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A Prospective, Randomized, Open-Label Study Comparing Recovery Characteristics between Desflurane and Sevoflurane Anesthesia in Elderly Patients Undergoing Elective Supratentorial Craniotomy

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Abstract

Background Sevoflurane and desflurane are the two commonly used volatile anesthetics and it is mandatory to comprehend their hemodynamic and recovery profiles to ensure safe administration and early recovery in elderly neurosurgical patients. The primary objective of the study was to compare the recovery profiles of sevoflurane and desflurane in elderly patients undergoing supratentorial craniotomy. The secondary outcome measures studied were intraoperative hemodynamic changes, intraoperative brain condition, and early postoperative cognition using short orientation memory concentration test (SOMCT).

Methods The prospective, open-labeled study involving 78 elderly patients undergoing elective supratentorial craniotomies randomized the subjects into sevoflurane and desflurane groups in the ratio of 1:1 (39 each). Pre- and early postoperative cognitive function of the patient was assessed using SOMCT. Time for emergence, extubation, and recovery were also compared between the groups. Hemodynamic parameters during surgery and brain relaxation were recorded. Student's *t*-test was used to find the significance of study parameters on a continuous scale and chi-squared test to find the significance of study parameters on a categorical scale between two groups.

Results The mean emergence time (minutes) was found to be significantly longer in sevoflurane group as opposed to desflurane (9.44 ± 2.07 vs. 8.28 ± 2.53, $p = 0.02$). Similarly, the mean recovery time was significantly longer for sevoflurane group than desflurane (17.33 ± 3.36 vs. 15.64 ± 4.63, $p = 0.03$). A statistically significant

Keywords
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difference in pre- and early postoperative SOMCT was observed between the two groups (5.31 ± 2.89 vs. 4.33 ± 1.74, $p = 0.04$) with better early postoperative SOMCT ($p = 0.05$) in desflurane group. However, extubation time, average duration of surgery, brain relaxation, and modified Aldrete score were comparable between the groups.

Conclusion Elderly patients who received desflurane had a shorter emergence and recovery time compared with sevoflurane. Improved early postoperative SOMCT scores were noted in desflurane group.

Introduction

The growing population of elderly and the extension of life expectancy have resulted in increase in demand for surgical services and associated workload without compromising the quality of care.[1] Due to the aging-related changes, diminished physiological reserve and high prevalence of co-occurring age-related disorders, elderly patients are more susceptible to perioperative morbidity and mortality.[2,3] Stress of trauma, surgery, and anesthesia pose greater risk for geriatric patients to develop postoperative complications.[4] The use of anesthetic agents in elderly is highly challenging due to reduced cardiorespiratory reserve, underlying organ system diseases and age-related variation in pharmacokinetic and pharmacodynamic factors.[5,6] Postoperative delirium and postoperative cognitive dysfunction are the most common anesthesia-related surgery risks found in elderly.[7] The use of volatile anesthetics that are quickly removed with little metabolic breakdown may lessen postoperative delirium and cognitive dysfunction in elderly patients by promoting quicker recovery.[8] In neurosurgical patients, an early recovery helps in identifying patients with new neurological deficits and triaging patients requiring immediate evaluation or reintervention.

It has been well established that lower blood:gas partition coefficient of volatile inhalation agent improves the recovery time following surgery. Hence, desflurane with low blood: gas partition coefficient (0.42) is preferred for ambulatory anesthesia and it has the shortest recovery time of approximately 5 minutes.[9] On the other hand, the blood:gas partition coefficient of sevoflurane is 0.65 and the recovery time is around 14 minutes.[9,10] Several clinical trials have reported the efficiency of desflurane and sevoflurane anesthesia in elderly patients.[5,8,11–13] Although the use of desflurane in neurosurgical patients is debatable due to its cerebral vasodilating properties, it does not cause any variation in intracranial pressure in normocapnic adult patients undergoing removal of supratentorial tumors.[14] Although the pharmacokinetic properties of both sevoflurane and desflurane favor rapid emergence from anesthesia, several studies have reported that recovery from anesthesia has been proven to be faster for desflurane than sevoflurane.[13–16]

Despite the wider use of sevoflurane and desflurane as inhaled anesthetics for outpatient surgeries, there are very few studies comparing the effect of these two agents in elderly patients undergoing supratentorial craniotomy. The primary objective of the study was to compare the two agents in elderly patients undergoing elective supratentorial craniotomy in terms of emergence time, extubation time and recovery time. As a secondary objective, the study has compared intraoperative hemodynamic changes, intraoperative brain conditions, and postoperative cognitive function between the two groups. This study has hypothesized that desflurane could offer better recovery profile in elderly neurosurgical patients than sevoflurane.

Materials and Methods

The prospective, randomized, open-label study considered elderly neurosurgical patients who visited a Bangalore based super specialty hospital between January 2020 and June 2021. The inclusion criteria considered for patient enrolment were American Society of Anesthesiologists (ASA) physical status 1 to 3, patients more than 65 years of age, and those scheduled to undergo elective supratentorial craniotomies for extra-axial lesions/pathologies (prolonged for >2 hours). Written informed consent and approval by the institutional review board and ethics committee (MSRMC/EC/AP-59/10–2019) were obtained prior to the study. The trial has been registered under the Clinical Trial Registry of India (CTRI/2020/03/024294). Patients with Glasgow coma scale score less than 15 prior to the surgery, body mass index (BMI) more than 30, computed tomography evidence of increased intracranial pressure, intracranial aneurysm or arteriovenous malformations, history of psychiatric illness, and/or receiving neuropsychiatric drugs, history of alcohol or substance abuse, and patients who required postoperative mechanical ventilation due to any intraoperative complications were excluded from the study. The sample size calculation was based on a previous study[5] that compared elderly patients undergoing craniotomy for extubation time between the groups with a minimum difference of 0.70 minutes and common standard deviation of 1.4 minute. To attain significance, with type I error of 5%, 85% statistical power, and 95% confidence interval, 78 was the total sample size estimated for the present study (after adjusting for lost to follow-up, drop-out rate, and nonresponse rate).

The selected patients were randomly allocated to either desflurane (group D) or sevoflurane (group S) arm and their demographic characteristics were recorded. Preanesthesia checkup for baseline cognitive function was done using short

orientation memory concentration test (SOMCT, total score of 28).[17] All the selected participants were induced with propofol (dose titrated to response), fentanyl 2 µg/kg, and vecuronium 0.1 mg/kg. Following intubation, radial artery cannulation was performed for invasive blood pressure monitoring. Central venous cannulation was performed at the discretion of attending anesthetists. A nasopharyngeal probe was used to measure temperature, and warm blankets and fluids were used to maintain normothermia. All subjects received scalp block 0.2% ropivacaine, and prior to the pin insertion, the skull pin sites had been injected with 2% lignocaine. The anesthesia workstation used was the GE ET (end-tidal) control machine (Datex-Ohmeda, Inc General Electric Company Madison, United States). Air oxygen mixture and sevoflurane/desflurane were used to attain a minimum alveolar concentration (MAC) of 1.0 with flows 0.5 to 1.0 L/min. End-tidal carbon dioxide (EtCO2) was maintained between 28 and 32 mm Hg using controlled ventilation. Depth of anesthesia was monitored with patient state index using MASIMO (United States) SedLine technology and was maintained between 25 and 50. Following exposure of the skull, all patients received 100 mL of 20% mannitol intravenously. Intraoperative heart rate (HR), systolic blood pressure, diastolic blood pressure, and mean arterial pressure (MAP) were recorded at baseline (before induction), immediately following induction and intubation, once either agent had achieved MAC of 1.0, at the time of head pin application, and every 15 minutes until the inhalation agents were tapered at the end of the surgery.

After dural opening, the operating neurosurgeon, who was blinded to the study, assessed the brain condition and graded on a 4-point scale as follows: (1) perfectly relaxed, (2) satisfactory relaxation, (3) firm brain, and (4) tight brain. Interventions like corrections in head position, further reduction of EtCO2, and additional doses of mannitol were undertaken to achieve better brain condition to the satisfaction of the neurosurgeon. Levetiracetam (1 gm) was administered intravenously, whenever indicated. At the beginning of skin closure, all the patients received 1 gm of paracetamol intravenously. Subsequently, neuromuscular blockade was reversed, and trachea was extubated in accordance with conventional standards (after confirming adequate oxygenation, ventilation, hemodynamic stability, sustained 5-second head lift/hand grip, and consciousness with intact cough/gag reflex).

All the outcome variables were recorded by the lead investigator. GE Aisys workstation monitor was used to measure HR, MAP, MAC, EtCO2, SPO2, and temperature. Anesthesia recovery was evaluated by timing the emergence, extubation time, and recovery time. Emergence time was defined as the time interval between the end of the anesthetic and the eye-opening either naturally or in response to verbal cues. The interval between cessation of volatile agent and tracheal extubation was considered as tracheal extubation time. The recovery time was defined as the period between the termination of an anesthetic drug and regaining consciousness to recollect their names. Scores of brain relaxation were recorded and the postoperative recovery was assessed using the modified Aldrete score. One hour after shifting the patients to intensive care unit (ICU), cognitive function was measured by SOMCT, and differences between the two groups were assessed. A language that the patient could understand was used to translate SOMCT.

Based on the anesthesiologist's discretion, patients with MAP and HR more than 20% from baseline were treated with boluses of intravenous fentanyl, esmolol, or labetalol. MAP less than or equal to 20% from the baseline were treated with ephedrine 6 mg intravenous boluses, crystalloids, colloids, blood, or noradrenaline infusion.

Statistical Analysis

Statistical analyses were performed using SPSS 22.0, and R environment ver.3.2.2. Descriptive variables were analyzed using a Student's *t*-test or chi-squared test. Continuous variables were compared by Student's *t*-test and categorical variables by chi-squared test. Line graphs were plotted using MS Excel (2019). A *p*-value less than 0.05 was considered as statistically significant.

Results

Hundred eligible elderly patients diagnosed with supratentorial extra-axial lesions were enrolled based on inclusion and exclusion criteria. These 100 subjects were randomized into sevoflurane and desflurane groups in the ratio of 1:1 (50 each) of which 78 (39 in each group) patients were analyzed as some on them were eliminated due to various reasons. The 2010 CONSORT flow diagram depicting the patient enrolment and allocation is provided as ►**Fig. 1**.

The demographic characteristics such as age, gender, BMI, ASA scores, and preoperative SOMCT were similar in both the groups. The diagnoses noted in the selected patients were meningioma (parasagittal, frontal/temporal convexity), chronic subdural hematoma, chordoma, depressed fracture without underlying brain parenchymal involvement, and subdural empyema. There was no statistical difference with regard to patients' diagnosis between the groups (►**Table 1**).

The mean emergence time was found to be significantly longer in sevoflurane group as opposed to desflurane ($p = 0.02$). Similarly, the mean recovery time was significantly longer for sevoflurane group than desflurane ($p = 0.03$). The mean extubation time was comparable between the groups ($p = 0.09$. non-significant). Early postoperative SOMCT difference between the groups was noted to be trending toward significance ($p = 0.05$) with desflurane having better scores. Average duration of surgery, the number of patients who attained satisfactory and perfect brain relaxation, and mean modified Aldrete score were also comparable (►**Table 2**). A statistically significant difference between pre- and postoperative SOMCT was observed between the two groups ($p = 0.04$). No statistically significant difference in the intraoperative HR and MAP was noted between the groups (►**Figs. 2** and **3**).

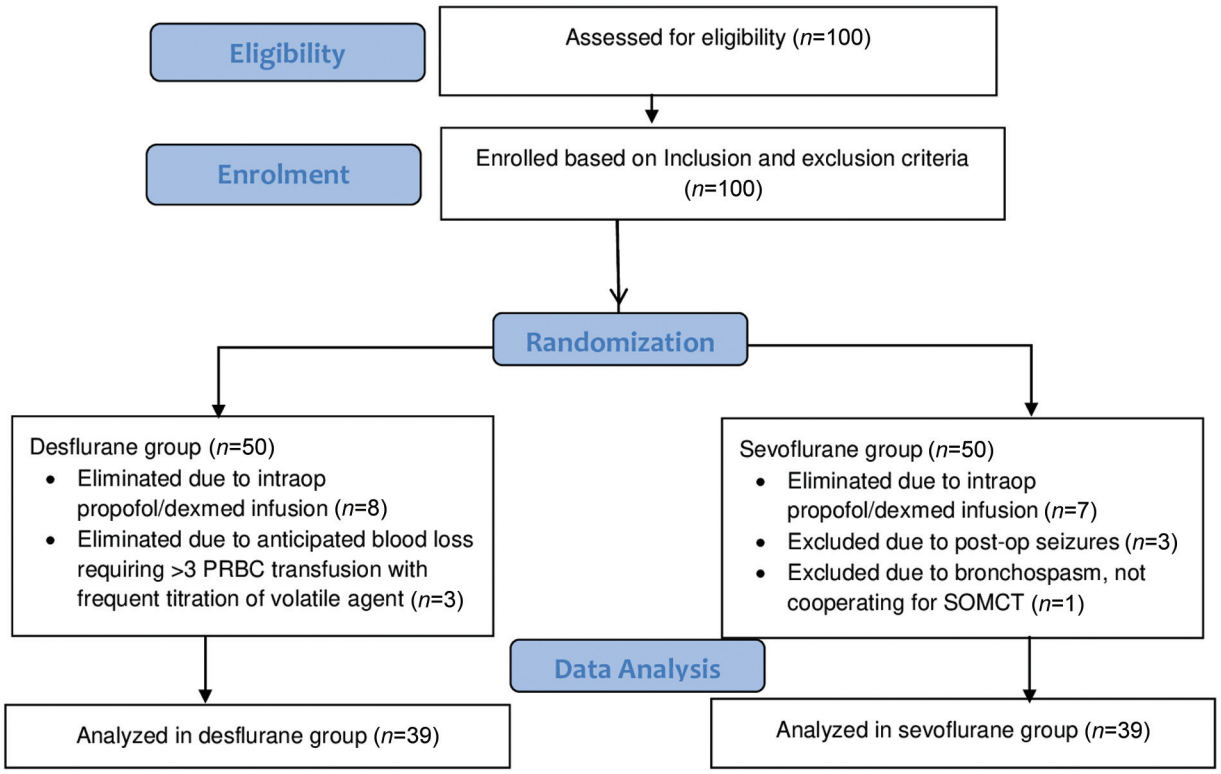

Fig. 1 The 2010 CONSORT flow diagram depicting the patient enrolment and allocation. PRBC, packed red blood cell; SOMCT, short orientation memory concentration test.

Table 1 Demographic, preoperative characteristics, and diagnoses noted in the two groups

Variables		Sevoflurane ($n = 39$)	Desflurane($n = 39$)	*p*-Value
Age (years)		69.21 ± 4.48	68.08 ± 3.56	0.11[a]
Gender (M/F)		27 (12)	23 (16)	0.48[b]
BMI (kg/m^2)		25.66 ± 3.15	25.08 ± 3.28	0.21[a]
ASA score	1	2 (5.13%)	2 (5.13%)	0.61[b]
	2	24 (61.54%)	28 (71.80%)	0.47[a]
	3	13 (33.33%)	9 (23.08%)	0.45[a]
Preoperative SOMCT		21.51 ± 3.01	21.69 ± 2.36	0.38[a]
Diagnosis	Frontal M	8 (20.51%)	7 (17.94%)	1.00[b]
	Temporal M	7 (17.94%)	4 (10.25%)	0.26[c]
	Parasagittal M	9 (23.07%)	10 (25.64%)	1.00[b]
	Chronic SDH	8 (20.51%)	10 (25.64%)	0.8[b]
	Chordoma	2 (5.13%)	3 (7.69%)	0.50[c]
	Depressed fracture	4 (10.25%)	4 (10.25%)	1.00[c]

Abbreviations: ASA, American Society of Anesthesiologists; BMI, body mass index; M, meningioma; SDH, subdural hematoma; SOMCT, short orientation memory concentration test.
[a]*t*-Test.
[b]Chi-squared test.
[c]Fisher's exact test.
$p \leq 0.05$ has been considered as significant.

Discussion

Emergence from anesthesia in elderly patients should be smooth and rapid to avoid further complications and to permit early recognition of neurological deficits or postsurgical complications. Due to the low solubility of sevoflurane and desflurane, these agents confer the advantages of better control of anesthetic depth and more rapid recovery from

Table 2 Comparison of intraoperative, postoperative, and recovery variables between the groups

Variables ($n = 78$)		Sevoflurane ($n = 39$)	Desflurane ($n = 39$)	*p*-Value
Brain relaxation	Satisfactory (%)	27 (69.23%)	28 (71.80%)	1.0[a]
	Perfect (%)	12 (30.77%)	11 (28.21%)	
Emergence time (minutes)		9.44 ± 2.07	8.28 ± 2.53	0.02[b]
Extubation time (minutes)		13.23 ± 2.88	12.23 ± 3.65	0.09[b]
Recovery time (minutes)		17.33 ± 3.36	15.64 ± 4.63	0.03[b]
Average duration of surgery (minutes)		292.31 ± 58.39	285.77 ± 80.92	0.34[b]
Postoperative SOMCT		16.21 ± 3.58	17.36 ± 2.55	0.05[b]
Difference in SOMCT		5.31 ± 2.89	4.33 ± 1.74	0.04[b]
Modified Aldrete score		9.08 ± 0.66	9 ± 0.56	0.29[b]

Abbreviation: SOMCT, short orientation memory concentration test.
[a]Chi-squared test.
[b]*t*-Test.
$p \leq 0.05$ has been considered as significant.

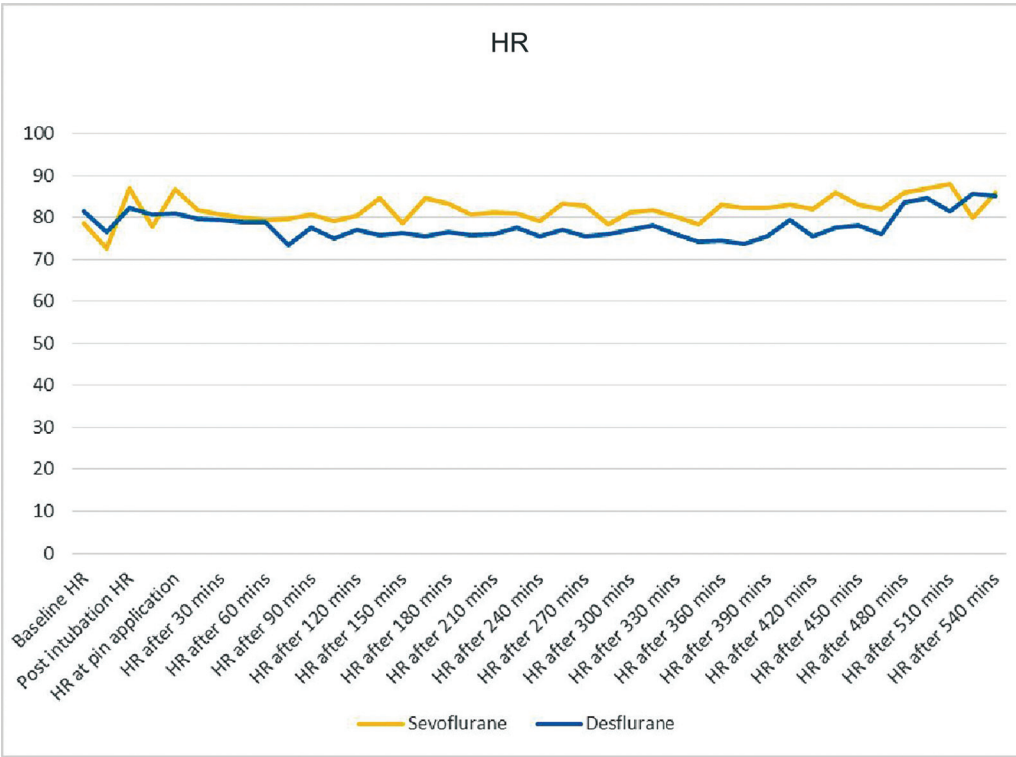

Fig. 2 Comparison of heart rate (HR) between sevoflurane and desflurane groups.

anesthesia.[18] Since desflurane has considerably lower blood: gas partition coefficient than sevoflurane, desflurane is anticipated to give an early and quick awakening from anesthesia.[19,20]

This study has noted significant difference in mean emergence time between the two groups ($p = 0.02$), shorter for desflurane than sevoflurane (8.28 ± 2.53 vs. 9.44 ± 2.07 minutes). This is in line with previous literature findings suggesting shorter emergence time for desflurane.[21,22] Nathanson et al reported significantly lesser emergence time for desflurane as opposed to sevoflurane (4.8 ± 2.4 vs. 7.8 ± 3.8 minutes) in outpatient surgeries.[21] In contrast, the study conducted by Dube et al in adult patients undergoing supratentorial craniotomy has reported that intraoperative brain condition, hemodynamics, and postoperative recovery profile were comparable for sevoflurane and desflurane (emergence time: group D 7.4 ± 2.7 minutes vs. group S 7.8 ± 3.7 minutes; $p = 0.65$).[14]

The study has also noted that the mean recovery time was significantly longer for sevoflurane group than desflurane (17.33 ± 3.36 vs. 15.64 ± 4.63, $p = 0.03$). This finding concurs with the studies by Magni et al and Dogru et al.[23,24] Magni

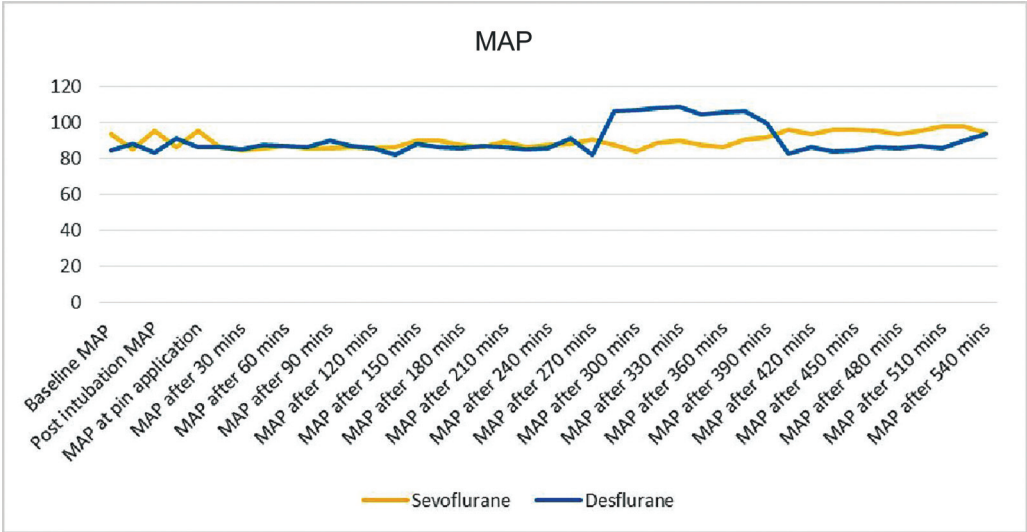

Fig. 3 Comparison of mean arterial pressure (MAP) between sevoflurane and desflurane groups.

et al have found that the mean emergence time was comparable between groups, whereas the mean extubation time and recovery time were longer for sevoflurane (15.2 ± 3.0 minutes for S vs. 11.3 ± 3.9 minutes for D and 18.2 ± 2.3 minutes for S vs. 12.4 ± 7.7 minutes for D, respectively; $p < 0.001$).[23] Dogru et al concluded that in patients undergoing hip replacement surgery, desflurane conferred significantly more rapid early recovery than sevoflurane, but there were no beneficial effects for desflurane on intermediate recovery.[24] Several other studies have also corroborated the rapid recovery time noted for sevoflurane.[16,25,26] Heavner et al have reported faster recovery time upon using desflurane in elderly patients undergoing surgical procedures requiring two or more hours of anesthesia ($p \leq 0.05$).[15]

The mean extubation time was found to be comparable between the two present study groups. A similar finding was reported by Dube et al, whereas other studies have noted that the extubation time was faster for desflurane than sevoflurane.[21–24] In clinical settings, 1 to 2 minutes difference in individual outcome parameters may not be very relevant. But the consolidated difference of 5 to 10 minutes noted with desflurane aids in early neurological assessment of elderly patients and effective usage of operation theaters in settings where case turnover is high.

The factors that may influence patient's postoperative cognition include patient's age, preoperative cognition, comorbid conditions, preoperative drugs, type of anesthetic agents used, and intraoperative events.[27] In this study, the pre and postoperative cognition function was assessed by SOMCT, which has been used extensively to study orientation levels of patients (either for comparison between pre and postoperative cognition or for screening or establishing baseline cognitive status in patients with neurological conditions).[28] This test, which is derived from the longer Blessed scale, correlates significantly ($r = 0.92$) with the latter and has comparable sensitivity. As per the scoring, score more than 20 is considered as normal.[17]

All the patients in this study had normal scores on preoperative assessment of SOMCT (>20). The postoperative cognition was evaluated only at early time point (1 hour after shifting to ICU) and it was better in desflurane group (17.36 ± 2.55 vs. 16.21 ± 3.58). Cognitive function studied at later time points would have given a clear picture, and this has been found to be comparable in both the groups in previous studies on non-neurological patients.[1,5] In clinical practice, improved early cognitive profile would help in the earlier recognition of neurological deficits.

Similar results were noted in studies by Dube et al and Magni et al in adult patients undergoing supratentorial craniotomy.[14,23] A study by Bilotta et al involving 18- to 75-year-old overweight and obese patients undergoing craniotomy reported desflurane had an earlier postoperative cognitive recovery than the sevoflurane group.[29] Similar cognitive recovery assessed by SOMCT by desflurane compared with sevoflurane was reported by Saha et al.[25] In this study, a statistically significant difference in SOMCT was observed between the two groups (5.31 ± 2.89 vs. 4.33 ± 1.74, $p = 0.04$). Although the preoperative SOMCT was comparable between the groups, the difference in SOMCT score noted could be due to comparatively lower postoperative SOMCT score observed in sevoflurane group. Brain relaxation, average duration of a surgery, and modified Aldrete score were also comparable between this study arms.

This study holds relevance in the field of neurosurgery, as there is very limited literature evidence comparing the recovery profile of these two volatile anesthetics in elderly neurosurgical population. Moreover, the power of the study (85%) is good to draw valuable conclusions. This study has certain limitations. The study findings are less generalizable due to the single-center study design. Though the study design was open label randomized, there was no influence of physician's assessment or opinion on parameters, as they were objective. The time of discontinuation of the inhalational agent was left to the discretion of the attending anesthesiologist and was not standardized. The effect of

postoperative hemodynamic variations on the postoperative SOMCT within the same group or between the groups was not assessed.

Conclusion

In conclusion, patients who received desflurane had a shorter emergence, recovery time, and better early cognitive function compared with sevoflurane, but intraoperative traits were similar in both the groups. The rapid emergence and recovery from anesthesia may enable conducting earlier neurological examination in elderly neurosurgical population and more effective usage of the operating room.

Conflict of Interest
None declared.

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