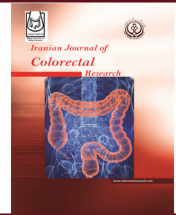


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Effect of Head-Up Positioning on Bispectral Index and Recovery Profiles in Patients Undergoing Laparoscopic Hysterectomy: A Randomized Controlled Clinical Trial

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Abstract

Background: Patient positioning during laparoscopic surgery can affect respiratory, cardiovascular, and cerebral physiology, thereby influencing processed electroencephalographic measures of anesthetic depth. This study evaluated the effect of head-up positioning on intraoperative bispectral index (BIS) values and perioperative recovery outcomes in patients undergoing laparoscopic hysterectomy.

Methods: In this randomized controlled clinical study, 105 adult patients undergoing elective laparoscopic hysterectomy were randomly assigned to either standard positioning (control, n=47) or approximately 30° head-up positioning (n=58). Anesthesia was induced with fentanyl, propofol, and atracurium and maintained with isoflurane at 1.2 MAC. The primary outcome was the mean intraoperative BIS. Secondary outcomes included measures of emergence, recovery, respiratory function, intra-abdominal pressure, sedation, and pain. Continuous variables were analyzed using independent-samples t-tests or Mann-Whitney U tests, as appropriate. ANCOVA was used to assess between-group differences in mean BIS after adjusting for age.

Results: The mean intraoperative BIS was significantly lower in the head-up group compared to the control group (45.46±6.27 vs. 50.18±4.55; P<0.001). This difference remained significant after adjusting for age (F(1,101)=17.574, P<0.001; partial η^2 =0.148), with an adjusted between-group difference of -4.556 BIS units. The time to reach a BIS of 80 was shorter with head-up positioning (13.2±2.8 vs. 15.4±3.2 minutes; P=0.028). The duration of anesthesia was longer in the head-up group (67 vs. 55 minutes; P=0.017), whereas surgery duration was similar between groups (P=0.729). Extubation time, PACU stay, postoperative pain, ETCO₂, mean airway pressure, and intra-abdominal pressure did not differ significantly between groups. RASS scores differed significantly (P=0.036).

Conclusion: Head-up positioning was associated with lower intraoperative BIS values during laparoscopic hysterectomy. However, without direct assessment of cerebral perfusion or oxygenation, these findings cannot conclusively indicate a greater depth of pharmacological hypnosis. Therefore, changes in BIS following positional interventions should be interpreted with caution.

Keywords: Consciousness Monitors; Hysterectomy; Laparoscopy; Anesthesia, General; Anesthesia Recovery Period

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Introduction

Monitoring the hypnotic component of general anesthesia is an important part of contemporary anesthetic practice, as both inadequate and excessive anesthesia can negatively impact perioperative management (1).

The bispectral index (BIS) is a processed electroencephalographic parameter widely used as an adjunctive measure of the anesthetic hypnotic state (2). Evidence from systematic reviews suggests that BIS-guided anesthesia can influence anesthetic administration and various recovery outcomes; however, the magnitude and consistency of these effects vary across clinical settings (3).

Importantly, BIS is not a direct measure of anesthetic drug concentration or pharmacological hypnosis and can be influenced by several non-anesthetic factors. Processed electroencephalographic indices may be affected by artifacts, neuromuscular blockade, drug effects, cerebral ischemia, and other physiological disturbances (4). Therefore, a decrease in BIS may occur in association with cerebral hypoperfusion and does not necessarily indicate an increased depth of pharmacological anesthesia (5).

Laparoscopic surgery induces additional physiological changes because pneumoperitoneum and changes in body position can affect venous return, arterial pressure, respiratory mechanics, carbon dioxide physiology, and cerebral hemodynamics (6). Studies have demonstrated that pneumoperitoneum and positional changes can alter cerebral oxygenation; however, the direction and magnitude of these changes depend on factors such as surgical position, intra-abdominal pressure, carbon dioxide levels, and hemodynamic conditions (7).

In gynecological laparoscopic surgery, Trendelenburg positioning has been associated with changes in regional cerebral oxygen saturation, with reductions becoming more pronounced in some patients during pneumoperitoneum and hypercapnia (8). Similarly, prospective studies have demonstrated that cerebral regional oxygen saturation can change during pneumoperitoneum and Trendelenburg positioning and may be related to arterial pressure and carbon dioxide tension (9).

Head elevation can influence cerebral physiology by changing the hydrostatic relationship between the heart and brain; however, its effects on cerebral perfusion pressure and oxygenation may vary across different clinical populations (10).

A recent systematic review and meta-analysis found that approximately 30° head elevation was associated with lower intracranial pressure, while cerebral perfusion pressure and measured cerebral oxygenation parameters generally did not differ significantly from those observed in the supine position (11). Consequently, a reduction in BIS following a positional change could theoretically reflect altered cerebral perfusion or cortical electrical

activity rather than a change in the pharmacological hypnotic effect (5).

Despite the clinical relevance of these considerations, evidence directly evaluating the relationship between head-up positioning and BIS during laparoscopic hysterectomy remains limited. Therefore, this randomized controlled study was designed to assess whether approximately 30° head-up positioning is associated with changes in intraoperative BIS values and selected recovery outcomes in patients undergoing laparoscopic hysterectomy. We hypothesized that head-up positioning would be associated with lower BIS values and potentially different early recovery characteristics, while recognizing that BIS changes could not be interpreted as direct evidence of altered pharmacological hypnosis in the absence of cerebral perfusion and oxygenation measurements.

Methods

Study Design and Participants

This randomized controlled clinical study included 105 adult patients undergoing elective laparoscopic hysterectomy.

Patients were eligible if they were between 18 and 80 years of age and classified as American Society of Anesthesiologists (ASA) physical status I or II.

Patients with a history of neurological disorders, significant prior head trauma, contraindications to general anesthesia, or indications for radical hysterectomy were excluded from the study.

The study was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethics Code: 402000181) and registered with the Iranian Registry of Clinical Trials (IRCT20230723058898N2).

Written informed consent was obtained from all participants prior to their enrollment.

Randomization and Intervention

Participants were randomly assigned to either the control group, which received standard positioning, or the head-up group, which received head-up positioning.

Randomization was conducted using a block randomization method. Allocation concealment was performed by a third party who was not involved in the clinical management of the participants.

Forty-seven patients were allocated to the control group, and 58 to the head-up group. Patients in the control group were maintained in the standard position used for the surgical procedure. In the intervention group, the head and upper body were elevated to approximately 30 degrees. Minor positional adjustments were permitted when required by surgical exposure or patient safety. The angle of head elevation was determined using a goniometer.

Blinding

Because the positioning intervention was visible

to the anesthesia and surgical teams, blinding of the anesthesiologist and surgical team was not feasible. However, patients were unaware of their group allocation. Postoperative recovery outcomes, including RASS scores and pain assessments, were recorded by a recovery-room nurse. Since the original study documentation did not specify prospective blinding of the recovery nurse, the present manuscript does not claim that the outcome assessor was blinded.

Anesthetic Management

All patients received a standardized general anesthesia protocol. Anesthesia was induced with fentanyl (2 µg/kg), propofol (2 mg/kg), and atracurium (0.5 mg/kg). Following endotracheal intubation, anesthesia was maintained with isoflurane at a target concentration of approximately 1.2 MAC. Additional doses of atracurium were administered as clinically required. At the end of surgery, residual neuromuscular blockade was reversed with neostigmine (2.5 mg) and atropine (1 mg).

BIS monitoring was performed continuously using a BIS monitor (BISTM Model A-2000, Aspect Medical Systems). Electrodes were placed on the forehead according to the manufacturer's recommendations. The mean intraoperative BIS was calculated by averaging five predefined BIS measurements recorded during the perioperative assessment.

Outcome Measures

The primary outcome was the mean intraoperative BIS.

Secondary outcomes included the time from discontinuation of anesthetic administration to extubation, the time to reach a BIS of 80 during emergence, duration of anesthesia, duration of surgery, PACU length of stay, ETCO₂ levels, mean airway pressure, intra-abdominal pressure, RASS score, and postoperative pain score.

Extubation time was defined as the interval between the discontinuation of anesthetic administration and the removal of the endotracheal tube.

The RASS assessment included measurements taken at extubation, upon arrival in the recovery unit, 15 minutes after admission, 30 minutes after admission, and at PACU discharge. The mean RASS value was calculated as the arithmetic mean of these five measurements.

Statistical Analysis

Data were analyzed using SPSS version 26 (IBM Corp., Armonk, NY, USA). The distribution of continuous variables was assessed using the Shapiro–Wilk test. Normally distributed continuous variables were summarized as mean ± standard deviation and compared between groups using the independent-samples t-test. Non-normally distributed continuous variables were summarized as median and interquartile range and compared using the Mann–Whitney U test.

Categorical variables were analyzed using the chi-square test or Fisher's exact test, as appropriate.

ANCOVA was used to evaluate the association between group allocation and mean intraoperative BIS after adjustment for age. Before conducting the final ANCOVA, the Group × Age interaction was examined to assess the homogeneity of regression slopes assumption. The interaction was not statistically significant ($F=3.841$, $P=0.053$, partial $\eta^2=0.037$), supporting the use of an additive ANCOVA model. Therefore, the final ANCOVA included group and age as model terms.

A two-sided P-Value of less than 0.05 was considered statistically significant.

For outcomes that were not normally distributed, Hodges–Lehmann estimates and corresponding 95% confidence intervals were obtained to describe the between-group location differences. Equivalence or non-inferiority testing was not performed.

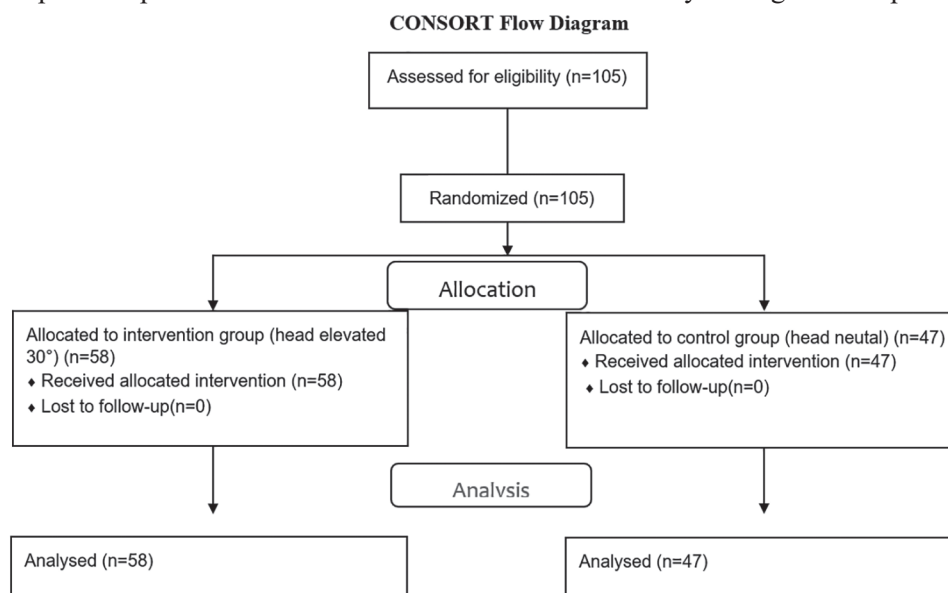


Figure 1: Illustrates the CONSORT flow diagram for patient inclusion.

Results

Participant Flow and Baseline Characteristics

A total of 105 patients were included in the final analysis, with 47 assigned to the control group and 58 to the head-up group. No participants were excluded after allocation. The CONSORT flow diagram is presented in Figure 1.

Baseline characteristics are summarized in Table 1. The mean age was 50.78 ± 9.77 years in the control group and 49.02 ± 9.80 years in the head-up group, with no statistically significant difference between the groups ($P=0.489$). Therefore, the two groups were comparable in terms of baseline age.

Primary Outcome: Intraoperative BIS

The mean intraoperative BIS was significantly lower in the head-up group than in the control group (Table 2). The unadjusted mean BIS was 50.18 ± 4.55 in the control group and 45.46 ± 6.27 in the head-up group, corresponding to an unadjusted mean difference of -4.72 points (95% CI, -6.82 to -2.62 ; $P<0.001$).

Because age was prespecified as a potential

covariate, an ANCOVA model was subsequently performed including treatment group and age as factors. The initial model also assessed the group-by-age interaction. Since the interaction term was not statistically significant ($F=3.841$, $P=0.053$, partial $\eta^2=0.037$), the final model was interpreted without the interaction term.

In the final ANCOVA model, the treatment group remained significantly associated with the mean BIS after adjusting for age ($F=17.574$, $P<0.001$, partial $\eta^2=0.148$), whereas age was not statistically significant ($F=3.762$, $P=0.055$, partial $\eta^2=0.036$).

The adjusted mean BIS was 50.212 (SE= 0.804 ; 95% CI, 48.617 – 51.806) in the control group and 45.656 (SE= 0.730 ; 95% CI, 44.200 – 47.103) in the head-up group. The adjusted between-group difference was approximately -4.56 BIS points (95% CI, -6.71 to -2.40).

These findings indicate that the association between head-up positioning and lower BIS remained statistically significant after adjusting for age.

Recovery Outcomes

Recovery-related outcomes are presented in Table 3.

Table 1: Baseline demographic and clinical characteristics of study participants

Variable	Control (n=47)	Head-up (n=58)	P value
Age, years, mean $\pm$ SD	50.78 $\pm$ 9.77	49.02 $\pm$ 9.80	0.489
Intra-abdominal pressure, median (Q1–Q3)	13(12–14)	13(12–14)	0.544
Mean airway pressure, median (Q1–Q3)	29(24.75–30)	29(25.25–32.50)	0.164
Duration of anesthesia, min, median (Q1–Q3)	55(43.75–75)	67(55–85)	0.017
Duration of surgery, min, median (Q1–Q3)	60(45–75)	60(45–70)	0.729
Extubation time, min, median (Q1–Q3)	10(10–15)	15(10–20)	0.051
PACU stay, min, median (Q1–Q3)	105(93.75–130)	102.50(85–115)	0.206
ETCO ₂ , mmHg, mean $\pm$ SD	27.26 $\pm$ 5.80	27.30 $\pm$ 5.40	0.973
RASS score, median (Q1–Q3)	-2(-2.20 to -1.20)	-2.20(-2.35 to -0.74)	0.036
Mean postoperative pain score, median (Q1–Q3)	2(0–2)	2(0–2)	0.127

P values for normally distributed continuous variables were obtained using independent-samples t-tests, whereas non-normally distributed variables were compared using the Mann–Whitney U test.

Table 2: Intraoperative BIS and ANCOVA results

Variable	Control	Head-up	Between-group difference / adjusted effect	P value
Mean BIS, mean $\pm$ SD	50.18 $\pm$ 4.55	45.46 $\pm$ 6.27	-4.72(95%CI -6.82 to -2.62)	<0.001
Adjusted mean BIS	50.21 $\pm$ 0.80	45.65 $\pm$ 0.73	-4.56(95% CI -6.71 to -2.40)	<0.001
Group effect, ANCOVA	—	—	$F=17.574$; partial $\eta^2=0.148$	<0.001
Age effect, ANCOVA	—	—	$F=3.762$; partial $\eta^2=0.036$	0.055
Group $\times$ age interaction	—	—	$F=3.841$; partial $\eta^2=0.037$	0.053

The final ANCOVA model included group and age without the interaction term.

Table 3: Recovery and perioperative outcomes

Outcome	Control (n=47)	Head-up (n=58)	P value
Time to BIS 80, min, mean $\pm$ SD	15.4 $\pm$ 3.2	13.2 $\pm$ 2.8	0.028
Duration of anesthesia, min, median (Q1–Q3)	55(43.75–75)	67(55–85)	0.017
Duration of surgery, min, median (Q1–Q3)	60(45–75)	60(45–70)	0.729
Extubation time, min, median (Q1–Q3)	10(10–15)	15(10–20)	0.051
PACU stay, min, median (Q1–Q3)	105(93.75–130)	102.50(85–115)	0.206
RASS score, median (Q1–Q3)	-2(-2.20 to -1.20)	-2.20(-2.35 to -0.74)	0.036
Mean postoperative pain score, median (Q1–Q3)	2(0–2)	2(0–2)	0.127

Table 4: Respiratory and intra-abdominal parameters

Variable	Control	Head-up	Between-group estimate (95% CI)	P value
ETCO ₂ , mmHg, mean±SD	27.26±5.80	27.30±5.40	0.04(-2.15 to - 2.23)	0.973
Intra-abdominal pressure, median (Q1–Q3)	13(12-14)	13(12-14)	0(0 to 0)	0.544
Mean airway pressure, median (Q1–Q3)	29(24.75-30)	29(25.25-32.50)	-1(-4 to 0)	0.164

The time to reach a BIS value of 80 was significantly shorter in the head-up group than in the control group (13.2±2.8 vs. 15.4±3.2 minutes, respectively; $P=0.028$).

The median RASS score was -2.20 (Q1–Q3, -2.35 to -0.74) in the head-up group, compared with -2.00 (Q1–Q3, -2.20 to -1.20) in the control group, representing a statistically significant difference ($P=0.036$).

The duration of anesthesia was significantly longer in the head-up group, with a median of 67 minutes compared to 55 minutes in the control group ($P=0.017$).

No statistically significant between-group differences were observed in the duration of surgery ($P=0.729$), PACU stay ($P=0.206$), or mean postoperative pain score ($P=0.127$).

Extubation time was numerically longer in the head-up group than in the control group (median 15 vs. 10 minutes); however, this difference did not reach conventional statistical significance ($P=0.051$).

Respiratory and Intra-abdominal Parameters

The respiratory and intra-abdominal parameters are summarized in Table 4.

Mean ETCO₂ was 27.26±5.80 mmHg in the control group and 27.30±5.40 mmHg in the head-up group, with no statistically significant difference between the groups ($P=0.973$). The estimated between-group difference was approximately 0.04 mmHg (95% CI, -2.15 to 2.23).

The median intra-abdominal pressure was 13 mmHg in both groups, with identical interquartile ranges of 12–14 mmHg, and no statistically significant difference was observed ($P=0.544$).

Median mean airway pressure was 29 mmHg in both groups, with no statistically significant difference ($P=0.164$). The adjusted estimated difference was approximately -1 mmHg, with a 95% CI ranging from approximately -4 to 0 mmHg.

As equivalence testing was not performed, these findings should be interpreted as a lack of statistically significant evidence for a between-group difference, rather than as evidence of equivalence.

Discussion

The principal finding of this study was that head-up positioning was associated with significantly lower mean intraoperative BIS values compared to standard positioning. Adjusted analyses confirmed that group allocation remained significantly associated with BIS values after controlling for age, supporting the

robustness of the observed between-group difference. BIS is widely used as an adjunctive processed electroencephalographic measure during general anesthesia; however, its clinical interpretation should always be considered within the context of the overall anesthetic and physiological state (1). Recent evidence suggests that BIS-guided anesthesia may reduce anesthetic exposure and facilitate selected recovery outcomes, although the magnitude of these effects varies across surgical populations (1).

The lower BIS observed in the head-up group should not be interpreted as definitive evidence of a greater pharmacological hypnotic depth. BIS reflects processed cortical electrical activity and may be influenced by physiological changes independent of anesthetic concentration, including alterations in cerebral perfusion and oxygenation (5). Head elevation can modify the hydrostatic relationship between arterial pressure measured at the heart and pressure at the brain level, potentially affecting cerebral perfusion physiology (10). A 2024 systematic review and meta-analysis found that approximately 30° head elevation reduced intracranial pressure while generally maintaining cerebral perfusion pressure and measured cerebral oxygenation parameters, indicating that the cerebral response to head elevation is complex and cannot be inferred from a single physiological variable (10).

The interpretation of the present findings is further complicated by the physiological effects of laparoscopic surgery. Pneumoperitoneum and changes in body position can modify intra-abdominal pressure, venous return, arterial pressure, respiratory mechanics, carbon dioxide physiology, and cerebral hemodynamics (12). Studies monitoring cerebral oxygenation during laparoscopic procedures have demonstrated measurable changes in regional cerebral oxygen saturation associated with pneumoperitoneum and positional changes; however, the direction and magnitude of these changes vary according to the surgical position and accompanying physiological conditions (9). More recent prospective evidence has also shown that pneumoperitoneum and Trendelenburg positioning can alter intracranial pressure and cerebral blood flow-related parameters, further supporting the importance of considering cerebral physiology when interpreting processed EEG changes during laparoscopy (13).

In the present study, the head-up group reached a BIS of 80 more rapidly and exhibited lower RASS scores, while extubation time showed only a non-significant numerical increase, and PACU stay did not differ significantly between groups.

These findings should be interpreted cautiously, as recovery endpoints are influenced by multiple factors, including anesthetic exposure, neuromuscular recovery, pain, respiratory function, and institutional recovery criteria (14). Similarly, the absence of statistically significant differences in ETCO₂, mean airway pressure, and intra-abdominal pressure should not be interpreted as evidence of clinical equivalence, since the study was neither designed nor powered as an equivalence trial.

Overall, the findings suggest that head-up positioning is associated with a measurable reduction in BIS during laparoscopic hysterectomy; however, the underlying mechanism remains uncertain. Because cerebral perfusion, cerebral blood flow, and cerebral oxygenation were not measured simultaneously, it is not possible to determine whether the lower BIS resulted from altered pharmacological hypnotic effects, changes in cerebral physiology, or a combination of these factors. Future randomized studies should standardize the degree of head elevation and simultaneously monitor BIS, cerebral regional oxygen saturation, arterial pressure referenced to brain level, and other relevant cerebral perfusion variables to clarify the physiological basis of the observed association.

Strengths and Limitations

This study has several strengths, including randomized allocation, third-party allocation concealment, objective measurement of head elevation angle using a goniometer, standardized anesthetic management, and prespecified assessments of both intraoperative and early recovery outcomes.

Several limitations should be considered. First, the study was conducted at a single center, which may limit the generalizability of the findings. Second, BIS is an indirect, processed EEG measure that can be affected by physiological, pharmacological, and technical factors. Third, although the target head elevation was approximately 30°, minor positional adjustments were permitted according to surgical requirements and patient safety, resulting in some exposure variability. Fourth, cerebral perfusion pressure, cerebral blood flow, and cerebral oxygenation were not directly measured, preventing determination of the mechanisms underlying the observed BIS differences. Fifth, quantitative neuromuscular monitoring was not routinely available, limiting the interpretation of extubation time. Sixth, the recovery nurse recorded RASS and pain outcomes; however, prospective blinding of the outcome assessor was not documented; therefore, assessor blinding cannot be confirmed. Seventh, the study was not designed as an equivalence or non-inferiority trial, and statistically nonsignificant findings for ETCO₂, mean airway pressure, and intra-abdominal pressure should not be interpreted as evidence of equivalence.

Finally, long-term postoperative outcomes were

not evaluated.

Conclusion

Approximately 30° head-up positioning was associated with significantly lower intraoperative BIS values in patients undergoing laparoscopic hysterectomy. This association remained statistically significant after adjusting for age. However, because cerebral perfusion and cerebral oxygenation were not directly measured, the lower BIS values cannot be conclusively interpreted as evidence of increased pharmacological hypnotic depth. The study found no statistically significant differences in ETCO₂, mean airway pressure, intra-abdominal pressure, or PACU stay. The duration of anesthesia was longer in the head-up group, while extubation time was numerically longer but did not reach statistical significance.

Overall, the findings emphasize that changes in BIS associated with patient positioning should be interpreted within a broader physiological context, rather than as isolated measures of anesthetic depth.

Future randomized studies incorporating standardized continuous positioning, along with simultaneous monitoring of cerebral oxygenation and perfusion, are warranted.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of Kerman University of Medical Sciences (Ethics Code: 402000181). Written informed consent was obtained from all participants prior to enrollment in the study.

Consent for publication

Not applicable. This manuscript does not include any individual patient data or identifying information.

Availability of Data and Materials

The datasets used and analyzed in the current study are available from the corresponding author upon reasonable request.

Competing Interests

The authors declare that they have no conflicts of interest.

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Authors' Contribution

All authors contributed to this work according to

the CRediT (Contributor Roles Taxonomy) system, as follows:

Mohammad Yousefi: Responsible for conceptualization of the study, designing the methodology, developing visual representations of data. Zahra Honarvar: Conducted data collection and curation. Roya Basirat: Contributed to reviewing and editing the manuscript. Fateme Ahmadi: performed the formal statistical analyses, and providing essential research resources, writing the original draft of the manuscript, Oversaw the project as supervisor, managed project administration tasks. All authors reviewed and approved the final version

of the manuscript.

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Trial Registration

The study was registered with the Iranian Registry of Clinical Trials (IRCT20230723058898N2).

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