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ORIGINAL RESEARCH

# Effects of Different Body Mass Indexes on the Induction Dose of Remimazolam in Patients Undergoing Gynaecological Day Surgery: A Propensity Score-Matched Study

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**Purpose:** This study compared the effects of different body mass indexes (BMI) on the induction dose of remimazolam in patients undergoing gynaecological day surgery, aiming to explore the appropriate weight index of remimazolam for overweight or obese people.

**Patients and Methods:** This was a retrospective, observational study based on propensity score matching (PSM). The patients were divided into two groups according to normal BMI boundaries: group N (BMI<24 kg/m²) and group F (BMI≥24 kg/m²). The primary observation of the study was the anesthetic induction dose per kg of remimazolam calculated on the basis of total body weight (TBW), ideal body weight (IBW), lean body weight (LBW) and corrected body weight (CBW).

**Results:** A total of 250 patients were included in the analysis. After PSM, 94 patients were finally included in each group. The primary observation: there was a significant difference between the two groups in the induction dose per kg of TBW and IBW ($P$=0.001), but not in the induction dose per kg of LBW and CBW ($P$>0.05). The Secondary observation:the time to loss of consciousness was shorter in group F than in group N ($P$=0.030), but there was no significant difference in recovery time ($P$=0.868). There were also no significant differences between the two groups in perioperative adverse effects and changes in circulating blood pressure before and after induction ($P$>0.05). In addition, the induction dose of remimazolam per kg calculated based on TBW exhibits a negative correlation with BMI (r=−0.362, $P$=0.001).

**Conclusion:** When calculated based on TBW, the induction dose of remimazolam per kilogram (mg/kg) was lower in overweight or obese patients compared to normal-weight patients. For these patients, we recommend using CBW for dose calculation when applying the 0.2–0.4 mg/kg dosing regimen.

**Keywords:** remimazolam, body mass index, induction dose, anesthesia, general

## Introduction

The increasing global prevalence of obesity has become a significant public health concern.[1] According to the World Health Organization (WHO), the global obesity rate has nearly tripled in recent decades, resulting in a larger proportion of individuals who are overweight or obese. This trend necessitates new approaches to managing chronic diseases[2] and poses challenges for perioperative anesthesia management.

Overweight or obese patients exhibit different pharmacokinetic and pharmacodynamic characteristics during anesthesia[3] and usually require higher drug doses to achieve the desired depth of anesthesia, but this does not mean that the dose is simply calculated on the basis of total body weight (TBW). Studies have shown that there are significant differences in drug dose-effect relationship between obese patients and non-obese patients.[4] Dosing based solely on TBW

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in overweight/obese patients may result in drug accumulation, potentially inducing adverse effects including excessive sedation, respiratory depression, and hemodynamic instability, while also elevating the risk of postoperative complications.[5]

Remimazolam is a novel short-acting sedative. It has the characteristics of rapid induction of awakening, little interference with respiratory and circulatory system, independent of liver and kidney metabolism, and can be antagonized by flumazenil with strong controllability.[6] However, there are few studies on the use of remimazolam in overweight or obese patients, and the relationship between body mass index (BMI) and the induction dose of remimazolam is still unclear. Because the traditional anesthetic propofol commonly uses lean body weight (LBW) rather than TBW to calculate the induction dose for overweight or obese patients,[7] we therefore raise a question: should lean body weight also be used as the basis for drug dosage when applying the more water-soluble remimazolam in these populations? Therefore, this study compared the effects of different body mass indexes (BMI) on the induction dose of remimazolam in patients undergoing gynaecological day surgery, aiming to explore the appropriate weight index of remimazolam for overweight or obese people, and provide a reference for clinical use.

## Materials and Methods

This study is a retrospective and observational study based on propensity score matching. The study followed the STROBE statement and was approved by the Ethics Committee of Weifang People's Hospital (KYLL20250307-1). Since the data were collected in an anonymised form, the institution waived the requirement for informed consent.

We retrospectively collected perioperative data on patients undergoing gynaecological day surgery from June 2022 to June 2023 at Weifang People's Hospital. Inclusion criteria: (1) Remimazolam was used for anesthesia induction and maintenance during the operation and the medication regimen was in line with the research process. (2) Aged 18–64 years. (3) American Society of Anesthesiologists (ASA) physical status of I-II. Exclusion criteria: (1) Patients with low body weight (BMI<18.5 $kg/m^2$) and morbid obesity (BMI≥35 $kg/m^2$) were excluded. (2) Exclude patients with missing data. (3) Patients who used psychotropic drugs before surgery were excluded. (4) Exclusion of patients with intraoperative use of sedative-hypnotic drugs other than remimazolam. (5) Exclusion of patients who change the method of anesthesia. Patients were stratified into two groups based on Chinese population-specific BMI cutoff values for normal weight range: group N (BMI<24 $kg/m^2$) and group F (BMI≥24 $kg/m^2$).

Building on our research team's prior investigations of remimazolam,[8–11] we have accumulated substantial clinical experience and established both standardized administration protocols and an associated medication database. All patients were unmedicated before surgery and their vital signs were monitored after entering the operating room. Dexamethasone 5 mg was given intravenously before anesthesia induction. Anesthesia induction: Remimazolam was intravenously infused at a rate of 6 mg/kg/h using a micropump until the patient's consciousness disappeared and the MOAA/S score reached ≤1. Subsequently, alfentanil 20ug/kg and mivacurium chloride 0.2 mg/kg were given. After the patient's spontaneous breathing disappeared, mask ventilation with positive pressure oxygen was performed. Three minutes later, a laryngeal mask airway (LMA) was inserted and secured, followed by mechanical ventilation. For anesthesia maintenance, remimazolam was infused at 0.5–1mg/kg/h and alfentanil at 20–40 ug/kg/h. The patient's BIS was maintained at 40–60 by adjusting the infusion rate of remimazolam and alfentanil during the operation. Discontinuation of anesthesia infusion at the end of surgery. The laryngeal mask was removed when the patient regained consciousness with eye opening and return of swallowing reflex. The patient was then transferred to the postanesthesia care unit (PACU) and discharged to the general ward upon achieving an Aldrete score of ≥9.

We use the Hospital Information Query System and the departmental anesthesia database to obtain the information we need for the study. The primary observation of the study was the anesthetic induction dose per kilogram of remimazolam calculated on the basis of TBW, ideal body weight (IBW), LBW and corrected body weight (CBW). Formula: IBW in women = height(cm)–105;[12] LBW in women = (9270×TBW)/(8780+244×BMI);[13] CBW in women = IBW+0.4×(TBW–IBW)[14].

The Secondary observation included the following:1.The time to loss of consciousness in the two groups (from the administration of remimazolam to the patient's MOAA/S score≤1). 2.Anesthesia time of the two groups (from the beginning of anesthesia induction to the end of drug infusion). 3.Recovery time of two groups of patients (from the

beginning of stopping drug infusion to the time of patients opening eyes). 4.Perioperative adverse events included intraoperative hiccups, cough, hypotension (systolic blood pressure less than 90 mmHg or MAP decreased by more than 20% from baseline), bradycardia (intraoperative heart rate less than 50 beats/min) and postoperative nausea and vomiting, dizziness, headache in PACU. 5. The hemodynamic changes of the patients were recorded before entering the operating room (T0), before induction of anesthesia (T1), after induction of anesthesia (T2), at the beginning of surgery (T3), 5 minutes after the beginning of surgery (T4), 10 minutes after the beginning of surgery (T5), 15 minutes after the beginning of surgery (T6), 20 minutes after the beginning of surgery (T7), at the end of surgery (T8), and after removal of the laryngeal mask (T9). 6.To explore the relationship between BMI and induction dose, and to form a linear regression equation.

In the statistical analysis of the data, normality of continuous variables was assessed by the Kolmogorov–Smirnov test. Variables that conformed to normal distribution were expressed as mean ± standard deviation, and independent samples *t*-tests were used for comparisons between groups. Within Group F, comparisons between two related samples were performed using paired-sample t-tests. Variables that were not normally distributed were expressed as median (interquartile range, IQR), and comparisons between groups were analysed using the Mann–Whitney *U*-test. The categorical variables were presented in the form of percentage (%), and the chi-square test or Fisher exact probability method was used for comparison between groups. Pearson correlation analysis was used to detect the relationship between induction dose and BMI, and a linear regression equation was constructed for further study.

In order to reduce the selection bias and control the influence of confounding factors, this study used propensity score matching (PSM) to balance the covariates of the two groups. The propensity score was estimated by logistic regression model. The included covariates included age and American Society of Anesthesiologist (ASA) Physical Status score. In the matching process, the optimal pair matching method was used, the matching ratio was 1:1, and no replacement was performed (the caliper value was set to 0.05). All the above data were statistically analyzed by R software (Version 4.2.1, R Foundation for Statistical Computing, Vienna, Austria). $P<0.05$ was considered statistically significant.

## Results

From June 2022 to June 2023, 259 patients underwent gynaecological day surgery under general anesthesia with remimazolam in our hospital. Among them, 4 cases were excluded due to incomplete intraoperative data, 3 cases were excluded due to low body weight, and 2 cases were excluded due to morbid obesity. The remaining 250 patients were included in the analysis and divided into 145 patients in group N and 105 patients in group F according to the patient ‘s BMI index. Because the main factors affecting the dosage of anesthetics are age, BMI and ASA Physical Status score, we matched the age and ASA Physical Status score between the two groups. After PSM, 94 patients were finally included in each group (Figure 1).

Baseline data before and after matching between the two groups (Table 1).

The primary observation: There was a significant difference in the induction dose per kg of TBW and IBW between the two groups (P=0.001). Based on TBW calculations, Group F required a lower induction dose per kilogram than Group N (P = 0.001). There was no significant difference in the induction dose per kg of LBW and CBW (P>0.05). On this basis, we compared the difference between the induced dose per kilogram calculated by LBW and CBW in group F. The induction dose per kg calculated based on LBW is higher than that calculated using CBW (P<0.05) (Table 2).

The Secondary observation: The time to loss of consciousness in group F was shorter than that in group N (P=0.030), but there was no significant difference between the two groups in terms of anesthesia duration and recovery time (P=0.868)(Table 1).In perioperative complications, there was no significant difference between the two groups (P>0.05) (Table 3). Figures 2 and 3 respectively illustrate the perioperative mean arterial pressure and heart rate of both groups. There were no significant differences in the changes of mean arterial pressure and heart rate between the two groups before and after anesthesia induction. At the commencement of surgery (T3), the blood pressure and heart rate of group F were higher than those of group N, with the difference being statistically significant.

To further investigate the impact of BMI on the induction dose of remimazolam anesthesia, we conducted a linear correlation analysis using the data prior to matching and generated a scatter plot (Figure 4). The induction dose of remimazolam per kg calculated based on TBW exhibits a negative correlation with BMI (r=-0.362, P=0.001). We further

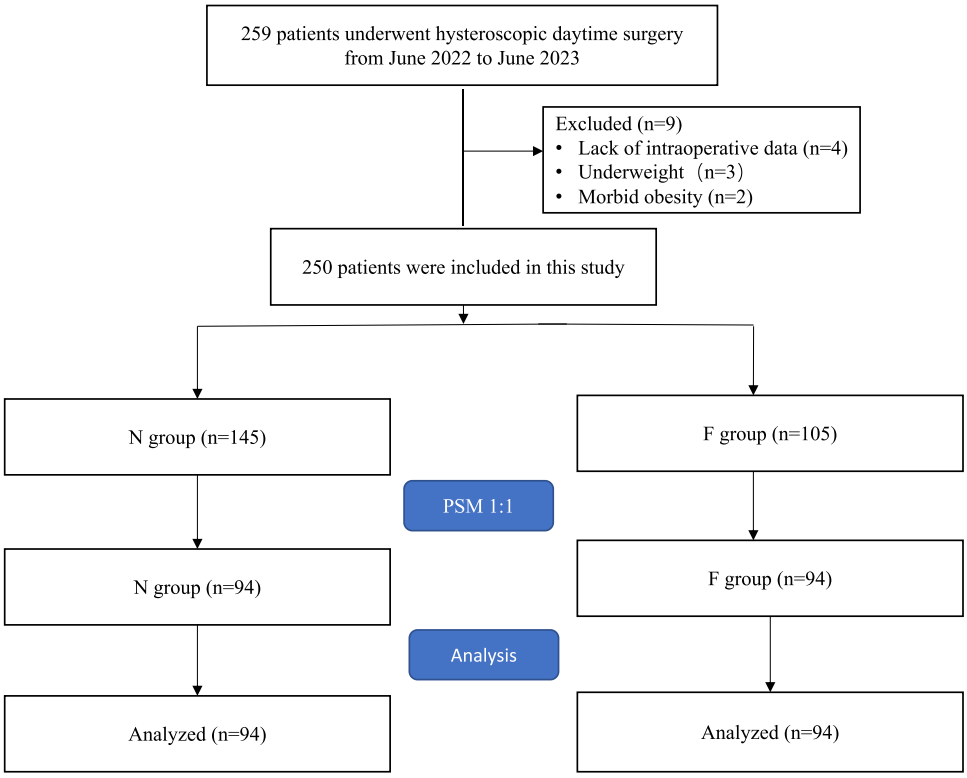


**Figure 1** Flow Chart Showing the Process Used to Select the Study Sample.

constructed a multiple linear regression equation: Y[remimazolam induction dose (mg/kg)]=0.413+(−0.001)×age +(−0.004)×BMI,($R^2$=0.165).

## Discussion

This study compares the impact of different body mass indices on the induction dose of remimazolam anesthesia using a propensity score matching method. In this study, we discovered that overweight or obese patients require a higher induction dose per kg based on TBW compared to patients with normal weight. Subsequent correlation analysis also

**Table 1** Comparison Between the Group N and Group F Before and After Propensity-Score Matching

| | Before Matching(n=250) | | | After Matching(n=188) | | |
|---|---|---|---|---|---|---|
| | **Group N** | **Group F** | ***P* value** | **Group N** | **Group F** | ***P* value** |
| Age (years) | 40.89±9.35 | 46.25±9.72 | 0.001 | 43.84±8.91 | 44.63±8.90 | 0.545 |
| BMI (kg/m²) | 21.16±1.71 | 26.75±2.23 | 0.001 | 21.38±1.70 | 26.79±2.29 | 0.001 |
| ASA-PS | | | 0.231 | | | 0.406 |
| I (n,%) | 40(27.6) | 22(21.0) | | 27 (28.7) | 22 (23.4) | |
| II (n,%) | 105(72.4) | 83(79.0) | | 67 (71.3) | 72 (76.6) | |
| Induction dose | | | | | | |
| Remimazolam(mg) | 15.52±3.04 | 16.82±2.93 | 0.001 | 15.18±2.98 | 16.98±2.95 | 0.001 |
| Alfentanil (mg) | 1.11±0.11 | 1.38±0.13 | 0.001 | 1.12±0.11 | 1.39±0.13 | 0.001 |
| Maintenance dose | | | | | | |
| Remimazolam (mg) | 17.99(13.25–25.64) | 22.33(16.25–29.60) | 0.008 | 17.85(12.01–25.13) | 22.73(17.01–30.88) | 0.002 |
| Alfentanil (mg) | 0.46(0.30–0.70) | 0.52(0.36–0.80) | 0.322 | 0.44(0.22–0.79) | 0.55(0.36–0.80) | 0.197 |
| Time of unconsciousness (s) | 162.40±31.32 | 148.08±26.18 | 0.001 | 158.81±30.32 | 149.97±24.62 | 0.030 |
| Duration of anesthesia (min) | 22.17±11.36 | 21.54±10.40 | 0.691 | 21.52±11.76 | 22.17±10.58 | 0.727 |
| Recovery time (min) | 8.61±3.41 | 8.70±3.07 | 0.857 | 8.58±3.29 | 8.49±2.95 | 0.868 |

**Notes**: Data are expressed as mean±SD, median (interquartile range) or number (%).
**Abbreviation**: ASA-PS, American Society of Anesthesiologist Physical Status.

**Table 2** Comparison of Induction Doses Between the Two Groups After Matching

| | Group N | Group F | *P* value |
|---|---|---|---|
| Total induction dose (mg) | 15.18±2.98 | 16.98±2.95 | 0.001 |
| Induction dose per kg TBW (mg/TBW) | 0.27±0.05 | 0.24±0.04 | 0.001 |
| Induction dose per kg IBW (mg/IBW) | 0.27±0.06 | 0.31±0.05 | 0.001 |
| Induction dose per kg LBW (mg/LBW) | 0.41±0.08 | 0.41±0.06 | 0.622 |
| Induction dose per kg CBW (mg/CBW) | 0.27±0.05 | 0.28±0.04* | 0.272 |

**Notes**: Data are presented as mean ± SD. *$P$<0.05: Comparison between the induction dose per kilogram calculated based on lean body weight and that calculated using corrected body weight.
**Abbreviations**: TBW, total body weight; IBW, lean body weight; LBW, ideal body weight; CBW, corrected body weight.

**Table 3** Perioperative Complications Between the Two Groups Before and After Propensity-Score Matching

| | Before Matching(n=250) | | | After Matching(n=188) | | |
|---|---|---|---|---|---|---|
| | Group N | Group F | *P* value | Group N | Group F | *P* value |
| Intraoperative | | | | | | |
| Hiccough | 8/145 (5.5) | 3/105 (2.9) | 0.311 | 4/94 (4.3) | 3/94 (3.2) | 1.000 |
| Cough | 4/145 (2.8) | 2/105 (1.9) | 0.663 | 0/94 (0) | 2/94 (2.1) | 0.497 |
| Hypotension | 30/145 (20.7) | 19/105 (18.1) | 0.610 | 18/94 (19.1) | 15/94 (16.0) | 0.565 |
| Bradycardia | 13/145 (9.0) | 11/105 (10.5) | 0.689 | 9/94 (9.6) | 10/94 (10.6) | 0.809 |
| Postoperative | | | | | | |
| Nausea and vomiting | 44/145 (30.3) | 34/105 (32.4) | 0.732 | 28/94 (29.8) | 30/94 (31.9) | 0.752 |
| Cephalalgia | 9/145 (6.2) | 7/105 (6.7) | 0.883 | 5/94 (5.3) | 6 /94 (6.4) | 0.756 |
| Dizziness | 35/245 (24.1) | 24/105 (22.9) | 0.814 | 17/94 (18.1) | 22/94 (23.4) | 0.368 |

**Notes**: All numbers are n/group N (%).

confirmed this finding, indicating a negative correlation between BMI and the induction dose of remimazolam per kg. Secondly, we found that the induction dose of remimazolam per kg calculated based on LBW and CBW showed no significant difference between the two groups, suggesting that equivalent sedative effects can be achieved in patients with different BMIs when the dose is calculated based on either LBW or CBW. This provides us with some indication that LBW or CBW can be used as appropriate weight metrics for calculating the ideal dosing of remimazolam in overweight or obese patients. However, we also identified an issue: the induction dose per kg calculated based on LBW is higher than that calculated based on CBW, which may result in the induction dose calculated using LBW failing to achieve

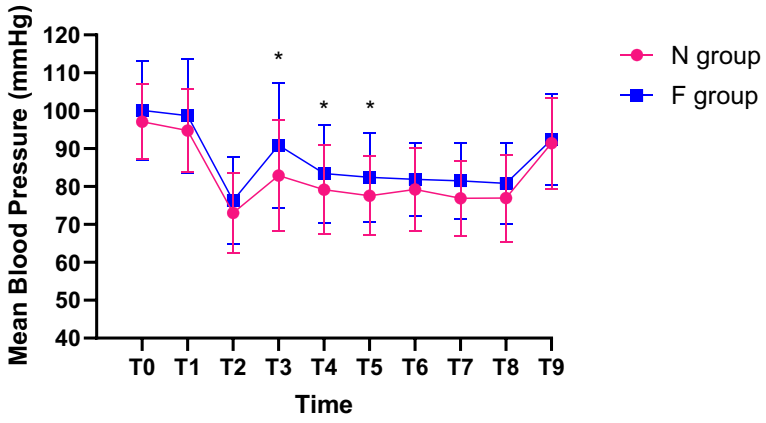


**Figure 2** Comparison of perioperative mean blood pressure between the two groups after matching. *$P$<0.05.


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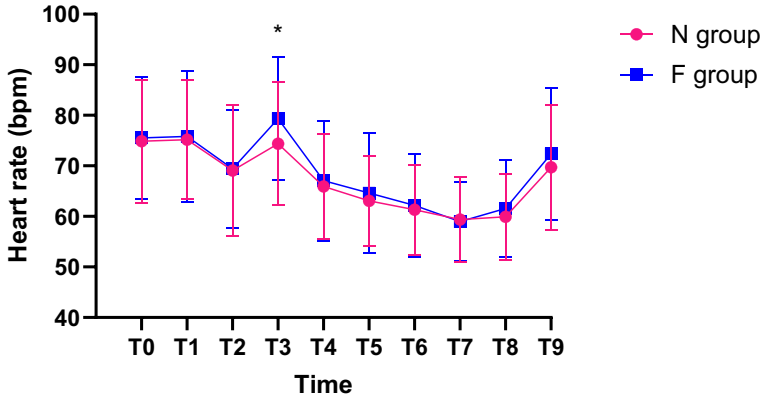


**Figure 3** Comparison of perioperative heart rate between the two groups after matching. *$P$<0.05.

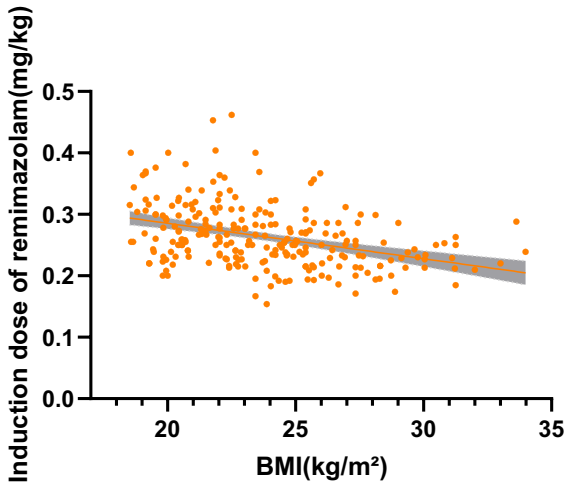


**Figure 4** Analysis of the correlation between the induction dose of remimazolam and BMI.

satisfactory anesthesia depth. Therefore, when calculating the dosage of remimazolam based on the induction dose per kilogram, we recommend using CBW as the preferred metric for dose calculation.

To date, there have been no studies on the dosing of remimazolam for overweight or obese patients. Only a limited number of articles have confirmed that, compared to the traditional anesthetic propofol, remimazolam exhibits a higher safety profile when used in obese patients.[15] The common methods for anesthesia induction with remimazolam can be divided into two types: one is continuous intravenous infusion at a rate of 6 mg/kg/h or 12 mg/kg/h until the patient falls asleep;[16] the other is administration based on body weight at a dose of 0.2–0.4 mg/kg.[17] In studies calculating the dosage of remimazolam based on the induction dose per kilogram, the total body weight of patients has been used for the calculation. This approach may lead to an increased induction dose for overweight or obese patients, potentially resulting in a series of perioperative adverse effects. In previous studies on anesthetic dosing for obese patients, it has been found that, except for the weakly lipophilic drug rocuronium, which should be dosed based on IBW rather than TBW,[18] the majority of anesthetic drugs, including opioids and sedatives, are most appropriately dosed using LBW.[7,19] However, some studies have also confirmed that using LBW may lead to insufficient dosing.[20]

In the comparison of other intraoperative observation indicators between the two groups, we observed that overweight or obese patients had a shorter time to loss of consciousness compared to patients with normal weight. This finding is consistent with the results of Lomher's study,[21] which revealed a correlation between the time to loss of consciousness during remimazolam induction and BMI. Specifically, when remimazolam was infused at a rate of 6 mg/kg/h, obese patients lost consciousness 20 seconds faster than those with normal weight. Furthermore, we found no significant difference in the recovery time between the two groups of patients. This may be attributed to the fact that remimazolam is primarily metabolized by nonspecific esterases in

the blood into CNS 7054, which is essentially inactive, and then excreted by the kidneys, resulting in no accumulation of the drug in the body.[22] Additionally, the pharmacokinetics of remimazolam are linear, and its clearance is independent of body weight, meaning the dosage does not need to be increased as weight increases.[23] Therefore, this further enhances the advantages of remimazolam in overweight or obese patients.

We also observed the incidence of perioperative adverse reactions and hemodynamic changes in both groups. The study found no significant difference in the rate of adverse reactions between the two groups. This result suggests that the use of remimazolam in obese patients does not increase the risk of perioperative adverse reactions, further supporting its safety in the obese population. In the perioperative hemodynamic changes, there was no significant difference in the variations of mean arterial pressure and heart rate between the two groups before and after induction. However, at the beginning of the surgery, the increase in blood pressure and heart rate was more pronounced in obese patients, which may be related to their heightened sensitivity to stimuli.

Limitations of this study: This research is a single-center retrospective clinical study that only included healthy patients classified as ASA I–II. Further studies are needed for patients classified as ASA ≥ III or those with liver or kidney diseases. Additionally, this study represents a retrospective exploratory investigation based on clinical data. We did not conduct a detailed analysis of the pharmacokinetic parameters of remimazolam in obese patients (such as volume of distribution, clearance rate, etc)., making it unable to fully explain the pharmacological basis of dosage differences. This study employed PSM to balance the two groups, focusing specifically on BMI's effect on remimazolam induction doses. Future research could further investigate the influence of age on induction requirements to develop more precise remimazolam dosing models.

## Conclusion

When calculated based on TBW, the induction dose of remimazolam per kilogram (mg/kg) was lower in overweight or obese patients compared to normal-weight patients. For these patients, we recommend using CBW for dose calculation when applying the 0.2–0.4 mg/kg dosing regimen.

## Abbreviations

MOAA/S, the Modified Observer's Assessment of Alertness/Sedation; BMI, body mass index; MAP, mean arterial pressure; HR, heart rate; SD, standard deviation; TWB, total body weight; IBW, ideal body weight, LBW, lean body weight; CBW, corrected body weight; ASA, American Society of Anesthesiologists.

## Data Sharing Statement

The datasets generated in this study are available from the first author (Hongyi Xiao, Email: 1185549168@qq.com) upon reasonable request.

## Ethics Approval

The study followed the STROBE statement and was approved by the Ethics Committee of Weifang People's Hospital (KYLL20250307-1). Since the data were collected in an anonymised form, the institution waived the requirement for informed consent. This study was conducted in accordance with the principles of the Declaration of Helsinki.

## Consent for Publication

All authors have agreed to submit and publish the manuscript.

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## Disclosure

The authors have no competing interests in this work.

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