



Comparing the effects of remifentanil with fentanyl on pain intensity, hemodynamic status and post-anesthesia complications of cataract surgery candidates

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Article info

Received: 02.04.2025

Accepted: 10.05.2025

Available Online: 11.05.2025

Checked for Plagiarism: Yes

Keywords:

Fentanyl, Remifentanil,
Hemodynamic Stability,
Anesthesia Recovery

ABSTRACT

Introduction: Opioids such as fentanyl and remifentanil are commonly used for anesthesia induction and maintenance, each with distinct pharmacokinetic and pharmacodynamic properties. This study aimed to compare their effects on hemodynamic stability, intraoperative excitability, neuromuscular blockade requirement, postoperative nausea, and recovery characteristics.

Materials and Methods: This prospective, randomized clinical trial included 400 patients, equally divided into fentanyl (n=200) and remifentanil (n=200) groups. Baseline characteristics, intraoperative hemodynamics, anesthesia recovery parameters, and postoperative complications were recorded. Data were analyzed using appropriate statistical tests, with $P < 0.05$ considered statistically significant.

Results: The remifentanil group exhibited significantly lower heart rate and blood pressure at all measured time points post-induction ($P < 0.05$). Intraoperative excitability and neuromuscular blocker requirement were higher in the remifentanil group ($P = 0.014$, $P = 0.009$). Postoperative nausea and antiemetic use were significantly higher in the fentanyl group ($P = 0.041$, $P = 0.038$). The remifentanil group had faster induction, earlier respiratory recovery, and shorter awakening time ($P < 0.05$).

Conclusion: Remifentanil ensures faster recovery with reduced postoperative nausea but causes greater hemodynamic suppression and intraoperative excitability. These findings support tailored opioid selection based on surgical needs and patient-specific factors.

Introduction

Cataract surgery is one of the most commonly performed ophthalmic procedures worldwide, significantly improving vision and quality of life in affected patients. Although generally considered a minimally invasive surgery, appropriate anesthetic management remains crucial to ensuring patient comfort, hemodynamic stability, and optimal surgical conditions (1).

Given the short duration of cataract procedures, anesthetic agents with rapid onset and offset, stable hemodynamic profiles, and minimal postoperative complications are preferred. Among the most commonly used opioids in this setting, remifentanil and fentanyl offer distinct pharmacological properties that may differentially impact intraoperative pain intensity, hemodynamic responses, and post-anesthetic recovery (2).

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Understanding these differences is essential to optimizing patient outcomes and minimizing perioperative risks.

Remifentanyl, an ultra-short-acting μ -opioid receptor agonist, is known for its rapid metabolism by nonspecific plasma and tissue esterases, leading to a swift recovery profile. This characteristic makes it particularly suitable for procedures requiring precise titration of analgesia with minimal residual effects (3). In contrast, fentanyl, a potent opioid with a longer duration of action, is frequently used in various surgical settings due to its reliable analgesic efficacy. However, its prolonged half-life can contribute to delayed recovery, respiratory depression, and postoperative nausea and vomiting (PONV). The choice between these two opioids in cataract surgery can significantly influence perioperative hemodynamic stability, patient comfort, and the incidence of post-anesthesia complications (4).

Pain intensity during cataract surgery is a crucial factor in determining the adequacy of intraoperative analgesia. While regional anesthesia techniques, such as topical or peribulbar anesthesia, are commonly employed, supplemental systemic opioids are often required to manage discomfort and anxiety(5). Remifentanyl's rapid onset allows for quick analgesic effects, potentially reducing intraoperative pain intensity more effectively than fentanyl. However, due to its short half-life, continuous infusion is necessary to maintain adequate analgesia. Fentanyl, with its longer duration, may provide more sustained pain relief but at the cost of prolonged postoperative effects, which could influence early recovery and patient discharge times (6).

Hemodynamic stability is another critical concern during cataract surgery, especially in elderly patients who often have comorbidities such as hypertension or cardiovascular disease. Sharp fluctuations in blood pressure and heart rate can lead to intraoperative complications, including ocular perfusion disturbances and increased surgical complexity(7). Remifentanyl, due to its potent but short-lived hypotensive effects, may lead to transient drops in blood pressure, necessitating careful titration. Fentanyl, while also capable of inducing hemodynamic changes, has a more prolonged and stable effect, which might be beneficial in patients prone to intraoperative fluctuations. However, excessive sedation or respiratory depression associated with fentanyl can pose additional risks, particularly in an ambulatory surgical setting (8).

Post-anesthesia recovery is a key determinant of overall surgical success, particularly in outpatient procedures like cataract surgery, where rapid discharge is desired. The short elimination half-life of remifentanyl facilitates quicker emergence from anesthesia, potentially allowing for earlier

ambulation and discharge. Conversely, fentanyl's lingering sedative and respiratory depressive effects may prolong the recovery period, increasing the likelihood of postoperative drowsiness, nausea, and delayed hospital discharge(9). Furthermore, the potential for opioid-induced hyperalgesia (OIH) following remifentanyl administration is a subject of ongoing research. Some studies suggest that remifentanyl may paradoxically increase postoperative pain sensitivity, necessitating additional analgesia during the recovery period(10). Complications associated with opioid use in cataract surgery extend beyond pain management and hemodynamic control. PONV, a common concern in ambulatory surgery, is influenced by the choice and dose of opioid analgesics. Remifentanyl, due to its rapid clearance, is less likely to contribute to prolonged nausea and vomiting compared to fentanyl, which has a higher propensity for emetogenic effects. Additionally, respiratory depression remains a critical safety concern, particularly in elderly patients with pre-existing pulmonary conditions (11). While both drugs can induce respiratory depression, fentanyl's longer half-life increases the duration of risk, necessitating careful postoperative monitoring.

The selection of an optimal opioid for cataract surgery must therefore be guided by a balanced consideration of analgesic efficacy, hemodynamic stability, and postoperative recovery profile (12). While remifentanyl offers rapid-onset analgesia with a favorable recovery profile, it requires continuous infusion and careful monitoring to prevent abrupt hemodynamic changes. Fentanyl, though more familiar to many anesthesiologists, may prolong recovery due to its residual sedative effects, necessitating a tailored approach based on patient-specific factors (13).

Several clinical studies have sought to compare the efficacy and safety of remifentanyl and fentanyl in ophthalmic surgeries, though findings remain variable. Some reports suggest that remifentanyl provides superior intraoperative pain control and faster recovery, while others highlight concerns regarding post-anesthetic hyperalgesia (14). Conversely, fentanyl's longer-acting analgesia may be beneficial in select patient populations, though at the cost of increased postoperative sedation. Given these nuances, further research is warranted to establish definitive guidelines on the optimal opioid regimen for cataract surgery patients (15).

In conclusion, the comparative evaluation of remifentanyl and fentanyl in cataract surgery is essential for refining anesthetic protocols and enhancing patient outcomes. By examining their respective effects on pain intensity, hemodynamic status, and post-anesthesia complications, clinicians can make more informed decisions tailored to the specific needs of each patient (16). Future studies should focus on individualized opioid dosing

strategies, multimodal analgesic approaches, and risk stratification to optimize perioperative care in cataract surgery candidates.

This study aims to provide a comprehensive analysis of the differential effects of remifentanyl and fentanyl in cataract surgery, contributing to the evolving landscape of anesthetic management in ophthalmic procedures. Through a systematic comparison of these opioids, this research will offer valuable insights into best practices for ensuring safe, effective, and patient-centered anesthesia care.

Material and methods

Study Design: This study was conducted as a randomized, double-blind, prospective clinical trial during the year 2023, involving patients undergoing cataract surgery at Nikookari Hospital. A total of 400 patients with a confirmed diagnosis of cataract who were hospitalized at Nikookari Hospital (affiliated with Tabriz University of Medical Sciences) and scheduled for cataract surgery were included in the study.

Inclusion Criteria

- Willingness to participate in the study and provision of written informed consent
- Candidates for elective cataract surgery
- Age over 18 years
- American Society of Anesthesiologists (ASA) classification I or II

Exclusion Criteria

- Patients younger than 18 years
- Patients with severe valvular heart disease
- Patients with known hypersensitivity to fentanyl or remifentanyl
- Patients with bradycardia
- Patients receiving antihypertensive medications
- Patients with hepatic or renal impairment

Sampling Method: A convenience sampling method was employed, wherein 400 patients meeting the inclusion and exclusion criteria were consecutively enrolled in the study.

Sample Size: The sample size was estimated using the standard formula for sample size determination. Considering a 90% confidence interval, a 10% margin of error, and the prevalence of cataract increasing with age (notably from 45 years and above), the required sample size was calculated to be 385. To enhance study power, a total of 400 patients were included.

Randomization and Blinding: Patients were randomly assigned into two groups of 200 each using the online software WWW.Randomize.org. Two study groups were predefined, and each eligible patient was assigned to one of them through this online randomization tool. Due to the nature of

the intervention, the anesthesiologist performing the procedure was aware of the administered drug, preventing full blinding on their part. However, the research intern responsible for recording study outcomes and the statistical consultant analyzing the results remained blinded to group allocation and drug type, ensuring a double-blind study design.

Study Procedure: Patients were randomly assigned to either the fentanyl group (Abidi Pharmaceutical Company) or the remifentanyl group (Abidi Pharmaceutical Company). For both groups, induction was performed using propofol, and anesthesia maintenance was achieved with 1% isoflurane (Sobhan Pharmaceutical Company). In the fentanyl group, atracurium (Abidi Pharmaceutical Company) was used as a muscle relaxant, whereas in the remifentanyl group, no muscle relaxant was administered. In the fentanyl group, after the return of spontaneous respiration, patients were reversed using neostigmine (Imen Daru Pharmaceutical Company) and atropine (Imen Daru Pharmaceutical Company).

For induction in the fentanyl group, the following regimen was used:

- Midazolam (1 mg) (Abidi Pharmaceutical Company)
- Fentanyl (0.7 µg/kg)
- Propofol (1–2 mg/kg) (Abidi Pharmaceutical Company)
- Lidocaine (1 mg/kg) (Pharmatek Pharmaceutical Company)
- Atracurium (10 mg)

For induction in the remifentanyl group, the regimen included:

- Midazolam (1 mg)
- Remifentanyl (2–4 µg/kg)
- Propofol (1–2 mg/kg)
- Lidocaine (1 mg/kg)

The induction time and postoperative complications in the recovery room were recorded alongside demographic data. Notably, a laryngeal mask airway (LMA) was used for airway management in all patients.

It is important to note that both remifentanyl and fentanyl are routinely used and widely accepted anesthetic agents, with no inherent superiority of one over the other. Both drugs may cause hypotension and bradycardia; however, these effects can be mitigated by dose adjustments based on patient weight. Any observed adverse effects were promptly managed by the research team using vasopressor agents.

Data Analysis

Data, including age, gender, comorbidities, and other recorded variables, were entered into SPSS version 20 for statistical analysis. The normality of data distribution was assessed initially. If normally distributed, descriptive statistics, including mean,

median, standard deviation, and mode, were calculated. If data were not normally distributed, the interquartile range (25th to 75th percentile) and median values were reported.

To evaluate associations between variables, linear regression analysis was performed. For group comparisons, if data were normally distributed, an independent t-test was used for continuous variables, and chi-square analysis was applied for categorical variables. If normality assumptions were not met, the Kruskal-Wallis test was used for statistical comparisons.

Ethical Considerations

- Ethical approval was obtained from the Regional Ethics Committee (Code: IR.TBZMED.REC.1402.420, dated September 4, 2023).
- The study was registered in the Iranian Clinical Trial Registry (IRCT Code: IRCT20190325043107N35).
- Institutional approval was secured from Nikookari Hospital for study implementation.

- Study objectives were explained to all participants.
- Written informed consent was obtained from all participants.
- The final manuscript was prepared using reputable sources to ensure scientific accuracy.
- The principles of integrity and transparency were strictly adhered to in reporting results.
- No data manipulation was performed to favor any specific outcome.

Results

The mean age of the study participants was 53.85 ± 5.97 years, with the majority being male. The mean height, weight, and body mass index (BMI) of the participants were 169.58 ± 15.69 cm, 85.27 ± 8.37 kg, and 29.57 ± 4.41 , respectively. Most participants were classified as ASA class II. The comparison of baseline variables between the study groups showed no statistically significant differences (table 1)

Table 1: Comparison of Baseline Variables between Study Groups

Variable	Fentanyl Group (N=200)	Remifentanyl Group (N=200)	P-Value
Age (years)	54.5 ± 8.27	53.5 ± 21.59	0.859
Height (cm)	168.14 ± 89.27	172.15 ± 27.44	0.744
Weight (kg)	86.5 ± 57.29	84.5 ± 96.28	0.695
BMI (kg/m ²)	29.4 ± 14.96	29.5 ± 49.22	0.859
Gender - Male	109 (54.5%)	111 (55.5%)	0.811
Gender - Female	91 (45.5%)	89 (44.5%)	
ASA Class I	75 (12.12%)	79 (39.5%)	0.739
ASA Class II	125 (12.12%)	121 (60.5%)	

Among all study participants, 101 patients in the fentanyl group and 109 patients in the remifentanyl group had comorbidities (hypertension, diabetes mellitus, and treated hypothyroidism) ($P = 0.559$). Evaluation of intraoperative and recovery complications indicated that the incidence of intraoperative excitability (involuntary movements during anesthesia) was significantly higher in the remifentanyl group compared to the fentanyl group ($P = 0.014$). Consequently, the need for neuromuscular blocking agents during anesthesia

was significantly higher in the remifentanyl group ($P = 0.009$), and the mean dose of muscle relaxants was also significantly higher in the remifentanyl group ($P = 0.036$). There was no significant difference in regurgitation between the two groups ($P = 0.744$). However, postoperative nausea in the recovery unit was significantly higher in the fentanyl group ($P = 0.041$), and the need for antiemetic drugs in the recovery unit was significantly higher in the fentanyl group ($P = 0.038$) (table 2)

Table 2: Comparison of Intraoperative and Recovery Complications between Study Groups

Variable	Fentanyl Group (N=200)	Remifentanyl Group (N=200)	P-Value
Excitability	31 (15.5%)	59 (29.5%)	0.014
Need for Muscle Relaxants	28 (14%)	66 (33%)	0.009
Mean Muscle Relaxant Dose	10.2 ± 27.29	25.5 ± 14.24	0.036
Regurgitation	14 (7%)	18 (9%)	0.744
Nausea in Recovery	63 (31.5%)	41 (20.5%)	0.041
Mean Antiemetic Drug Dose	8.2 ± 78.59	5.2 ± 57.14	0.038

Evaluation of hemodynamic variables between the two study groups showed no significant differences in heart rate, systolic blood pressure, or diastolic blood pressure before induction. However, after induction, the heart rate (Figure 1) and blood pressure (Figures 2 and 3) were significantly lower

in the remifentanyl group at all time points compared to the fentanyl group. The degree of hemodynamic variation was significantly greater in the remifentanyl group than in the fentanyl group (table 3).

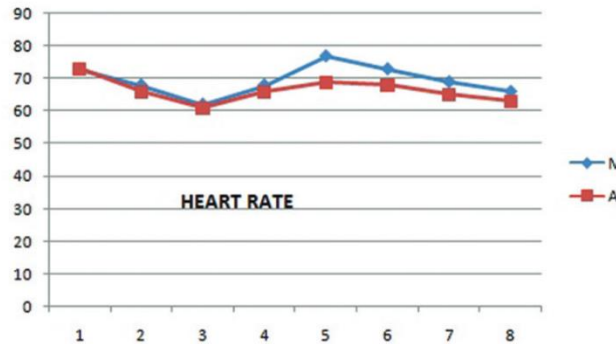


Figure 1: Comparison of Heart Rate between the Two Study Groups (M refers to Macintosh, and A refers to Videolaryngoscope).

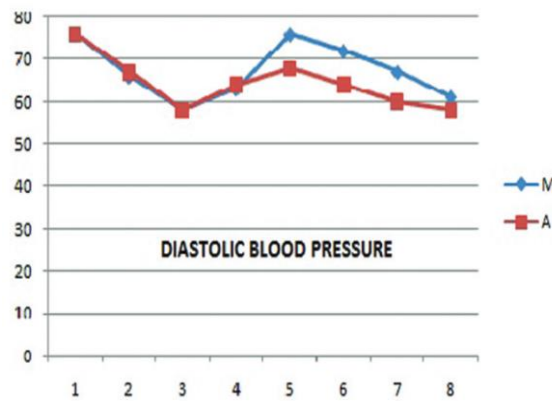


Figure 2: Comparison of Diastolic Blood Pressure between the Two Study Groups (M refers to Macintosh, and A refers to Videolaryngoscope).

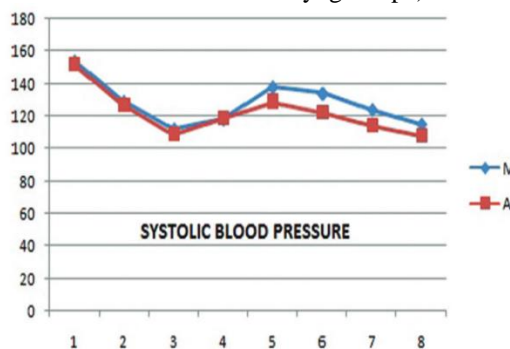


Figure 3: Comparison of Systolic Blood Pressure between the Two Study Groups (M refers to Macintosh, and A refers to Videolaryngoscope).

Table 3: Comparison of Hemodynamic Changes Between Study Groups at Different Time Points

Variable	Fentanyl Group (N=200)	Remifentanyl Group (N=200)	P-Value
Heart Rate (bpm)			
Before Induction	95.5 ± 17.27	86.9 ± 57.39	0.547
2 min After Induction	80.5 ± 27.96	75.5 ± 57.69	0.041
1 min After LMA Insertion	82.5 ± 27.63	71.5 ± 19.39	0.038
5 min After LMA Insertion	81.5 ± 41.96	70.6 ± 55.37	0.036
Systolic Blood Pressure (mmHg)			
Before Induction	145.14 ± 89.39	131.9 ± 29.88	0.447

2 min After Induction	125.12 ± 87.96	112.8 ± 27.73	0.033
1 min After LMA Insertion	129.7 ± 30.85	109.7 ± 64.23	0.031
5 min After LMA Insertion	125.9 ± 22.96	105.8 ± 27.33	0.028
Diastolic Blood Pressure (mmHg)			
Before Induction	95.8 ± 37.99	92.5 ± 44.67	0.509
2 min After Induction	83.5 ± 37.27	72.5 ± 26.33	0.041
1 min After LMA Insertion	86.9 ± 77.35	76.8 ± 57.74	0.036
5 min After LMA Insertion	84.7 ± 22.09	80.9 ± 44.57	0.036

The mean duration of anesthesia after complete propofol injection was significantly shorter in the remifentanyl group compared to the fentanyl group ($P = 0.041$). Additionally, the time to spontaneous

respiration return was significantly shorter in the remifentanyl group ($P = 0.048$), and the recovery time was also significantly shorter in the remifentanyl group ($P = 0.042$) (table 4)

Table 4: Comparison of Anesthesia Induction and Recovery Between Study Groups

Variable	Fentanyl Group (N=200)	Remifentanyl Group (N=200)	P- Value
Time to Anesthesia Induction After Propofol (sec)	39.5 ± 27.29	21.1 ± 74.57	0.041
Time to Spontaneous Respiration Recovery (sec)	245.40 ± 57.59	175.50 ± 55.57	0.048
Time to Recovery (min)	25.5 ± 57.96	18.4 ± 73.27	0.045
Pain Intensity in Recovery	3.1 ± 57.33	4.1 ± 11.08	0.095
Opioid Use in Recovery	10.3 ± 27.11	18.4 ± 47.55	0.111

Discussion

This study aimed to compare the effects of fentanyl and remifentanyl on intraoperative and postoperative outcomes, including hemodynamic stability, anesthesia induction and recovery time, and perioperative complications. The findings highlight significant differences between the two opioid agents, particularly in terms of intraoperative excitability, neuromuscular blockade requirement, hemodynamic stability, nausea in recovery, and recovery speed (17).

A key finding of this study was the significant reduction in heart rate and blood pressure (both systolic and diastolic) in the remifentanyl group after anesthesia induction. These hemodynamic parameters remained consistently lower in the remifentanyl group compared to the fentanyl group at all measured time points. This observation aligns with the known pharmacokinetics of remifentanyl, a short-acting μ -opioid receptor agonist with rapid metabolism by nonspecific plasma and tissue esterases. Its ultra-short half-life leads to quick onset and offset of action, resulting in faster hemodynamic changes compared to fentanyl, which has a longer context-sensitive half-life (18).

While remifentanyl-induced bradycardia and hypotension have been reported in previous studies, our findings confirm that these effects are more pronounced compared to fentanyl. The significant reduction in hemodynamic parameters in the remifentanyl group suggests that patients receiving remifentanyl require closer intraoperative hemodynamic monitoring and possible pharmacologic interventions to maintain cardiovascular stability. The rapid decline in blood

pressure and heart rate observed with remifentanyl may be attributed to greater inhibition of sympathetic outflow, reinforcing the need for individualized dosing and vigilant titration to hemodynamic responses (19).

One of the most notable differences between the two groups was the significantly higher incidence of intraoperative excitability (involuntary movements during anesthesia) in the remifentanyl group. This led to a higher requirement for neuromuscular blocking agents (NMBAs) and higher total doses of muscle relaxants in this group. This phenomenon can be explained by remifentanyl's ability to induce acute opioid-induced hyperalgesia (OIH) and excitatory motor effects, particularly when used in bolus doses or high infusion rates (20).

The mechanism underlying this excitability is not entirely understood but is believed to involve increased N-methyl-D-aspartate (NMDA) receptor activity, which contributes to hyperalgesia and muscle rigidity. This finding is clinically relevant as it highlights the potential need for adjunct medications (such as low-dose benzodiazepines or magnesium sulfate) to reduce excitatory responses when using remifentanyl. Additionally, careful titration and gradual dose escalation may help mitigate these motor responses (21).

While intraoperative excitability was higher in the remifentanyl group, the incidence of nausea in the recovery unit was significantly higher in the fentanyl group. Consequently, the fentanyl group had a greater requirement for antiemetic drugs. This finding aligns with fentanyl's longer duration of action, which may prolong opioid-induced nausea

and vomiting (PONV) compared to remifentanyl (22).

Remifentanyl's rapid metabolism reduces its residual opioid effect in the postoperative period, which likely explains the lower incidence of nausea. These results support the preferential use of remifentanyl in patients at high risk of PONV, such as those undergoing ambulatory surgery or individuals with a prior history of opioid-induced nausea. However, it is crucial to balance remifentanyl's benefits with its potential drawbacks, including hemodynamic instability and intraoperative excitability(23).

The study found that the time to achieve surgical anesthesia after propofol administration was significantly shorter in the remifentanyl group compared to the fentanyl group. This suggests that remifentanyl enhances the hypnotic effects of propofol, allowing for faster anesthesia induction(11)

Similarly, spontaneous respiratory recovery and awakening time in the recovery unit were significantly shorter in the remifentanyl group. This is consistent with remifentanyl's ultra-short elimination half-life (~3–5 minutes), which facilitates rapid recovery following discontinuation. This advantage makes remifentanyl a preferred opioid in short-duration surgeries, particularly when fast emergence and extubation are desired, such as in ambulatory anesthesia and neurosurgical procedures(18).

Despite faster recovery, pain intensity in the recovery unit was slightly higher in the remifentanyl group compared to the fentanyl group, although this difference was not statistically significant. The need for postoperative opioids in the recovery phase was also higher in the remifentanyl group, though this difference did not reach statistical significance. These findings suggest that remifentanyl's rapid elimination can result in opioid withdrawal-like effects or hyperalgesia in the early postoperative period. The clinical implication is that patients receiving remifentanyl may benefit from multimodal analgesia approaches, such as regional anesthesia techniques, NSAIDs, or gabapentinoids, to optimize postoperative pain control.

Conclusion

In summary, this study demonstrates that remifentanyl is associated with greater intraoperative hemodynamic suppression, increased excitability, and a higher requirement for neuromuscular blockade compared to fentanyl. However, remifentanyl provides faster induction and emergence from anesthesia with a lower incidence of postoperative nausea. The findings support the selective use of each opioid based on patient and procedural factors, emphasizing the need for individualized anesthetic strategies to optimize safety and recovery. Future research should explore strategies to minimize opioid-induced hyperalgesia

and excitability, particularly in remifentanyl-based anesthetic protocols.

Disclosure Statement

No potential conflict of interest reported by the authors.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' Contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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