ORIGINAL RESEARCH ARTICLE

Outcome of an intervention based on adjusting the threshold for hyponatremia in patients undergoing myomectomy: A case control study

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Abstract

This study evaluated the effect of increasing the critical value threshold for hyponatremia combined with systematic intervention on sodium regulation in patients undergoing myomectomy. A retrospective analysis was performed. Patients who underwent myomectomy and received conventional care between March 2014 and March 2019 (n=844) served as the reference group (threshold: 120 mmol/L), while those treated between March 2019 and March 2024 (n=1385) formed the observation group. In the observation group, the hyponatremia critical threshold was raised to 129 mmol/L, alongside targeted interventions including patient education, dynamic sodium monitoring, use of normal saline as the oxytocin solvent, and dietary management. The observation group showed a significantly lower overall incidence of hyponatremia compared with the reference group (21.3% vs. 25.8%, P<0.05). The reduction was more pronounced for moderate-to-severe hyponatremia, decreasing from 5.6% (0.9% severe, 4.7% moderate) to 2.2%, with no severe cases observed. Symptomatic episodes were also reduced (8/31 vs. 25/48). Acute moderate-to-severe hyponatremia occurred predominantly in patients receiving intravenous oxytocin. In conclusion, elevating the hyponatremia critical threshold combined with multidimensional intervention effectively reduces both the incidence and severity of postoperative hyponatremia following myomectomy, supporting its value in early warning and clinical management *(Afr J Reprod Health 2026; 30 [16]:123-131).*

Keywords : Gynecology; Hyponatremia; Critical value; Uterine fibroid surgery

Résumé

Cette étude a évalué l'effet de l'augmentation du seuil critique de l'hyponatrémie, combinée à une intervention systématique, sur la régulation du sodium chez les patientes subissant une myomectomie. Une analyse rétrospective a été réalisée. Les patientes ayant subi une myomectomie et reçu des soins conventionnels entre mars 2014 et mars 2019 (n=844) ont constitué le groupe de référence (seuil : 120 mmol/L), tandis que celles traitées entre mars 2019 et mars 2024 (n=1385) ont formé le groupe d'observation. Dans ce dernier, le seuil critique de l'hyponatrémie a été relevé à 129 mmol/L, avec la mise en œuvre simultanée d'interventions ciblées, incluant l'éducation des patientes, la surveillance dynamique du sodium, l'utilisation de solution saline normale comme solvant de l'ocytocine, et une prise en charge diététique. Le groupe d'observation a présenté une incidence globale d'hyponatrémie significativement plus faible que le groupe de référence (21,3 % vs 25,8 %, P<0,05). La réduction était plus marquée pour l'hyponatrémie modérée à sévère, passant de 5,6 % (0,9 % sévère, 4,7 % modérée) à 2,2 %, sans aucun cas sévère observé. Les épisodes symptomatiques ont également diminué (8/31 vs 25/48). L'hyponatrémie aiguë modérée à sévère est survenue principalement chez les patientes recevant de l'ocytocine par voie intraveineuse. En conclusion, l'élévation du seuil critique de l'hyponatrémie, associée à une intervention multidimensionnelle, permet de réduire efficacement l'incidence et la sévérité de l'hyponatrémie postopératoire après myomectomie, soulignant sa valeur pour l'alerte précoce et la prise en charge clinique. *(Afr J Reprod Health 2026; 30 [16]: 123-131).*

Keywords: Gynécologie ; Hyponatrémie ; Valeur critique ; Chirurgie des fibromes utérins

Introduction

Hyponatremia is defined as a serum sodium concentration below 135 mmol/L and can be classified according to plasma osmolality, severity of hyponatremia, progression rate, and clinical symptoms.[1] As the most common type of water–electrolyte disturbance in clinical practice, hyponatremia occurs in approximately 30% of hospitalized patients and involves multiple clinical disciplines. It frequently leads to neurological complications such as seizures and cerebral edema, In severe cases, it may result in irreversible sequelae or even death; therefore, it receives considerable attention from clinicians.[2] Although hyponatremia in hospitalized patients is often mild and accompanied by few obvious symptoms, it still holds important clinical significance[3]. Particularly, acute hyponatremia poses substantial risks. Studies have shown that even mild hyponatremia can prolong hospitalization duration and increase mortality.[4]

To reduce postoperative bleeding after myomectomy for uterine fibroids, the most commonly used clinical method currently is intravenous infusion of oxytocin. which promotes uterine contraction and thereby compresses the blood vessels in the myometrium to achieve hemostasis[5]. Since oxytocin contains trace amounts of antidiuretic hormone (ADH), it can bind to ADH receptors on kidney-related cells, significantly enhancing its antidiuretic effect, promoting water reabsorption, and leading to an increase in body fluid volume with decreased output. However, the increased water is mainly distributed intracellularly (accounting for approximately two-thirds) and only one-third accumulates in the extracellular fluid, thereby resulting in hypotonic hyponatremia.[6]

Of note, post-myomectomy hyponatremia induced by oxytocin tends to progress rapidly and develop insidiously, with acute onset features that differ from those of general hospital-acquired hyponatremia. Currently, domestic medical institutions adopt 120 mmol/L as the general critical value for hyponatremia, a threshold corresponding to severe hyponatremia with life-threatening neurological manifestations8.However, this universal cutoff is designed for general inpatients and fails to support early warning in high-risk gynecological postoperative patients. Rapid sodium decline after myomectomy means that neurological injury may already occur before serum sodium drops to 120 mmol/L, resulting in delayed intervention.

To optimize postoperative safety management and compensate for the deficiency of the general critical value in this specific population, our department raised the specialized hyponatremia critical threshold to 129 mmol/L in March 2019 and implemented standardized targeted interventions. Existing studies mainly focus on the general management of hyponatremia, while few investigations have optimized critical values for high-risk gynecological surgical patients. This study therefore aimed to evaluate the clinical efficacy of this individualized threshold strategy. We sought to verify whether the elevated specialized critical value combined with systematic interventions could reduce the incidence and severity of acute post-myomectomy hyponatremia and improve patient postoperative outcomes, so as to provide practical evidence for the early prevention and standardized management of this postoperative complication.

Methods

Study subjects

A retrospective data analysis was conducted on patients who received intravenous oxytocin infusion after uterine fibroid surgery in the gynecology ward of Peking University Shenzhen Hospital between March 3, 2014, and March 4, 2024. Patients hospitalized from March 3, 2014 to March 3, 2019, were assigned to the reference group (n=844), while those treated from March 4, 2019 to March 4, 2024, comprised the observation group (n=1,385). The reference group included 844 cases, with ages ranging from 19 to 80 years and a mean age of (39.33 ± 6.48) years. The observation group consisted of 1,385 cases, aged 16-76 years, with a mean age of (38.86 ± 6.93) years. Comparison of baseline characteristics between the two groups showed no statistically significant difference ($P > 0.05$), indicating comparability.

Inclusion criteria were: ① Diagnosed with uterine fibroids in accordance with the relevant diagnostic criteria specified in Gynecology and Obstetrics[8], and underwent laparoscopic or open myomectomy; ② Received intraoperative and/or postoperative oxytocin infusion; ③ Had complete case records.

Exclusion criteria were: ① Patients with hyponatremia before or during surgery;② Patients with severe postoperative complications such as massive hemorrhage, pulmonary embolism, or systemic infection; ③ Patients who underwent hysteroscopic or vaginal surgery; ④ Patients who received hypertonic saline or other medications interfering with serum sodium after surgery; ⑤ Patients with underlying diseases affecting water and sodium metabolism, such as diabetes, heart failure, or chronic kidney disease; ⑥ Incomplete medical records.

Control of confounding factors: Pre-analysis revealed that the distribution of surgical approaches (open vs. laparoscopic) might differ between the two groups, as minimally invasive techniques became more widely adopted clinically after 2019, and the surgical approach could influence postoperative sodium metabolism and the risk of developing hyponatremia. To eliminate the potential confounding effect of this factor on study outcomes, we included "surgical approach" as a covariate in the subsequent multivariate logistic regression model. This adjustment allowed us to account for its impact on the incidence of hyponatremia and ensured an objective comparison of intervention effects between the two groups.

Nursing interventions

Reference group

Patients in the reference group received conventional nursing care, which included: health education upon admission regarding the disease and related surgical procedures; completion of preoperative preparation; and postoperative guidance on diet and physical activity.

Observation group

Patients in the observation group received systematic interventions based on a specialized early-warning system for critical hyponatremia values: ① Critical value adjustment: In collaboration with the clinical laboratory, the critical value threshold for serum sodium was adjusted from the hospital standard of 120 mmol/L to 129 mmol/L. ② Health education on hyponatremia: Educational brochures were developed to provide patients and their families with comprehensive knowledge regarding hyponatremia, including its definition, risk factors, clinical manifestations, potential complications, and preventive interventions. This education was specifically targeted at postoperative patients receiving intravenous oxytocin infusion after myomectomy. ③ Solvent selection: Normal saline was selected as the diluent for oxytocin administration.[6] ④ Dietary intervention: Postoperative dietary interventions were implemented according to the patient's serum sodium level.

Observed indicators

The primary observation indicator of this study is the incidence of hyponatremia, with a particular focus on evaluating the occurrence of moderate to severe hyponatremia and its associated clinical symptoms. Diagnostic Criteria: Based on laboratory blood sodium test results, hyponatremia is defined as a blood sodium concentration < 135 mmol/L, and is further classified as follows: • Mild: 130 ≤ serum sodium < 135 mmol/L; Moderate: 125 ≤ serum sodium < 130 mmol/L; Severe: serum sodium < 125 mmol/L.[9] We will compare the changes in the above indicators between the two groups of patients before and after the implementation of the intervention to assess its effectiveness.

Quality control

This study was a retrospective analysis of hospital electronic medical and laboratory records. All data were retrieved from standardized hospital information systems to ensure original authenticity and traceability. To ensure data accuracy and validity, two trained researchers independently extracted and double-entered all data according to uniform inclusion and exclusion criteria. Any inconsistent data were verified and corrected by checking the original medical records. A random 5% of cases was further manually reviewed for quality control. These measures minimized selection and entry bias and ensured reliable study results.

Statistical analysis

Data were analyzed using Statistic Package for Social Science (SPSS) Statistics version 27.0 (IBM Corp., Armonk, NY, USA). Continuous variables that were normally distributed, as assessed by the Shapiro–Wilk test and Levene's test for equality of variances, are presented as mean ± standard deviation ($\bar{x} \pm s$). Intergroup comparisons for normally distributed continuous variables were performed using independent samples t-tests. Categorical variables are expressed as frequencies (n) or percentages (%), with between-group differences evaluated using the chi-square (χ^2) test. For cells in Table 3 with an expected count <5, Fisher's exact test was additionally applied to enhance the reliability of the statistical analysis. A two-sided P-value <0.05 was considered statistically significant.

Ethical considerations

This retrospective study was approved by the Ethics Committee of Peking University Shenzhen Hospital (Approval No. PKUSH-IRB-[2026]-031) and performed in accordance with the Declaration of Helsinki. Regarding patient autonomy, no additional interventions or changes to routine patient management were implemented; therefore, informed consent was waived by the ethics committee. Regarding confidentiality, all patient data were de-identified to remove personal identifiable information. Only trained researchers accessed the dataset for analysis, and no individual patient information was disclosed during the study, ensuring full protection of patient privacy and rights..

Results

Baseline characteristics of the study population

A total of 2,229 participants were enrolled in this study, including 844 in the reference group and 1,385 in the observation group. The age distribution in both groups was approximately normal. The reference group ranged from 19 to 80 years with a mean age of 39.33 ± 6.48 years, and the observation group ranged from 16 to 76 years with a mean age of 38.86 ± 6.93 years.

There was no statistically significant difference in age between the two groups (P= 0.128). A significant difference was found in the distribution of surgical procedures between the groups (P< 0.001). However, after adjustment for this potential confounding factor using a multivariate logistic regression model, the baseline characteristics of the two groups were well balanced and comparable, thus meeting the requirements for further efficacy analysis.

Incidence of postoperative hyponatremia between two groups

The overall incidence of postoperative hyponatremia in the observation group was lower than that in the reference group, with a particularly marked reduction in the rate of moderate-to-severe hyponatremia, as well as a decreased number of symptomatic patients. Despite the significant intergroup difference in the composition of surgical procedures, multivariate Logistic regression analysis confirmed that early intervention with adjusted critical value thresholds served as an independent predictive factor for the occurrence of hyponatremia, which was not confounded by variables such as surgical approach. On this basis, a comparative analysis of hyponatremia incidence between the two groups (Table 3) revealed that the total incidence of hyponatremia in the observation group was 21.3%, which was significantly lower than the 25.8% observed in the reference group (P < 0.05). The intergroup difference was even more prominent in terms of moderate-to-severe hyponatremia: the incidence of moderate-to-severe hyponatremia in the control group was 5.6% (0.9% for severe and 4.7% for moderate), whereas no severe hyponatremia cases were detected in the observation group, and the moderate incidence was merely 2.2%. These findings demonstrated that the incidence of all grades of hyponatremia in the observation group was lower than that in the control group, with the most remarkable decline detected in moderate-to-severe cases, indicating that the targeted intervention strategy exerted a prominent effect in preventing severe postoperative hyponatremia events.

As shown in Table 4, among patients with moderate-to-severe hyponatremia, 25 symptomatic episodes were recorded in the reference group (48 cases), whereas only 8 symptomatic episodes occurred in the observation group (31 cases). The difference in symptom distribution between the two groups before and after the intervention was statistically significant (P< 0.05).

Postoperative oxytocin infusion and acute moderate-to-severe hyponatremia in uterine fibroid patients

In patients undergoing surgery for uterine fibroids, those who received intravenous oxytocin infusion were predominantly diagnosed with acute moderate-to-severe hyponatremia.As shown in Table 5, a total of 98.7% of the cases with moderate-to-severe hyponatremia were recorded in both the reference and observation groups.

Table 1: Comparison of general data between two groups

Group	age (years, $\bar{x}$±*s*)	surgical method *[n (%)]*		χ^2/t	*P*
		Laparotomy	Laparoscopic surgery		
Reference group (n=844)	39.33±6.48	343 (40.6)	501 (59.4)	1.523	0.128
Observation group (n=1385)	38.86±6.93	274 (19.8)	113 (80.2)	120.433	<0.001

Note: Continuous data are presented as mean ± standard deviation ($\bar{x}$±*s*). Comparisons of age were performed using the independent samples t-test. Categorical data are expressed as the number of cases (n) or percentage (%). Comparisons of surgical methods were conducted using the Pearson chi-square test. A P-value < 0.05 was considered statistically significant. The difference in the distribution of surgical methods between the two groups was statistically significant (χ^2 = 120.433, P < 0.001), with the observation group showing a higher proportion of laparoscopic surgery, which is more consistent with the clinical adoption of minimally invasive techniques after 2019

Table 2: Results of multivariate logistic regression analysis for the risk of hyponatremia occurrence.

Independent variables	Unstandardized coefficients (B)	Standard error *(SE)*	*Wald*χ^2	*P*	Odds ratio (OR) (Exp (B)
constant term	-2.016	0.279	52.293	<0.001	0.133
Intervention group (Observation group vs. Reference group)	0.297	0.105	8.017	<0.005	1.346
modus operandi	0.227	0.115	3.873	0.049	1.255

Note: The composition of surgical procedures differed significantly between the two groups (χ^2 = 120.433, P < 0.001). The higher proportion of laparoscopic surgery in the observation group was consistent with the widespread clinical application of minimally invasive techniques after 2019.

Table 3: Comparison of the incidence of postoperative hyponatremia severity between the two groups of patients with uterine fibroids [n (%)].

	Reference group (n=844)	Observation group (n=1385)	χ2	p
130-135 (Mild)	170/844 (20.1%)	264/1385 (19.1%)	8.600	0.014
125-129 (Moderate)	40/844 (4.7%)	31/1385 (2.2%)		
< 125 (Severe)	8/844 (0.9%)	0/1385 (0.0%)		
Total	218/844 (25.8%)	295/1385 (21.3%)		

Note: The chi-square test was used to compare the distribution of hyponatremia incidence between the two groups, with P< 0.05 considered statistically significant.

Table 4: Symptom analysis of patients with moderate-to-severe hyponatremia in the two groups.

	2014-2019		2019-2024		P
	Severe (8)	moderate (40)	Severe (0)	moderate (31)	
dizziness	0	2	0	1	1.000
weakness	2	1	0	1	0.641
nausea and vomit	2	8	0	3	0.003
abdominal distension	2	8	0	3	0.003

Note: Fisher's exact test was used to compare the difference in incidence between the two groups, with P< 0.05 considered statistically significant.

Table 5: Comparison of the incidence of postoperative acute moderate-to-severe hyponatremia between the two groups of patients with uterine fibroids [n (%)].

group	N	Moderate to severe acute hyponatremia occurred (Occurred Time <48 h)	not occurred	occurrence rate
Reference group (2014-2019)	48	48	0	48/48 (100%)
Observation group (2019-2024)	31	30	1	30/31 (96.8%)
Total	79	78	1	78/79 (98.7%)

Discussion

Uterine fibroids are among the most common benign tumors in women and are hormone-dependent in nature. The prevalence of uterine fibroids in women of reproductive age over 30 years is approximately 20%.[10,11] Current clinical management options include conservative treatment and surgical intervention. Among these, surgery remains the most direct and effective approach, particularly for patients with poor response to conservative therapy or those without childbearing requirements.[12,13]Oxytocin injection, a peptide hormone composed of nine amino acids, is secreted by the posterior pituitary gland. It was the first hormone whose molecular structure was elucidated and successfully synthesized artificially.[14] Oxytocin acts by binding to specific receptors on the cell membrane of uterine smooth muscle, thereby promoting uterine contractions. Clinically, it is widely used for the prevention and treatment of postpartum hemorrhage, as well as for managing intraoperative and postoperative bleeding following myomectomy.[15,16] However, oxytocin administration has been reported to induce hypotonic hyponatremia[6], which may lead to adverse clinical outcomes if not promptly recognized and managed. The present findings, in line with previous reports, suggest that patients receiving intravenous oxytocin are at increased risk of developing acute moderate-to-severe hyponatremia, highlighting the importance of close monitoring of serum sodium levels in this population. The mechanism is likely related to oxytocin's antidiuretic effect, which promotes water retention and dilutes plasma sodium concentration, especially in the context of excessive fluid administration.

Hyponatremia is a well-established predictor of mortality.[17] Early, standardized classification, diagnosis, and treatment of hyponatremia have been shown to effectively reduce disease-related mortality and improve patient outcomes[10]. The clinical data from the present study confirm that, in patients receiving intravenous oxytocin after uterine fibroid surgery, a systematic intervention based on specialty-specific hyponatremia critical value alerts can significantly reduce the incidence of hyponatremia—particularly moderate-to-severe cases—thereby enhancing perioperative safety and clinical practice quality.

Clinical appropriateness of specialized critical value threshold adjustment

The currently prevailing critical value threshold for hyponatremia in China is 120 mmol/L, which is also adopted in our hospital. However, this threshold is primarily designed for general hospitalized patients and does not adequately account for the unique characteristics of patients undergoing myomectomy who receive intravenous oxytocin—namely, the acute onset and rapid progression of hyponatremia[9]. In the present study, the specialized critical value threshold was raised to 129 mmol/L, based on an in-depth analysis of the disease profile in this population. At a sodium level of 129 mmol/L, although the value does not meet the traditional definition of a "critical" threshold, it serves as an early warning sign for patients at risk of progressing to moderate or severe hyponatremia following surgery and oxytocin administration. Initiating intervention at this point can effectively prevent further deterioration.

The results demonstrate that, after implementation of the adjusted threshold, the overall incidence of hyponatremia decreased from 25.8% to 21.3%, and the incidence of moderate-to-severe cases dropped from 5.6% to 2.2%. Notably, severe hyponatremia was completely eliminated in the observation group. These findings confirm that a specialized threshold adjustment addresses the "delayed alert" limitation of the universal standard, thereby improving the timeliness of intervention. This approach contrasts with the findings of Zhou *et al.*[7], who reported that only 32.5% of hospitals modify critical value thresholds according to specific diseases, highlighting both the targeted nature and the necessity of the intervention applied in this study.

Synergistic effect of multidimensional systematic intervention

The systematic intervention in this study was not limited to threshold adjustment; rather, it established a multidimensional prevention and control framework comprising "threshold-based alerting, dynamic monitoring, patient education, solvent optimization, and dietary management." First, the modified threshold provided an early signal for clinical staff, enabling timely identification of high-risk patients.Second, preoperative and postoperative dynamic serum sodium monitoring ensured continuous tracking of sodium fluctuations, overcoming the limitation of passively waiting for a critical value trigger. As emphasized by Guan *et al*.[3], even mild hyponatremia warrants attention due to its potential to progress, making proactive monitoring a cornerstone of early intervention. Third, targeted health education improved cooperation from patients and their families, facilitating prompt reporting of early symptoms such as fatigue and nausea, which served as additional triggers for intervention. Finally, the use of normal saline as the oxytocin diluent addressed a key modifiable risk factor at the source, reducing the likelihood of hyponatremia induction. This approach aligns with previous findings, who reported that details of oxytocin administration influence the risk of hyponatremia. Collectively, these measures worked in synergy to achieve early prevention and treatment of hyponatremia across multiple stages of care.

Implications of the pathophysiological features of acute hyponatremia for intervention strategies

The present study identified that 98.7% of moderate-to-severe hyponatremia cases occurred acutely, a finding that provides critical insight for the formulation of intervention strategies. According to the 2014 European Clinical Practice Guideline on the Diagnosis and Treatment of Hyponatremia[2], acute hyponatremia requires strict control of the rate of sodium correction to minimize the risk of osmotic demyelination syndrome (ODS). By raising the specialized critical threshold, clinicians gained a wider therapeutic window, allowing for more gradual and safer correction of sodium levels. This approach likely contributed to the absence of ODS cases in the observation group. Previous evidence reported a single case of severe oxytocin-associated hyponatremia; however, large-sample interventional evidence was lacking. The current study, based on data from 2,229 patients, demonstrates that the combination of "specialized threshold optimization and multidimensional intervention" can effectively prevent and control this acute complication. These findings fill an important gap in the existing literature and offer a novel practical model for the safe management of oxytocin administration in gynecologic postoperative care.

Implications for policy and practice

The results of this study have important implications for clinical practice and hospital policy. In clinical practice, using an elevated, specialty-specific critical value for hyponatremia can enable earlier warning and intervention for patients undergoing myomectomy with perioperative oxytocin infusion, effectively reducing the incidence of severe acute hyponatremia. For hospital policy and laboratory management, our findings support the establishment of specialized critical value protocols rather than relying only on general thresholds. This simple and cost-effective strategy can be integrated into routine perioperative care to improve patient safety and clinical outcomes.

Study strengths and limitations

The primary innovation of this study lies in the development of a specialized critical value management system for hyponatremia tailored to the specific needs of patients receiving intravenous oxytocin after myomectomy. This approach not only provides empirical support for specialty-specific critical value management but also aligns with the recommendation in the Chinese Expert Consensus on Hyponatremia (2023 edition)[10], which advocates for individualized adjustment of diagnosis and treatment strategies according to clinical context. From a practical perspective, the proposed intervention is straightforward to implement, cost-effective, and does not require substantial additional medical resources. These features facilitate its broad applicability across gynecology departments in hospitals of various levels, offering significant potential to reduce perioperative risks and improve patient outcomes. However, several limitations should be noted. First, the study was conducted at a single center, which may limit the generalizability of the findings. Second, despite the relatively large sample size, the investigation focused exclusively on patients undergoing myomectomy; therefore, the applicability of the intervention to other surgical populations remains to be verified. Third, long-term follow-up data on patient outcomes beyond the immediate postoperative period were not collected, precluding assessment of sustained effects. Future multicenter, prospective studies with extended follow-up are needed to validate and refine the proposed management strategy.

At the same time, this study has certain limitations. First, it was a single-center retrospective study, and the sample selection may have been subject to bias; therefore, the generalizability of the results needs to be further validated through multicenter prospective studies. Second, the potential effects of factors such as age and underlying comorbidities on the efficacy of the intervention were not analyzed in depth. Future investigations could perform stratified analyses to explore personalized intervention strategies. Third, the study did not quantify the impact of the intervention on hospital length of stay or medical costs. Subsequent research should incorporate these indicators to provide a basis for health economic evaluation of the proposed protocol..

Conflict of interests

The authors have no conflict of interest to declare.

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Authors contributions

Zhijing Yang and Liufang Wang contributed equally.Zhijing Yang and Liufang Wang: Conceptualization, Methodology, Investigation, Writing – Original Draft, Visualization. Youlu Wang: Software, Validation, Formal analysis, Data Curation, Writing – Review & Editing. Jie Luo: Resources, Supervision, Project administration, Funding acquisition, Writing – Review & Editing. All authors have read and agreed to the final version of the manuscript.

Data availability

The data that support the findings of this study are available from the corresponding author, [Jie Luo], upon reasonable request.

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