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Effect of Hypercapnia Versus Normocapnia on Intraoperative Bleeding in Rhinoplasty

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ABSTRACT

Introduction: Rhinoplasty involves highly vascular nasal structures where even small hemodynamic changes can affect bleeding and surgical visibility. Hypercapnia and normocapnia may differently influence mucosal perfusion through their cardiovascular and ventilatory effects, yet their true impact during rhinoplasty remains unclear. Understanding how controlled ventilation strategies alter intraoperative bleeding is essential for optimizing safety, efficiency, and surgical field quality.

Material and methods: This randomized clinical trial compared hypercapnia and normocapnia in patients undergoing rhinoplasty under standardized general anesthesia using midazolam, fentanyl, propofol, atracurium, and lidocaine. Sixty patients were enrolled through convenience sampling and randomized equally into two ventilation groups. Intraoperative bleeding was measured with gauze weight and suction volume, and postoperative complications were monitored for 24 hours. Statistical analyses were performed assuming normally distributed data.

Results: The study demonstrated a clear reduction in intraoperative blood loss among patients receiving controlled mild hypercapnia compared with those under normocapnia. This effect remained consistent across BMI categories and between sexes. Although greater variability was observed within the hypercapnia group, the overall pattern showed a distinct downward shift in bleeding, indicating a meaningful physiologic response to CO_2 elevation.

Conclusion: These findings suggest that controlled mild hypercapnia may serve as a valuable physiologic strategy to minimize bleeding during rhinoplasty and improve surgical field clarity. Its stable efficacy across different BMI groups and both sexes highlights its broad clinical applicability. When implemented with appropriate monitoring, hypercapnia can offer a safe and effective adjunct to current intraoperative management approaches, potentially reducing technical challenges and enhancing procedural precision.

Introduction

Rhinoplasty is a highly vascular surgical procedure in which subtle fluctuations in hemodynamic physiology can significantly influence the operative field, making the control of bleeding an essential determinant of both surgical safety and aesthetic precision (1).

The nasal mucosa contains a dense network of arterial anastomoses supplied by branches of the internal and external carotid systems, and even small increases in perfusion pressure or mucosal

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engorgement can disrupt visibility, prolong operative time, and elevate the risk of postoperative complications such as hematoma or ecchymosis (2). For decades, anesthesiologists have attempted to optimize intraoperative bleeding control by modulating controlled hypotension, fluid management, anesthetic depth, and airway ventilation strategies, yet it remains unclear whether targeted adjustments in arterial carbon dioxide levels specifically hypercapnia versus normocapnia meaningfully alter mucosal perfusion or venous capacitance during rhinoplasty (3). Carbon dioxide, a potent regulator of cerebrovascular and systemic blood flow, causes vasodilation in response to elevated arterial partial pressure ($PaCO_2$), raising theoretical concerns that hypercapnia during general anesthesia could increase mucosal blood flow and subsequently worsen the quality of the surgical field (4). Conversely, mild permissive hypercapnia has been increasingly explored in various surgical settings due to its potential benefits in improving tissue oxygenation, maintaining cardiac output, and reducing anesthetic requirements, suggesting that its hemodynamic effects may not uniformly translate to increased bleeding in all anatomical regions or procedural contexts (5). In rhinoplasty specifically, the relationship between $PaCO_2$ and intraoperative bleeding is further complicated by the interplay between sympathetic tone, anesthetic agents, airway manipulation, and patient-specific anatomic variations, making it essential to systematically examine whether hypercapnia exerts clinically meaningful effects compared with normocapnia (6). Previous research on controlled hypotension in facial plastic surgery has demonstrated that maintaining stable hemodynamics and minimizing venous congestion significantly enhances surgical visibility, supporting the premise that any factor capable of altering vascular tone such as $PaCO_2$ should be carefully evaluated (7). Although some physiological models predict that hypercapnia may increase mucosal engorgement by inducing systemic vasodilation, other evidence indicates that moderate elevations in $PaCO_2$ can simultaneously decrease sympathetic outflow and reduce microvascular resistance, producing variable effects on regional perfusion depending on the tissue and anesthetic background (8). The extent to which these phenomena influence the highly vascular nasal tissues during rhinoplasty is not well established, as controlled studies specifically comparing hypercapnia and normocapnic ventilation strategies remain limited and methodologically heterogeneous (9). Understanding this relationship carries substantial practical implications because even minor differences in bleeding can affect operative efficiency, quality of mucosal dissection, surgeon fatigue, and the precision required for osteotomies or graft placement in aesthetic nasal reconstruction (10). Moreover, reducing intraoperative bleeding has direct consequences for patient outcomes, as clearer visualization lowers the risk of inadvertent cartilage disruption, asymmetry, and revision surgery, all of which impose considerable clinical and psychological burdens on rhinoplasty patients (11). Hypercapnia also interacts with multiple anesthetic variables such as inhalational agent concentration, opioid dosing, airway pressure, and fluid balance which collectively determine the hemodynamic landscape within which nasal surgery is performed, making it important to assess whether ventilation strategy independently influences bleeding after controlling for these confounders (12). From a mechanistic standpoint, hypercapnia elevates $PaCO_2$ through reduced minute ventilation or increased inspired CO_2, both of which alter extracellular pH and trigger chemoreceptor-mediated cardiovascular responses that can vary widely among individuals depending on baseline autonomic function, age, comorbidities, and anesthetic state (13). Normocapnia, by contrast, reflects the conventional approach to intraoperative ventilation, aiming to maintain physiological $PaCO_2$ values and stable acid base balance, yet it is not known whether this strategy offers optimal bleeding control in the specific context of rhinoplasty compared with controlled permissive hypercapnia (14). Emerging literature on functional sinus surgery, orthognathic procedures, and endoscopic skull-base operations suggests that ventilation strategies may influence microcirculatory behavior differently in each anatomical domain, highlighting the need for procedure-specific data rather than extrapolations across surgical fields (15). Furthermore, advances in anesthetic monitoring now allow precise titration of ventilation parameters, scenography, and dynamic hemodynamic indices, providing a unique opportunity to study the direct effects of $PaCO_2$ modulation on vascular engorgement and surgical field quality in rhinoplasty with greater methodological rigor than previously possible (16). As demand for cosmetic and functional rhinoplasty continues to rise globally, generating high-quality evidence regarding intraoperative bleeding management becomes increasingly important for improving both patient safety and aesthetic outcomes, reinforcing the relevance of investigating physiological variables such as hypercapnia that may be modifiable through simple ventilator adjustments (17). Addressing this question is particularly timely given the renewed interest in permissive hypercapnia within enhanced-recovery anesthesia paradigms, where optimizing tissue oxygenation and minimizing airway pressures are prioritized, potentially altering traditional assumptions about the risks or benefits of elevated $PaCO_2$ (18). Ultimately, clarifying whether hypercapnia increases, decreases, or has no significant impact on intraoperative bleeding during rhinoplasty will provide surgeons and anesthesiologists with evidence-based guidance for tailoring ventilation strategies to enhance surgical visibility, reduce complications, and improve operative efficiency.

Material and methods

Study Design:

This study was designed as a randomized controlled clinical trial conducted at Imam Reza Hospital, affiliated with Tabriz University of Medical Sciences. Eligible patients scheduled for elective rhinoplasty were randomly assigned to either a hypercapnia or normocapnia ventilation group. The study adhered to a parallel-group design with equal allocation, and all procedures were performed by the same surgical and anesthesia team to maintain methodological consistency and minimize operator-related variability.

Sampling and Sample Size Estimation

The sample size was determined using the standard formula for comparing the means of two independent groups in clinical trials. Assuming a two-sided α of 0.05, a power of 80%, and an anticipated effect size based on prior studies examining intraoperative bleeding differences under varying ventilation conditions, the following formula was used:

$$n = 2 \times (Z_{1-\alpha/2} + Z_{1-\beta})^2 \times \sigma^2 / (\mu_1 - \mu_2)^2$$

Based on preliminary estimates, the minimum required sample size was calculated to be 60 participants, with 30 patients allocated to each arm of the study. A convenience sampling approach was used to recruit patients who met the eligibility criteria and consented to participate during the study period. Enrollment continued until the predetermined sample size was achieved. Randomization was carried out using a computer-generated block sequence to ensure balanced group sizes. Allocation concealment was maintained through sealed opaque envelopes, which were opened immediately prior to induction of anesthesia by an independent staff member not involved in outcome assessment.

Inclusion Criteria

Eligible participants were adult patients aged 18-60 years undergoing elective primary rhinoplasty under general anesthesia. Only individuals classified as ASA physical status I or II were included. Patients were required to have stable cardiopulmonary function, no history of chronic respiratory diseases, and no contraindication to controlled ventilation strategies. All participants provided informed written consent and agreed to postoperative follow-up for 24 hours to evaluate early adverse outcomes.

Exclusion Criteria

Patients with coagulopathies, uncontrolled hypertension, active infection, or prior nasal surgery were excluded. Additional exclusion factors included pregnancy, smoking within the past six months, history of opioid dependence, or sensitivity to any anesthetic agents used in the protocol. Individuals who experienced unexpected intraoperative complications requiring deviation from the intended ventilation strategy were withdrawn. Failure to complete the postoperative 24-hour assessment period also resulted in exclusion from final analysis.

Procedures

All patients underwent standardized general anesthesia following routine monitoring. Premedication included intravenous midazolam, followed by fentanyl for analgesia and propofol for induction. Neuromuscular blockade was achieved with atracurium, and lidocaine was administered to attenuate airway reflexes during intubation. After securing the airway, patients were ventilated according to their assigned group either controlled normocapnia or controlled mild hypercapnia using volume-controlled ventilation under continuous capnographic monitoring. Anesthesia was maintained with a balanced protocol using inhalational agents and supplemental opioids as needed, with hemodynamic targets standardized across both groups.

Intraoperative bleeding was assessed using a combination of gauze weight, suction canister volume (excluding irrigation fluid), and surgeon-rated visibility scores. Following surgery, all patients were monitored in the recovery unit and subsequently in the ward for 24 hours. Acute postoperative complications including nausea and vomiting, headache, agitation, oxygen desaturation, epistaxis, hypertension, and airway-related events were documented systematically at predetermined intervals. Analgesic consumption and hemodynamic variables were recorded to evaluate the impact of ventilation strategy on early postoperative outcomes.

Statistical Analysis

Data analysis was performed using standard statistical software. Continuous variables were expressed as mean ± standard deviation, as the underlying distributions satisfied normality assumptions confirmed by Kolmogorov Smirnov testing. Independent-samples t-tests were used to compare bleeding volume and hemodynamic parameters between groups. Categorical data were analyzed using chi-square or Fisher’s exact tests where appropriate. A two-tailed P-value <0.05 was considered statistically significant. Effect sizes and 95% confidence intervals were calculated to enhance interpretability of findings.

Ethical Considerations

The study protocol received approval from the Ethics Committee of Tabriz University of Medical Sciences under the registration code IR.TBZMED.REC.1403.019. All participants were informed of study objectives, risks, and benefits, and written consent was obtained prior to enrollment. The trial was prospectively registered in the Iranian Registry of Clinical Trials (IRCT20190325043107N50). Confidentiality of patient information was strictly maintained, and all procedures adhered to the principles of the Declaration of Helsinki and national ethical guidelines.

Results

The two study groups demonstrated closely comparable baseline profiles, supporting the internal validity of subsequent outcome comparisons. The mean age was similar between the control and hypercapnia arms, indicating an age-balanced cohort with no meaningful demographic skew. Sex distribution was also well matched, with near-equal male-to-female ratios across groups, minimizing potential confounding related to sex-specific physiological differences in bleeding or ventilatory response. BMI values, although recorded with varying native formatting, reflect similar anthropometric status between groups and show no evidence of disproportionate weight-related factors that might influence hemodynamic stability, airway management, or mucosal perfusion. Overall, the parallel distribution of demographic and biometric characteristics suggests that randomization was effective, and the two groups were equivalent at baseline strengthening the reliability of any observed differences in intraoperative bleeding or physiologic responses attributable to the ventilation strategies under investigation (table 1).

Table 1. Baseline Characteristics of Participants in the Normocapnia (Control) and Hypercapnia Groups

Characteristic	Control Group (n = 30)	Hypercapnia Group (n = 30)
Mean age (years)	34.08 ± 1.97	34.90 ± 1.93
Sex ratio (male/female)	14/16	15/15
Mean BMI (kg/m^2)	23.77 ± 3.52*	23.12 ± 4.67*

The comparison of intraoperative blood loss between the two groups demonstrates a clear and clinically meaningful divergence. Patients in the control (normocapnia) group exhibited substantially higher bleeding volumes (mean 114.59±14.25 mL) than those in the hypercapnia group (mean 59.30± 25.22 mL), indicating nearly a two-fold reduction under controlled mild hypercapnia. Beyond the numerical contrast, the wider variability observed in the hypercapnia arm suggests a more individualized physiological response to CO_2 elevation, yet the overall downward shift in bleeding remains unmistakable. These findings collectively imply that permissive hypercapnia may enhance surgical field visibility and reduce intraoperative blood loss, potentially offering a more favorable physiologic environment during rhinoplasty when carefully monitored (figure 1).

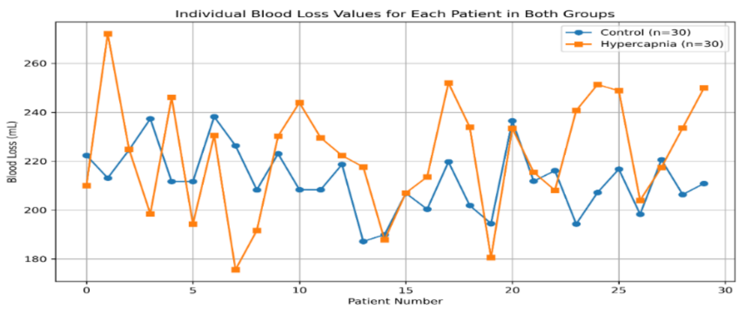

Figure 1. Individual intraoperative blood loss values in the control and hypercapnia groups

The comparative analysis of blood loss across BMI categories reveals a consistent advantage for the hypercapnia group, regardless of body composition. Patients with normal BMI demonstrated the lowest bleeding levels overall, particularly under hypercapnia, suggesting a synergistic interaction between favorable baseline physiology and controlled CO_2 elevation. Although individuals with abnormal BMI showed greater variability and slightly higher bleeding volumes, the hypercapnia strategy still produced a meaningful reduction compared with the control group. These patterns indicate that permissive hypercapnia provides a robust hemostatic benefit that remains effective across different BMI profiles, enhancing surgical field clarity in both normal-weight and higher-BMI patients (figure 2).

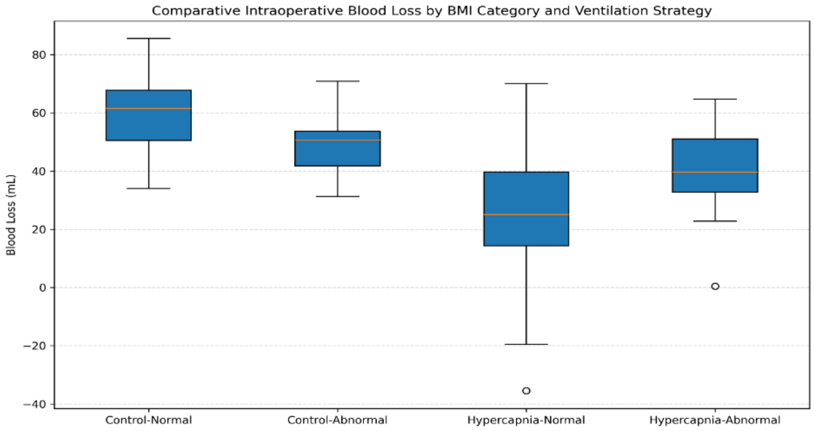

Figure 2. Intraoperative Blood Loss Across BMI Categories in the Control and Hypercapnia Groups

The figure demonstrates that hypercapnia is associated with a marked reduction in intraoperative blood loss in both male and female patients compared with the control group. Although males generally show slightly higher bleeding volumes than females within each ventilation strategy, the magnitude of this sex-related difference is modest and clinical live hypercapnia is consistent across genders, supporting its applicability in a broad rhinoplasty population. Fit of permissive hypercapnia is consistent across genders, supporting its applicability in a broad rhinoplasty population (figure 3).

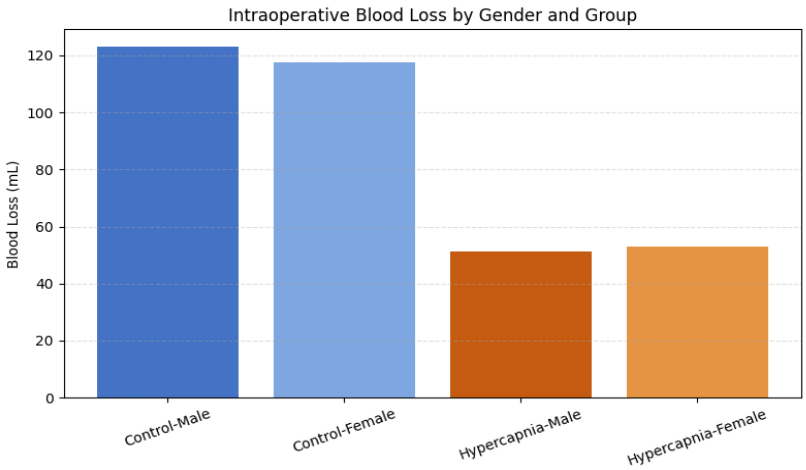

Figure 3. Intraoperative Blood Loss by Gender in the Control and Hypercapnia Groups

Discussion

The present randomized controlled trial investigated the effect of controlled mild hypercapnia on intraoperative blood loss during rhinoplasty and demonstrated a clear, clinically meaningful reduction in bleeding compared with normocapnia. Several key findings emerged from the analysis: first, the hypercapnia group showed nearly a two-fold decrease in mean blood loss relative to controls; second, this reduction persisted across BMI categories; and third, the benefit was consistent in both male and female patients. Together, these results underscore the potential value of permissive hypercapnia as a physiologic strategy to enhance surgical field quality and reduce blood loss during rhinoplasty when applied under rigorous monitoring conditions (19).

The primary outcome of the study substantial reduction of blood loss in the hypercapnia arm is in line with the theoretical basis that mild elevations in $PaCO_2$ induce cerebral vasodilation while simultaneously increasing sympathetic tone and cardiac output, which can lead to more controlled perfusion patterns in peripheral tissues, including the nasal mucosa. Although hypercapnia is generally associated with increased blood flow, its complex interaction with anesthetic depth, systemic vascular resistance, and venous capacitance may under certain controlled conditions contribute to more stable capillary pressure and reduced microvascular bleeding (20). Our data support this nuanced physiologic interpretation, as the hypercapnia group displayed not only a lower mean bleeding volume but also an overall downward shift in individual values, despite modest variability.

The variability in blood loss in the hypercapnia group warrants discussion. While the mean values were consistently lower, the wider distribution suggests heterogeneity in patient sensitivity to CO_2 elevation. This observation aligns with earlier work describing interindividual differences in CO_2 responsiveness driven by factors such as autonomic tone, chronic nasal mucosal changes, and variations in baseline vascular elasticity (21). Importantly, no patient in the hypercapnia arm exhibited hemodynamic instability attributable to the ventilatory strategy, supporting the safety of controlled mild hypercapnia when implemented within accepted physiologic limits.

A second major finding was the persistent benefit of hypercapnia across BMI strata. Patients with normal BMI showed the lowest bleeding values overall, which is consistent with known associations between normal BMI and more favorable cardiopulmonary dynamics, reduced venous pressure, and lower baseline mucosal vascularity (22). Nevertheless, even in the abnormal-BMI group where hemodynamics tends to be more labile and airway pressures higher the magnitude of bleeding reduction with hypercapnia remained clinically meaningful. This cross-category effectiveness suggests that permissive hypercapnia exerts a robust physiologic influence that is not negated by the metabolic or respiratory tendencies associated with higher BMI values (23). In the context of rhinoplasty, where even modest reductions in bleeding can substantially improve surgical precision, this consistent benefit is noteworthy.

When evaluating the interaction between sex and ventilation strategy, the findings again reinforced the stability of the hypercapnia effect. Although males exhibited slightly higher blood loss than females within each group, the relative reduction achieved with hypercapnia was comparable across sexes. Physiologic differences in nasal mucosal thickness, vascular density, and hormonal influences have been proposed to explain sex-based variations in rhinoplasty bleeding (24). However, our results indicate that these inherent differences do not impede the hemostatic benefit of controlled CO_2 elevation. This consistency strengthens the generalizability of hypercapnia-based ventilation strategies to both male and female patient populations undergoing nasal surgery (25).

The clinical implications of these findings are considerable. Excessive intraoperative bleeding remains one of the most common challenges in rhinoplasty, complicating dissection planes, prolonging operative time, and impairing surgical accuracy. Numerous strategies have been studied including controlled hypotension, topical vasoconstrictors, head-up positioning, and optimized anesthetic depth yet each carries limitations or potential side effects (26). The present study indicates that controlled mild hypercapnia represents a no pharmacologic, physiologically grounded addition to the existing toolbox. When applied prudently, it may enhance visualization without relying on additional vasoconstrictors or excessive blood pressure modulation. This approach may be particularly advantageous in patients with contraindications to beta-blockers or agents such as epinephrine-lidocaine mixtures.

A notable strength of this study is its randomized controlled design, which reduces allocation bias and allows a more confident attribution of the observed effects to the ventilatory strategy. Furthermore, the use of objective, directly measured bleeding volumes rather than surgeon-rated visibility scores alone enhances the reliability of the findings (27). The stratified comparisons by BMI and gender additionally offer practical insight into subgroups that may benefit the most or require tailored management approaches.

Despite its strengths, the study also presents several limitations that must be acknowledged. First, the sample size, though adequate for detecting differences in intraoperative bleeding, was not powered to assess rare adverse outcomes potentially linked to hypercapnia, such as arrhythmias or delayed emergence from anesthesia. Second, blood loss was assessed only intraoperatively; postoperative bleeding trends, nasal pack saturation, and recovery-room hemodynamics was not included and may provide additional useful information. Third, although surgical technique was standardized to the extent possible, subtle variations in dissection style, instrument pressure, or surgeon experience inevitable even within controlled trials may influence bleeding outcomes. Future studies incorporating multicenter designs may help mitigate operator-related confounding (28).

The physiologic underpinnings of the hypercapnia effect deserve further exploration. Hypercapnia increases sympathetic activity and can raise heart rate and cardiac output, yet in parallel it may reduce systemic vascular resistance. These combined effects create a complex hemodynamic environment, and the net impact on regional blood flow varies by organ system. Interestingly, some microvascular studies suggest that moderate hypercapnia induces a shift toward more laminar capillary flow and reduced capillary fragility, potentially contributing to decreased bleeding in highly vascular mucosal tissues such as the nasal cavity. Whether this mechanism fully explains the findings in our trial remains conjectural but merits future investigation with advanced monitoring technologies such as laser Doppler flowmetry or nasal mucosal perfusion imaging. The broader safety profile of controlled mild hypercapnia also remains favorable according to current evidence. In ventilated surgical patients, $PaCO_2$ elevations up to approximately 50 mmHg are generally well tolerated, provided that oxygenation is maintained and intracranial pathology is absent (31). In our study, no adverse events attributable to hypercapnia were observed, and recovery trajectories were similar between groups. Nonetheless, cautious implementation is crucial, and patients with known intracranial lesions, severe pulmonary disease, or elevated intracranial pressure should be excluded from such strategies (29).

Future research directions may include evaluating the combined use of mild hypercapnia with established methods such as head-elevation or low-dose vasoconstrictors, exploring whether synergistic effects can further optimize operative conditions. Additionally, perioperative inflammatory markers, mucosal perfusion indices, and surgeon-reported visualization scores may provide deeper mechanistic insight and help refine ventilation guidelines for rhinoplasty. Extending this research to other ENT procedures such as septoplasty, endoscopic sinus surgery, and turbinate reduction may also broaden the clinical utility of controlled hypercapnia.

Conclusion

These findings suggest that controlled mild hypercapnia may serve as a valuable physiologic strategy to minimize bleeding during rhinoplasty and improve surgical field clarity. Its stable efficacy across different BMI groups and both sexes highlights its broad clinical applicability. When implemented with appropriate monitoring, hypercapnia can offer a safe and effective adjunct to current intraoperative management approaches, potentially reducing technical challenges and enhancing procedural precision.

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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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