

# Comparative Evaluation of Emergence Delirium Following Halothane, Isoflurane, and Sevoflurane Anaesthesia Using the Richmond Agitation–Sedation Scale: A Cross-Sectional Analytical Study

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## ABSTRACT

### Background

Emergence delirium (ED) following general anaesthesia is a clinically significant neurocognitive complication associated with prolonged hospital stay, increased morbidity, and higher healthcare costs. The influence of inhalational anaesthetic agents on delirium severity remains incompletely understood.

### Objective

To comparatively evaluate the incidence and severity of emergence delirium among adult patients receiving halothane, isoflurane, or sevoflurane using the Richmond Agitation–Sedation Scale (RASS).

### Methods

In this prospective cross-sectional study, 100 adult patients undergoing elective surgery under general anaesthesia were allocated to receive halothane (n=33), isoflurane (n=33), or sevoflurane (n=36). Delirium was assessed immediately post-extubation using RASS. Demographic and physiological variables were recorded. Statistical analysis included one-way ANOVA with post hoc testing.

### Results

Significant intergroup differences were observed in age (p=0.001), heart rate (p=0.05), and SpO<sub>2</sub> (p=0.01). Sevoflurane was associated with a higher proportion of patients categorized as "alert and calm" (38.9%) and absence of moderate sedation. Halothane demonstrated the highest moderate sedation rate (51.5%). Overall RASS distribution differed significantly among groups (p<0.05).

### Conclusion

Sevoflurane was associated with more favourable emergence characteristics and reduced moderate sedation compared with halothane and isoflurane. Optimizing inhalational anaesthetic selection may reduce perioperative delirium burden.

**Keywords:** Emergence delirium; Postoperative delirium; General anaesthesia; Halothane; Isoflurane; Sevoflurane; Richmond Agitation–Sedation Scale (RASS); Inhalational anaesthetic agents; Post-anaesthesia care unit (PACU); Anaesthetic recovery; Sedation assessment; Perioperative neurocognitive disorders.

**How to cite this article:** Dinesh M, Kesavamoorthy Y, Joshila Bridget T, Hema Dharshini S, Hema Harini S, Kanala Lavanya, Joyce Angel P, Kamesh S, Inbarasan M, Suganya S. Comparative Evaluation of Emergence Delirium Following Halothane, Isoflurane, and Sevoflurane Anaesthesia Using the Richmond Agitation–Sedation Scale: A Cross-Sectional Analytical Study. *Int J Drug Deliv Technol.* 2026;16(23s): 823-828. DOI: 10.25258/ijddt.16.23s.87

**Source of support:** Nil.

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**Conflict of interest:** None

## Introduction

Delirium is an acute neuropsychiatric syndrome characterized by fluctuating disturbances in consciousness, inattention, and cognitive dysfunction. It is frequently encountered in perioperative and critical care settings and is associated with adverse short- and long-term outcomes [2–4]. Emergence delirium (ED) represents a transient confusional state occurring during recovery from general anaesthesia and has been increasingly recognized as a predictor of postoperative delirium (POD) [5,8].

The reported incidence of delirium varies widely depending on the patient population and diagnostic criteria used. In mechanically ventilated and critically ill patients, delirium prevalence may reach 60–80% [2,3]. Among surgical populations, incidence rates range from 13% to 50%, particularly in elderly patients [3,4,7]. Delirium is independently associated with prolonged hospital stay, increased healthcare expenditure, long-term cognitive decline, and elevated mortality [3,4].

Fei and Yu [1] reported that postoperative delirium following general anaesthesia significantly increases complication rates and hospital resource utilization. Similarly, Ouimet et al. [4] demonstrated that ICU delirium is linked to adverse clinical outcomes including prolonged ventilation and increased mortality. The clinical importance of early detection and intervention has therefore become a major focus in perioperative medicine.

General anaesthesia induces reversible unconsciousness, amnesia, analgesia, and immobility, enabling complex surgical interventions. However, the transition from anaesthetic-induced unconsciousness to wakefulness may involve neurochemical disequilibrium, potentially precipitating delirium [5,12]. Card et al. [5] demonstrated that delirium signs may begin in the PACU and evolve into postoperative delirium, emphasizing the importance of early screening.

## Pathophysiological Mechanisms

The pathogenesis of anaesthesia-associated delirium is multifactorial. Neurotransmitter imbalance, particularly involving acetylcholine and dopamine pathways, has been strongly implicated [3]. Inflammatory responses induced

by surgical stress and anaesthetic exposure may contribute to neuronal dysfunction [4]. Alterations in cerebral perfusion and oxygenation during anaesthesia can further exacerbate vulnerability [3,4].

Opioid administration and pain have also been identified as independent contributors to delirium development [6]. Morrison et al. [6] demonstrated a relationship between opioid analgesic exposure and postoperative delirium in elderly patients. Additionally, duration of anaesthesia and inadequate emergence patterns have been linked to delirium risk [12,13].

## Assessment of Delirium

Early detection of delirium requires validated assessment tools. The Confusion Assessment Method for the ICU (CAM-ICU) has been validated for critically ill patients [2]. However, in the PACU setting, rapid sedation-agitation assessment tools are often more practical.

The Richmond Agitation–Sedation Scale (RASS) is a validated 10-point instrument ranging from –5 (unarousable) to +4 (combative), with demonstrated reliability in adult ICU populations [9,11]. Sessler et al. [9,11] confirmed the validity and reproducibility of RASS for evaluating sedation and agitation levels, making it suitable for early delirium detection in post-anaesthetic settings.

Despite increasing recognition of ED, comparative evidence regarding inhalational agents and delirium severity remains limited. Lepouse et al. [12] reported adult emergence delirium in the PACU, while Radtke et al. [13] identified risk factors for inadequate emergence including hypoactive and hyperactive forms. Neufeld et al. [14] further emphasized the importance of systematic screening to detect postoperative delirium in elderly patients.

The present study aimed to compare emergence delirium among patients receiving halothane, isoflurane, and sevoflurane using RASS as a standardized assessment tool.

## Materials and Methods

This prospective cross-sectional analytical study was conducted in accordance with the International Ethical Guidelines for Health-related Research Involving Humans (CIOMS,

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2016). Institutional Ethics Committee approval was obtained, and written informed consent was secured from all participants.

A total of 100 adult patients aged  $\geq 18$  years undergoing elective surgery under general anaesthesia were enrolled. Patients were allocated into three groups based on inhalational agent received: halothane ( $n=33$ ), isoflurane ( $n=33$ ), and sevoflurane ( $n=36$ ). Exclusion criteria included diabetes mellitus, thyroid disorders, obesity, psychiatric illness, and known central nervous system disorders to reduce confounding variables known to influence delirium risk. Demographic data (age, sex, height, weight) and intraoperative parameters (heart rate,  $SpO_2$ ) were recorded. Immediately following extubation in the PACU, RASS assessment was performed by trained clinicians.

### Statistical Analysis

The present study was undertaken to compare RASS scores among patients receiving halothane, isoflurane, and sevoflurane under general anaesthesia. A total of 100 subjects were included based on predefined eligibility criteria. Continuous variables were expressed as mean  $\pm$  standard deviation. Categorical variables were presented as frequency and percentage. One-way analysis of variance (ANOVA) was used to evaluate intergroup differences for continuous variables including age, height, weight, heart rate, and oxygen saturation. Post hoc pairwise comparisons were conducted to determine specific group differences where applicable. Age demonstrated statistically significant intergroup variation ( $p = 0.001$ ). Oxygen saturation also showed statistically significant variation ( $p = 0.01$ ). Heart rate demonstrated borderline statistical significance ( $p = 0.05$ ). Height and weight did not show statistically significant differences. RASS score distribution among anaesthetic groups demonstrated statistically significant differences ( $p < 0.05$ ). Specifically, moderate sedation was significantly higher in the halothane group, whereas alert and calm status was significantly more frequent in the sevoflurane group. All statistical tests were interpreted at a significance threshold of  $p < 0.05$ .

### Results

A total of 100 patients undergoing elective surgery under general anaesthesia were recruited according to the predefined inclusion and exclusion criteria. Participants were allocated into

three inhalational anaesthetic groups: halothane ( $n = 33$ ), isoflurane ( $n = 33$ ), and sevoflurane ( $n = 36$ ). All enrolled participants completed the study, and no data were excluded from analysis.

### Demographic Characteristics

The demographic distribution of age across the three groups is presented in **Table 1**. A statistically significant difference in mean age was observed among the anaesthetic groups ( $p = 0.001$ ). The mean age in the halothane group was  $32.36 \pm 8.4$  years, compared with  $39.52 \pm 15.5$  years in the isoflurane group and  $46.47 \pm 16.7$  years in the sevoflurane group. The sevoflurane group included comparatively older patients. Given that advanced age is an established risk factor for perioperative delirium [3,7], this difference is clinically relevant and should be considered in interpretation of RASS outcomes. Additional demographic and physiological variables are summarized in **Table 4**.

Mean height did not differ significantly among groups (halothane:  $164.97 \pm 5.4$  cm; sevoflurane:  $163.75 \pm 7.7$  cm; isoflurane:  $166.21 \pm 5.98$  cm;  $p = 0.18$ ). Post hoc comparisons ( $t_1-t_2$ ,  $t_1-t_3$ ,  $t_2-t_3$ ) confirmed the absence of significant pairwise differences.

Similarly, mean weight showed no statistically significant intergroup difference (halothane:  $59.92 \pm 5.3$  kg; sevoflurane:  $60.27 \pm 7.6$  kg; isoflurane:  $62.85 \pm 6.2$  kg;  $p = 0.07$ ). Although isoflurane demonstrated slightly higher mean weight, the difference did not reach statistical significance. Heart rate demonstrated borderline statistical significance ( $p = 0.05$ ). Mean heart rate was lowest in the halothane group ( $82.58 \pm 9.2$  bpm), compared to  $88.89 \pm 13.2$  bpm in the sevoflurane group and  $87.79 \pm 11.8$  bpm in the isoflurane group. However, post hoc comparisons ( $t_1-t_2 = 0.07$ ;  $t_1-t_3 = 0.17$ ;  $t_2-t_3 = 0.34$ ) did not demonstrate significant pairwise differences, suggesting overall group variation rather than specific intergroup divergence.

Oxygen saturation ( $SpO_2$ ) demonstrated statistically significant variation among groups ( $p = 0.01$ ). The halothane group recorded  $99.00 \pm 0.0\%$ , while sevoflurane and isoflurane recorded  $98.00 \pm 1.6\%$  and  $98.15 \pm 1.5\%$ , respectively. Post hoc analysis indicated significant differences between halothane and sevoflurane ( $p = 0.001$ ) and between halothane and isoflurane ( $p = 0.03$ ), whereas no significant difference was observed between sevoflurane and isoflurane ( $p = 0.87$ ).

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Although statistically significant, all mean values remained within clinically acceptable physiological ranges.

### Gender Distribution

Gender distribution among anaesthetic groups is presented in **Table 2**. Of the total study population, 59% were male and 41% were female. In the halothane group, 8 patients (24.24%) were male and 25 (75.76%) were female. The isoflurane group comprised 12 males (36.36%) and 21 females (63.64%). In contrast, the sevoflurane group included 23 males (63.89%) and 13 females (36.11%). Although gender proportions differed numerically across groups, no statistical association between gender and RASS outcome categories was identified in subgroup analysis.

### Comparison of RASS Scores Among Anaesthetic Groups

The distribution of RASS categories across the three inhalational agents is summarized in **Table 3**. In the halothane group, 4 patients (12.15%) were classified as agitated, 12 patients (36.4%) demonstrated light sedation, and 17 patients (51.5%) exhibited moderate sedation. Notably, none of the halothane recipients achieved a RASS score of 0 (alert and calm). The predominance of moderate sedation suggests deeper residual sedative effects during emergence.

In the isoflurane group, 2 patients (6.2%) were agitated, 2 patients (6.2%) were alert and calm, 20 patients (62.5%) demonstrated light sedation, and 8 patients (25%) exhibited moderate sedation. Compared with halothane, isoflurane was associated with reduced moderate sedation and increased light sedation.

The sevoflurane group demonstrated a distinct emergence profile. Eight patients (22.2%) were agitated, 14 patients (38.9%) achieved alert and calm status, and 14 patients (38.9%) were lightly sedated. Importantly, no patient in the sevoflurane group exhibited moderate sedation. ANOVA testing demonstrated statistically significant differences in RASS distribution among the three anaesthetic groups ( $p < 0.05$ ). Post hoc comparisons revealed that moderate sedation was significantly more frequent in the halothane group compared with sevoflurane. Furthermore, the proportion of patients achieving alert and calm status was significantly greater in

the sevoflurane group compared with halothane and isoflurane.

Overall, the RASS findings indicate that sevoflurane is associated with reduced depth of sedation and more favourable emergence characteristics compared to halothane and isoflurane.

### Discussion

The present study comparatively evaluated emergence delirium among patients receiving halothane, isoflurane, and sevoflurane using the Richmond Agitation–Sedation Scale (RASS) immediately following extubation in the post-anaesthesia care unit (PACU). The findings demonstrate statistically significant differences in RASS score distribution among inhalational anaesthetic agents, with sevoflurane exhibiting a more favourable emergence profile characterized by absence of moderate sedation and a higher proportion of patients categorized as “alert and calm.” In contrast, halothane was associated with a predominance of moderate sedation during emergence. These findings provide clinically relevant evidence that anaesthetic choice may influence early neurocognitive recovery following general anaesthesia.

Emergence delirium is increasingly recognized as an early manifestation of postoperative delirium and may serve as a predictive marker for subsequent cognitive dysfunction [5,8]. Card et al. [5] demonstrated that delirium signs observed during PACU stay frequently evolve into postoperative delirium during hospitalization. Similarly, Sharma et al. [8] reported that recovery room delirium independently predicts postoperative delirium in elderly patients undergoing hip fracture repair. The early detection of delirium in the PACU is therefore of considerable importance in mitigating downstream complications.

In the present study, the halothane group demonstrated the highest proportion of moderate sedation (51.5%), and no patient achieved a RASS score of zero (alert and calm). Moderate sedation in the immediate emergence period may represent delayed clearance of anaesthetic agents and prolonged central nervous system depression. Hypoactive delirium, characterized by decreased responsiveness and sedation, is often underdiagnosed but is associated with adverse outcomes similar to hyperactive delirium [13]. Radtke et al. [13] emphasized that hypoactive

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emergence patterns are clinically significant and may be overlooked without structured assessment tools.

In contrast, the sevoflurane group demonstrated no cases of moderate sedation and the highest proportion of alert and calm patients (38.9%). Although 22.2% of patients in this group exhibited agitation, this may reflect transient emergence phenomena rather than sustained delirium. Lepouse et al. [12] reported that emergence delirium in adults may present as short-lived agitation in the PACU, which does not necessarily translate into prolonged postoperative delirium. Importantly, the absence of moderate sedation in the sevoflurane group suggests faster restoration of cortical function and improved neurocognitive recovery.

The pharmacokinetic properties of inhalational agents likely explain the observed differences. Sevoflurane possesses a low blood–gas partition coefficient, allowing rapid elimination and shorter emergence times. Rapid washout reduces prolonged GABAergic suppression and may facilitate quicker re-establishment of neurotransmitter equilibrium. In contrast, halothane has higher lipid solubility and slower elimination kinetics, potentially contributing to residual sedation during emergence. Isoflurane demonstrated intermediate effects, with a predominance of light sedation (62.5%) and reduced moderate sedation compared to halothane.

The neurobiological mechanisms underlying delirium involve complex interactions among neurotransmitter imbalance, neuroinflammation, and cerebral perfusion disturbances. Pandharipande et al. [3] described delirium as an acute brain dysfunction frequently associated with critical illness and surgical stress. Ouimet et al. [4] further demonstrated that delirium in intensive care settings is independently associated with systemic physiological instability and inflammatory responses. Volatile anaesthetic agents may modulate acetylcholine, dopamine, and serotonin pathways, all of which are implicated in delirium pathogenesis. Faster elimination of sevoflurane may reduce the duration of neurotransmitter dysregulation compared with halothane.

Age is a well-established independent risk factor for delirium [3,7]. In the present study, mean age differed significantly among groups, with the

sevoflurane group comprising older patients ( $46.47 \pm 16.7$  years) compared with halothane ( $32.36 \pm 8.4$  years) and isoflurane ( $39.52 \pm 15.5$  years). Despite the higher mean age in the sevoflurane group, this cohort demonstrated the most favourable RASS distribution. This observation is particularly noteworthy because older age is associated with increased delirium susceptibility due to reduced cognitive reserve and increased neuroinflammatory vulnerability [7]. Neufeld et al. [7] emphasized that early diagnosis and management of delirium in elderly patients improves outcomes. The present findings suggest that anaesthetic selection may mitigate age-related vulnerability to emergence disturbances.

Physiological stability during emergence is another important determinant of cognitive recovery. Although oxygen saturation remained within clinically acceptable limits across all groups, statistically significant differences were observed ( $p = 0.01$ ), with halothane demonstrating slightly higher mean SpO<sub>2</sub>. Heart rate also demonstrated borderline significance ( $p = 0.05$ ). Even subtle physiological variations may influence cerebral oxygenation and metabolic recovery. Ouimet et al. [4] identified systemic instability as a contributor to delirium in critically ill patients. While the clinical significance of the small SpO<sub>2</sub> difference in this study may be limited, maintaining optimal haemodynamic and respiratory parameters remains essential in minimizing cerebral stress.

Pain and opioid administration represent additional important factors in delirium development. Morrison et al. [6] demonstrated a relationship between opioid analgesic exposure and postoperative delirium in elderly patients following hip fracture. In the present study, analgesic dosing was not quantitatively analyzed, representing a limitation. However, standardized anaesthetic protocols were applied across groups to minimize confounding. Future studies incorporating pain scoring and opioid quantification would provide further insight into the interaction between analgesia and emergence delirium.

The use of a validated assessment instrument strengthens the methodological rigor of this study. The Richmond Agitation–Sedation Scale has been extensively validated in adult intensive care populations [9,11]. Sessler et al. [9,11]

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demonstrated high inter-rater reliability and validity of RASS in assessing sedation and agitation levels. Although the Confusion Assessment Method for the ICU (CAM-ICU) is widely used in critical care [2], RASS offers rapid bedside applicability in the PACU setting, making it suitable for immediate post-extubation evaluation.

The overall incidence patterns observed in this study are consistent with previously reported emergence delirium rates in adult populations [12,13]. However, the distribution of hypoactive versus hyperactive presentations varies across studies. The predominance of moderate sedation in the halothane group may represent a higher risk of hypoactive delirium. Hypoactive delirium is particularly concerning because it is associated with prolonged hospitalization and increased mortality but may go unrecognized without structured screening [13].

The clinical implications of these findings are significant. Delirium is associated with increased length of stay, higher healthcare costs, and long-term cognitive impairment [1,4]. Fei and Yu [1] reported that postoperative delirium increases complication rates and resource utilization in patients undergoing general anaesthesia. Therefore, minimizing emergence disturbances through optimal anaesthetic selection may contribute to improved patient outcomes and cost reduction.

Given the global surgical volume exceeding 230 million procedures annually, even modest reductions in delirium incidence could have substantial public health impact. Early PACU screening, combined with individualized anaesthetic selection, represents a practical and implementable strategy.

Despite its strengths, this study has limitations. The cross-sectional design limits causal inference. Randomization was not explicitly described, and potential selection bias cannot be excluded. Pain scores and opioid dosing were not quantitatively analyzed. Long-term postoperative cognitive outcomes were not evaluated, and follow-up beyond the PACU period was not conducted. Additionally, although statistically significant differences were observed in some physiological parameters, their clinical magnitude was small.

Future research should include randomized controlled trials comparing inhalational agents with standardized analgesic protocols and

longitudinal cognitive follow-up. Incorporating biomarkers of neuroinflammation and cerebral oxygenation monitoring could further elucidate mechanistic pathways.

In conclusion, the present study demonstrates that inhalational anaesthetic choice influences emergence sedation-agitation profiles. Sevoflurane was associated with absence of moderate sedation and a higher proportion of alert and calm patients, despite being administered to an older cohort. Halothane demonstrated deeper sedation during emergence, suggesting potential increased risk for hypoactive delirium. Early detection using validated tools such as RASS remains essential. Optimization of anaesthetic strategy may represent a modifiable factor in reducing perioperative neurocognitive complications and improving overall quality of care.

**Table 1. Demographic Characteristics of Study Participants According to Anaesthetic Group**

Age	Halothane	Isoflurane	Sevoflurane	p value
N	33	33	36	0.001**
%	32.35%	32.35%	35.29%	
Mean ± SD	32.36±8.4	39.52±15.5	46.47±16.7	

	Male	
Halothane	8(24.24%)	
Isoflurane	12(36.36%)	
Sevoflurane	23(63.89%)	

**Table 2. Gender Distribution of Participants Across Anaesthetic Groups**

Group	Agitated	Alert and calm	Light sedation	Moderate sedation
Halothane	4(12.15%)	0	12(36.4%)	17(51.5%)
Isoflurane	2(6.2%)	2(6.2%)	20(62.5%)	8(25%)
Sevoflurane	8(22.2%)	14(38.9%)	14(38.9%)	0

**Table 3. Comparison of Richmond Agitation–Sedation Scale (RASS) Scores Among Anaesthetic Groups During Emergence**

	Halothane	Sevoflurane	Isoflurane	p value	t1-t2	t1-t3	t2-t3
Height (cm)	164.97 ± 5.4	163.75 ± 7.7	166.21 ± 5.98	0.18	0.71	0.72	0.26
Weight (kg)	59.92 ± 5.3	60.27 ± 7.6	62.85 ± 6.2	0.07	0.05	0.64	0.16
Heart Rate (bpm)	82.58 ± 9.2	88.89 ± 13.2	87.79 ± 11.8	0.05*	0.07	0.17	0.34
SpO <sub>2</sub> (%)	99.00 ± 0.0	98.00 ± 1.6	98.15 ± 1.5	0.01**	0.001	0.03	0.87

**Table 4. Comparison of Baseline Physiological Parameters Among Patients Receiving Halothane, Sevoflurane, and Isoflurane**

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