (ICH or venous infarction). This is consistent with the report by Ben-Haim *et al*.,[2] who found that the mean age was significantly higher in patients with than without hemorrhage ($P = 0.020$). The authors concluded that the potential for an increased incidence of hemorrhage might be associated with various factors in the aging brain, including generalized atrophy, more brittle or fragile blood vessels, and an increased number of comorbidities. Sansur *et al*.[8] also reported that age was a contributive factor to hemorrhage in 567 electrodes placed into 259 patients (DBS to treat movement disorders, 219 electrodes; radiofrequency lesioning for movement disorders, 74 electrodes; and intracerebral depth electrodes for seizure localization, 274 electrodes) ($P = 0.010$). Voges *et al*.[9] retrospectively evaluated serious adverse events during the first 30 postoperative days after stereotactic surgery for DBS performed in 1183 patients from 5 German stereotactic centers. They found that ICH occurred more frequently in patients aged ≥60 years (16/26) than in younger patients aged <60 years (10/26 patients). However, Binder *et al*.[10] found no statistically significant relationship between the risk of hematoma and patient age among 481 lead implantations; other authors have reported similar results.[11,12] In the present study, age was associated with cerebral vascular injury ($P = 0.039$), but in ≥60-year-old patients, hemorrhage more easily occurred in the cortex and the puncture channel (5 patients, $P = 0.016$). Deep ICH (2 patients, $P = 1.000$) and infarction (0 patients, $P = 0.527$) were not associated with age. We concluded that elder patients are more prone to cerebrovascular amyloidosis involving the cerebral cortex of small arteries, arteries, arterioles, and capillaries. Guide tubes damaged the cerebral vasculature in patients with amyloidosis and increased the rate of hemorrhage. Elder patients are more likely to have cerebral atrophy, and cerebrospinal fluid is easily lost after cutting of the dura mater, resulting in shifting of the brain. The planned approach and practical approach often differ, resulting in the guide tube being mistakenly advanced into the sulcus and increasing the risk of damage to the sulcus vessels.

With respect to the association between cerebral vascular injury and MER, whether the use of MER increases the incidence of ICH remains controversial. Some reports have suggested that there is no significant relationship between hemorrhage and MER;[8,13] however, other reports have reached the opposite conclusion, showing a statistically significant correlation between hemorrhage and MER.[1,14] Kimmelman *et al*.[12] analyzed 109 studies (6237 patients and 9890 trajectories to deep nuclei) and found a significant positive relationship between MER and ICH; the estimated per-trajectory ICH rate was 1.57% (95% confidence interval, 1.26–1.95%)[12] In the present study, the application of intraoperative MER significantly increased the risk of vascular injury. Vascular accidents occurred in all patients who underwent MER ($P = 0.000$), especially those with ICH ($P = 0.002$). However, compared with the performance of one MER, the performance of more than two MERs did not increase the rate of vascular injury ($P = 0.335$).

With respect to the association between deep ICH (basal ganglia and target areas) and multi-channel MER, few reports have addressed whether multi-channel MER increases the risk of ICH. Tonge *et al*.[11] reported that in a comparison of multiple MER electrodes versus a single electrode, multiple electrodes did not increase the risk of ICH. In the present study, however, ICH was observed in 3 (2.59%) of 116 patients with single-channel MER and 2 (22.22%) of nine patients with multi-channel MER, and comparison between these two groups showed that multi-channel MER distinctly increased the risk of deep ICH ($P = 0.044$). We conclude that multi-channel MER, particularly five-channel MER, increases the volume of the cortex injured and increases the brain volume of the target region injured. The area of puncture is larger, the sulci vessels are not completely avoided, and the probability of vascular injury is increased.

The association between cerebral venous infarction and DBS was also assessed. Bleeding complications have been frequently reported in association with DBS surgery, but only four reports mentioned venous infarction[4-6] and only eight patients complicated with venous infarction have been reported. Chang *et al*.[6] analyzed the potential risk of intracranial hemorrhage in 23 patients (46 electrodes) who underwent single-track MER during DBS procedures and found that one patient developed intracranial hemorrhage that appeared to be due to venous infarction. Umemura *et al*.[15] reported that among 16 serious adverse events related to DBS surgery that occurred in 109 patients (179 electrodes), only one patient had a venous infarction. Binder *et al*.[10] reported two infarct-related cases: one was a hemorrhagic venous infarct that evolved several minutes after coagulation of a bridging vein that was interrupted during dural opening (subthalamic nucleus target), and the other was an ischemic capsular infarction that developed 1 week after subthalamic nucleus DBS. Morishita *et al*.[5] reported four cases (0.8%/lead, 1.3%/patient) of symptomatic cerebral venous infarction among 500 DBS lead implantation procedures (301 patients). The authors suggested that venous infarction commonly results from intraoperative injury to cortical veins. In the present study, two patients were complicated with venous infarction after the CT scans and exhibited minor psychiatric symptoms. Both were located in the frontal lobe, and around the lead, we found no infarction in the basal ganglia or target. We determined that the veins around the hole included cortical veins, venous sulci, and bridging veins. Any damage to the veins will result in venous hypertension and congestion secondary to obstruction of venous outflow. Venous infarction is often accompanied by local bleeding. Dural incision, coagulation of the cortex, and passage of ducts through sulci can lead to venous injury. The performance of multi-channel MER and multiple punctures with single-channel MER increases the risk of venous damage. Venous infarction always occurs in the frontal lobe, around the lead, or adjacent to the lead and always results in mild clinical symptoms without permanent loss of function.

In conclusion, patients aged ≥60 years are more likely to develop vascular injury, which more readily occurs in the cortex and puncture channel. The application of intraoperative MER significantly increases the risk of vascular injury, especially ICH. Compared with single-channel MER, multi-channel MER increases the risk of deep ICH (basal ganglia and target areas). Both arterial hemorrhage and venous infarcts are complications of DBS surgery.

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Conflicts of interest

There are no conflicts of interest.

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