



Patients' caring experience during procedures under regional anesthesia in Mainland China: A phenomenology study

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ABSTRACT

Background: Although regional anesthesia is common, the procedure results in feelings of uncertainty and anxiety in some patients. Increased care is needed for these patients under general anesthesia. Few studies have focused on the intraoperative caring experience of patients during regional anesthesia. This study focused on the caring experience of patients during procedures involving regional anesthesia.

Methods: The descriptive phenomenology method of Husserl was employed. Semi-structured interviews were conducted with a purposive sample in five Grade III-A hospitals in Zhengzhou City, Henan Province. The seven-step analysis method of Colaizzi was applied for the analysis, summation, and theme refinement of the interview data.

Results: A total of 14 patients from five hospitals participated in the interviews. Four domains and 16 themes emerged during analysis: be informed (about the operation site, progression of the operation, informed in advance, receive explanation for abnormal experience); take care of my body (painless, gentle movements, special care); be protected (work seriously, favorable atmosphere, skilled, authority); and treated as an individual (pay attention, accompany, ask for opinions, encourage patient expression, humorous).

Conclusion: Patients during procedure under regional anesthesia had specific caring experiences relative to other patients. Medical staff should recognize the importance of regional anesthesia patients' intraoperative caring experience. Hospital administrators should offer support to allow healthcare staff to provide targeted caring for patients during procedure under regional anesthesia.

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1. Introduction

Medical improvements, advancements in rapid recovery, and the demands of fast-paced modern lifestyles have driven revolutionary changes in surgical methods. Surgical procedures performed under regional anesthesia have become more widely used in many disciplines [1]. In such procedures, a stable physiological support of applying anesthetic drugs to the central nervous system is not required [2]. The significant benefits of procedures under regional anesthesia include low risk of anesthesia [3], short surgery time [4], reduced incidence of adverse reactions [3,4], low incidence of complications [2,4,5], improved surgical outcomes [2,6], shortened hospital stays [3,4,7,8], and reduced healthcare costs [4,9–11]. More importantly, in the context of the global COVID-19 pandemic, medical teams are more inclined to perform procedures under regional anesthesia if conditions permit. This is because surgeries involving general anesthesia generate a large amount of aerosol due to essential intubation, whereas regional anesthesia greatly reduces the risk of virus transmission and infection of medical personnel [12–14].

However, reported weaknesses of procedures performed under regional anesthesia include increased surgery-related anxiety [15, 16], aggravated pain [17], worse discomfort [3], and lower patient satisfaction compared to general anesthesia surgeries [7]. Despite their low risk, procedures under regional anesthesia still have uncertainties and risks, like all surgeries. In addition, patients may struggle with the reality of experiencing the entire surgical process, rather than being unconscious. Thus, the caring received from healthcare staff is important for patients. This caring can help patients cope with the difficulties they experience and remain comfortable. Unfortunately, little attention has been paid to the caring experience of patients during procedures performed under regional anesthesia. Increased knowledge can provide a reference for medical staff and help in targeted caring for patients. Provision of caring can reduce the negative feelings and increase satisfaction for regional anesthesia patients.

In the present study, a qualitative analysis examined the caring experience of patients during procedure under regional anesthesia. The intent was to help medical and healthcare staff better understand patients' caring experience during surgeries, support them in providing more comprehensive caring for such patients, and improve the quality of caring in the future.

2. Methods

Husserl's descriptive phenomenology [18] was applied. Interpretivism was selected as the research paradigm. This study was deemed exempt by the Luoyang Orthopedic Hospital of Henan Province Institutional Review Board (KT2020-004-01).

2.1. Study subjects

Patients admitted to five Grade III-A hospitals in Zhengzhou for procedures involving regional anesthesia from June to August 2021 were enrolled by purposive sampling. Procedure performed under regional anesthesia were defined as surgeries in which patients were at any level of anesthesia and retained the ability to understand, recognize, and respond to verbal stimuli [19]. After anesthesia, the Montreal Cognitive Assessment (MoCA) [20] scores of all patients were not <26. The first author had friends or classmates in all the departments in which samples were selected, so that the desired samples could be obtained. The information of patients, including age, sex, education background, occupation, surgical history, and anesthesia method, were considered in the sampling process.

Patients at least 18-years-old who remained conscious during surgeries, had good expression and communication skills, stable conditions, and agreed to participate in this study by signing the informed consent form were included. Patients whose anesthesia was switched to general anesthesia, suffered from mental disorders, or refused interview recording by audio or text were excluded. The data of patients whose interview was stopped due to physical discomfort and other reasons were deleted.

2.2. Data collection

Data were collected via personal interviews that took place from June 21, 2021 to August 19, 2021. Among the selected patients, outpatient surgery patients were followed up by telephone within 24 h after surgery. Inpatients were interviewed at the bedside within 48 h after surgery. All the interviews were conducted in private environments, such as in private wards or at the bedside enclosed by curtains. All patients signed the informed consent form and confidentiality was ensured. Semi-structured interviews were conducted by the first author (Rui Chen) following an outline. Before data collection, the research team pre-formulated an interview outline and carried out pre-interviews on two patients; one had received a hysterectomy and the other cataract surgery. Another study author (Ying Chen) observed the nonverbal actions of patients, and provided mutual evidence after interviews to improve the reliability and internal consistency of the research results. Only the two aforementioned individuals were involved in the interviews. Two research assistants (Meng Yang and Xinhui Zhang) were recruited to assist the first and second authors in reviewing the refined themes. All four researchers had a master's degree and had received training in qualitative research.

The interviews were recorded with a model SR901 smart voice recorder (iFLYTEK), which was placed at a suitable position within 90 cm from the patient's mouth. The interviews started with a general discussion to build a relationship with interviewees, followed by an open-ended question about how the patient felt when entering the operating room. Other questions included what patient-perceived caring behaviors, language, and other aspects of the medical staff in the operating room; whether someone impressed them in the operating room; and what that individual did. During interviews, prompts, reflections, and open-ended questions were used to promote participant conversation. Those interviewed were prompted to explain their experience, which was verified by asking questions. The researchers briefly recorded the interview experience, including their immediate impressions. The sample size was determined based on the repeated interviewee data. The interview finished when no new themes emerged. The present study employed

Table 1
Demographics of patients.

No.	Sex	Age, years	Educational background	Job	Surgical history	Surgery type	Anesthesia method	Surgery duration, h:min	Anxiety score	Pain score
1	Male	32	Senior high school	Self-employed	0	Intervertebral disc radiofrequency ablation	Regional block anesthesia	1:05	17	2
2	Male	35	Senior high school	Driver	0	Intervertebral disc radiofrequency ablation	Regional block anesthesia	1:23	13	0
3	Male	61	College	Retired worker	1	High ligation of saphenous vein of right lower extremity	Spinal anesthesia	2:23	24	0
4	Male	65	Primary school	Farmer	0	Vertebroplasty	Regional nerve blockade	1:07	18	2
5	Female	51	Senior high school	Salesperson	4	Anal fissure resection	Spinal anesthesia	0:27	19	1
6	Female	31	Postgraduate	Teacher	0	External hemorrhoidectomy, internal hemorrhoid suture	Spinal anesthesia	0:19	15	1
7	Female	40	Postgraduate	Civil servant	2	Hysterotokotomy	Spinal anesthesia	0:22	9	1
8	Female	32	Postgraduate	Doctor	0	Hysterotokotomy	Spinal anesthesia	0:38	7	1
9	Female	23	College	Self-employed	0	Hysterotokotomy	Spinal anesthesia	0:44	14	1
10	Female	56	Junior high school	Freelance	1	Corneal laceration debridement and suture	Local anesthesia	2:24	/	3
11	Male	32	Undergraduate	Administrative	0	Fibromectomy	Local anesthesia	0:33	17	1
12	Male	49	Primary school	Farmer	0	Glioma resection	Spinal anesthesia	2:54	13	0
13	Female	69	Primary school	Farmer	1	Glioma resection	Spinal anesthesia	1:47	16	0
14	Male	63	Junior high school	Farmer	1	Cataract phacoemulsification combined with lens implantation	Local anesthesia	0:29	22	0

Table 2
Sample responses from thematic domains.

Domain	Theme	Sample responses [†]
be informed	Be informed about the operation site	During the operation, the doctor said “you see, you have serious problems,” and then told me that my perianal eczema problem was more serious. (Participant 5) The doctor said “Your sore is not big, but you have eczema.” (Participant 6) At the end of the operation, he told me that it went well, and told me to go back to the ward to rest. (Participant 14)
	Be informed about progression of operation	The doctor said “It’s half-done, so far all went well.” (Participant 3) I was told “We are about to start your anesthetic.” (Participant 13)
	Be informed in advance	[The doctor] stopped and said it might feel painful later. (Participant 5) [The doctor told] me about my disease and also told me about the situation of other people who has the same disease. (Participant 10).
	Receive explanation for abnormal experience	The nurses were very amiable. When the surgery was stimulating and I felt painful, they would tell me that all these were normal. [They advised me to] relax and not to be nervous. Then, I felt relieved. (Participant 7)
	take care of my body	Painless
Gently movements		[Relocation was quick and painless, and took] just a few seconds. I thought it would take a long time. They just shouted one, two, and then moved me to another bed. Three girls did it for me. (Participant 2) I was very [carefully and gently] moved from the operating bed to the transportation bed. (Participant 6)
Special care		[I was covered with a heated blanket]. (Participant 13) The anesthetist said “I will give you a kid’s tube later, you will feel better.” (Participant 9) I said I was a little sick, and the nurse said I could vomit, and put a cloth on me. I vomited twice, and the nurse then wiped my mouth. (Participant 7)
be protected		Work seriously
	Favorable atmosphere	The doctors and nurses were chatting, and they were chatting with me. I was so happy. I liked the atmosphere here. I knew if they are working without talking, it [meant that the task was serious] (Participant 8) The atmosphere was good. The healthcare staff were all very nice. It was not scary [and]. Not as [I had] expected. (Participant 4) Each of them was very good. I suddenly had a feeling that the unfamiliar environment was [more familiar]. I felt I could actively control the environment. (Participant 7) She asked me which songs she can play for me ... I just focused on the music and thought [about] nothing. (Participant 8) The doctor did not know me, but she was very friendly and [talked] to patients. (Participant 10) They talked [in a friendly way]. You won’t be afraid when she comforts you. (Participant 13)
	Skilled	The doctor was very skilled in suturing, and it was just finished in a few seconds. (Participant 9)
	Authoritative	After a while, I heard them call [for the Director]. I [felt a] weight off my shoulder. (Participant 10)
	As an individual	Pay attention
Accompany		The doctor was with me the whole time. Unexpectedly, she held my hand, including the anesthesia process. Based on this, I trusted her. (Participant 10) I said I was scared, and she (the doctor) touched my head and said “It will be okay, it’s almost over.” (Participant 7)
	Asking for opinions	[The doctor] asked could [they] we take a picture just of [the surgery site]. (Participant 11) The director asked if [I wanted help in treating perianal eczema]. I said yes. (Participant 5)

(continued on next page)

Table 2 (continued)

Domain	Theme	Sample responses ¹
	Encourage expression	A healthcare staff person told me “If you have any questions, let me know.” (Participant 4) The doctor kept telling me that if I felt uncomfortable I should speak out. (Participant 1) [The doctor told me that] when it hurts, not to bear it. [He kept] asking me if it hurt or not. (Participant 13)
	Humorous	After the operation, the doctor said that I could slow down. I rolled over and jumped down, and the doctor said “Hey, you are still a flexible fat man.” (Participant 11) The doctor said “You must be a good drinker.” When I said why, he said you could not feel your lower body after giving you so much anesthetic. He said “I have never seen someone so strong, and I guess you can drink half a pound.” (Participant 11)

the method of theoretical saturation testing through interview samples and expert validation. Theoretical saturation testing was used to determine when to stop the interview process, when no new theoretical insights could be generated from the collected new data. Based on the preliminary themes and sub-themes, three experts reviewed and validated all data and coding processes. The three experts identified no errors or new themes, indicating that the study had achieved theoretical saturation. The study followed the principle of triangulation, selecting interviewees with different educational backgrounds, ages, and surgical experiences to ensure the specificity and comprehensiveness of the information obtained. Additionally, relevant literature was continuously collected to validate the themes formed during the research process to ensure completeness and validity.

2.3. Data analysis

Within 24 h after the interviews, the recordings were transferred into text sentence-by-sentence. Data storage and management utilized NVivo 9.0 software (QSR International, 2010). The Colaizzi seven-step analysis method was adopted to analyze interview data, including careful reading of the text, extracting key statements, coding and summarizing recurring ideas, providing descriptions that were as detailed as possible, analyzing similar ideas, and summarizing and refining themes. Any ambiguous conclusion was determined through feedback with interviewees. A total of six themes were obtained after two researchers (Rui Chen and Ying Chen) separately analyzed the research data. Five themes were generated by the other two research assistants (Xinhui Zhang, Jianlei Li) after they analyzed the interview recordings. Through the discussion among the four researchers, the two themes of “sense of trust” and “participation” were incorporated into other themes. The entire study group agreed on the final four domains.

3. Results

3.1. Participants

Among the 19 patients invited to participate in the interviews, one patient suffered from wound pain during the interview, one patient stopped the interview due to nausea and vomiting, and three patients refused interviews because they objected to recording of the conversations. Finally, 14 patients completed the interviews, which lasted for 22–91min. 2 and 12 patients were recruited in the outpatient and inpatient department, respectively. The Chinese version of the Hamilton Anxiety Scale was used to measure anxiety during the preoperative visit on the evening before surgery. A Numerical Rating Scale was used to assess pain in the first 6 h after surgery for patients. In addition to routine anesthetic drugs, antibiotics were used before surgeries for patients 4, 7–9, and 12–14, and ibuprofen was used as a painkiller for patient 4. Compound tropicamide eye drops were used as a mydriatic for patient 14. Sedatives, such as dexmedetomidine and diazepam, were used for patients 3, 4, 6, 12, and 13 during the procedures. The general data of the interviewees are listed in [Table 1](#).

Zhengzhou hospitals usually enhance the patient surgical experience in the following four aspects. First, regarding preoperative education, doctors assess the patient’s physical condition before surgery and provide detailed surgical information and precautions to inform patients of the entire process and potential risks, which can help alleviate patient anxiety and fear. Second, regarding pain control and sedatives, analgesics are administered to patients before surgery to relieve preoperative pain. During surgery, the dose and concentration of local anesthetics are adjusted according to the patient’s response to ensure that the patient does not experience pain during surgery. For some anxious or worried patients, the hospital may administer oral or intravenous sedatives before surgery to reduce patient tension and anxiety. Third, concerning intraoperative attention, doctors maintain communication with patients during surgery to monitor the patient’s condition and feelings, which can inform adjustments of the dose and concentration of local anesthetics, to increase patient confidence and safety. In addition, nurses pay attention to the patient’s vital signs and promptly handle any abnormalities. Finally, in terms of the environment, the operating room is kept clean, tidy, and comfortable, so that patients feel warm and safe.

According to the interview results, the caring experience of patients could be classified into four domains: be informed, take care of my body, be protected, and treated as an individual. These domains are addressed in detail below. Representative comments of patients for the various domains are presented in [Table 2](#).

3.2. Be informed

Eight patients mentioned that they considered being informed as caring. Four themes were evident in this domain: be informed

about the surgical site, be informed about progression of surgery, be informed in advance, and receive an explanation for an abnormal experience. In terms of being informed about the surgical site, the medical staff delivered information to the patient in simple, clear, and easy-to-understand words, so that the patient could promptly and accurately understand their disease condition and the progress of surgery. These actions were important indicators of caring experience. The medical staff could also inform the patient of things that might happen in advance, so that the patient would be aware of these subsequent situations and stay calm when they occurred. During surgery, patients could often experience abnormal situations, such as pain. Anxiety could be lessened if medical staff explained in a timely manner that these abnormal situations were normal.

3.3. *Take care of my body*

Eight patients mentioned that attention given to their bodies during surgery was caring. During surgery, a patient is often passive and unable to move independently, with poor self-care ability. Assistance from medical staff is needed, which can generate patients' concern about physical caring. Physical trauma is inevitable in surgery, and it often causes pain. This is a major reason for patients' fear of surgery. In the interviews, patients frequently mentioned that the absence of pain during surgery was a sign of caring. When transferred after surgery, an anesthetized patient cannot move independently. Medical staff with professional skills can help gently and quickly transfer the patient, and reduce pain and suffering. This aspect was highly praised by patients. In addition, special care for a patient is also considered caring. The ambient temperature of the operating room is often low. Medical staff can help keep the patient warm, which can minimize their discomfort and pain. Medical staff also provided help and care to the patient in the case of an accident during surgery.

3.4. *Be protected*

Eleven patients regarded being protected as caring. A patient undergoing surgery in an unfamiliar environment is in a passive position that can be distressing due to their lack of relevant medical knowledge. Fear and dependence emerge, and the patient even becomes sensitive and vulnerable. Special support and protection are required from medical staff. At this time, medical staff can create an environment where the patient feels protected. The patient will have an enhanced sense of trust and feel reassured and relaxed. In the patient's view, being protected is manifested as follows: medical staff carefully check and discuss difficult problems, quietly focus on the surgery, and correct the mistakes of colleagues in a timely manner. All these actions are expressions of caring. In terms of a favorable atmosphere, after the patient entered the operating room, music was played and noise was reduced to create a relaxing environment and effectively relieve anxiety throughout the surgery. Medical staff also communicated with the patient to build a relaxed atmosphere. In terms of technical proficiency, the conscious patient could directly perceive the proficiency of the medical staff. Realization of this technical proficiency could make the patient feel more at ease. In terms of authoritative experts, the patient will be more confident in the surgery and will obtain psychological comfort after knowing that the chief surgeon is an authoritative expert.

3.5. *Treated as an individual*

Eleven patients regarded being treated as an individual as caring. The patient will feel more like a whole person when treated as an individual, with medical staff providing full attention to the patient and respecting his/her uniqueness and dignity. Being treated as an individual is manifested in five aspects. The first is to pay attention. A patient is especially eager for the attention of medical staff due to physical discomfort and surgical fear. The attention of medical staff can make the patient feel that they are being taken seriously. The second aspect is to accompany the patient. During surgery, medical staff accompanies and made physical contact with the patient, such as by touch. This could instill a sense of caring and being sheltered during a vulnerable time. The third aspect was to ask for opinions. During surgery, the patient had a weaker role, rather than a social role. However, the patient's subjective initiative could be inspired when medical staff allowed him/her to participate in the surgical process and seek opinions on treatment. The fourth aspect was to encourage expression. Medical staff with caring characteristics often encouraged the patient to express their positive and negative emotions, so that true feelings and condition could be understood and psychological pressure relieved. The fifth aspect was humorous communication. The medical staff created a relaxed and happy atmosphere using humorous and witty language, closing the distance with the patient and making the patient feel recognized.

4. Discussion

Surgery is a major source of mental stress for patients. As a response, patients will try to restore the intraoperative situation through previous life experiences and guesses [21]. Surgical fear is a normal and complex emotional response often caused by patients' guesses about whether the surgery is successful or not, and how they will recover after surgery, which is essentially the fear of bodily injury and death. Ramirez et al. [22] and Theunissen et al. [23] conducted surveys on patients using the surgical fear questionnaire (SFQ). The results showed that the patients were fearful and anxious about their short- and long-term surgical consequences. In the regional anesthesia state during surgery, the patients can fully and clearly perceive the surgical process and focus on the surgery. At the same time, they are also unfamiliar with the operating environment and have little understanding of the surgical situation and progress, which exacerbates their fear.

Therefore, caring is important in procedures performed under regional anesthesia, in which the patients lose autonomous control of their own bodies. With the caring relationship established between the patient and the medical staff, the patients will feel that they are

in a safe and secure state, and regain a sense of identity during surgery to meet their physical and emotional needs. When caring becomes the foundation of healthcare system, the patients' intraoperative experience will be improved, surgical outcomes may be affected, and the quality of caring will be better. This is good for patients and for the hospital's reputation and profitability. Therefore, all aspects of healthcare system will benefit.

Surprisingly, the themes identified in this study were largely consistent with the domains of the holistic caring inventory (HCI). The HCI assesses the holistic caring delivered and patients' feelings about caring [24]. The inventory covers four dimensions (physical, interpretive, spiritual, and sensitive). These four dimensions correspond respectively to the presently-identified domains of being informed, take care of my body, be protected, and treated as an individual. The possible reason is that HCI emphasizes the whole, while the patients in this study preferred to be considered as a complete individual during surgery, and expressed their caring perceptions more when they needed holistic caring.

In a study on the surgical process of various patients under local anesthesia, Hudson et al. [25] found that the patients felt unprepared for the surgical process, had insufficient information, and experienced anxiety and restlessness, highlighting the importance of communication. The explanation of the themes were also refined in a paper on the surgical process of patients under local anesthesia [26], consistent with the implication of being informed in this study. If patients who are conscious during surgery do not have sufficient information, they cannot predict what will happen next or how long something will last. The patients sense of uncertainty and anxiety will be enhanced and they will be more eager for information. Once the surgical process becomes completely opaque, the patients will feel disorientated, more sensitive, and isolated. Therefore, adequate, timely, and comprehensive information support is crucial for surgical patients.

As previous studies described, physical caring and being treated as an individual are important for surgical patients. Hudson [25] showed that the physical support from the nursing staff in the operating room greatly helped patients. Zemmoura et al. [26] argued that conscious patients who felt pain during skin suture were concerned about physical caring, while those who felt no pain thought that they were cared for. These findings are consistent with the results in this study and bolster the view that the physical comfort of the patient is an important part of the patient's perception of the surgical success [27]. Kim et al. [28] emphasized being a person, which is essentially consistent with being an individual in the present study. Patient-centered caring may improve patient experience and satisfaction, and make patients feel caring.

Interestingly, patients rarely mentioned the technical proficiency of medical staff. Instead, they cared more about the working attitude of medical staff and their attitude towards patients. In most previous studies, patients ranked technical proficiency first among all caring attributes [29]. In this study, surgical patients placed more emphasis on the medical staff's perception and response to them. Such differences also represented the specific caring experience of surgical patients.

How can healthcare workers improve the intraoperative experience of patients under regional anesthesia? Undoubtedly, the answer lies in the diligent execution of their professional roles, as patients expect healthcare providers to "do your job well, focus on what needs to be done, and do it well." [30] At the hospital level, relevant organizational structures should be established, standardized procedures and evaluation tools developed based on the results of relevant research. Furthermore, healthcare providers should receive standardized education, training, supervision, and assessments to truly understand the importance of caring and how to care for patients receiving regional anesthesia. This ensures homogeneous caring and effective treatment for patients. The critical role of administrative and physician leadership should be emphasized. Specifically, a guideline [31] and a cohort study [32] suggest that clinical physicians should provide patient and family-centered personalized education and sufficient information to patients (and/or responsible caregivers), which can improve patient experience and reduce fear of surgery. Similarly, hypnosis and acupuncture can replace sedatives to reduce intraoperative anxiety in patients receiving regional anesthesia, and intelligent surgical beds that allow patients to watch movies, listen to music, and video chat with family members are all paths that can improve the patient caring experience [33–35].

In this study, patients were interviewed within 48 h after surgery, so their memory of their surgical process was still fresh. The patients were from five hospitals in Zhengzhou, but came from different cities in Henan Province. The health system in Henan Province is in the middle level in China, which can represent to a certain extent the condition of medical institutions in China. The patients in this study were enrolled from orthopedics, obstetrics, ophthalmology, and general surgery departments. Thus, the results are applicable to a majority of regional anesthesia patients, making it easy to find potential implications.

There were limitations of this study. Due to the impact of the COVID-19 pandemic, data were not collected from other cities, and all patients were from Grade III-A hospitals in Zhengzhou City, Henan Province. Thus, the conclusions may not be applicable to primary medical institutions and private hospitals. All the patients were older than 18 years of age. The caring experiences of underage patients were not described. In the future, relevant scales can be developed combined with literature review and qualitative research results to more specifically understand the caring perception of regional anesthesia patients during surgery, which will provide guidance for clinical improvement.

Caring is vital to patients. This study revealed four aspects of the caring experience of regional anesthesia patients during surgery. The findings established a basic conceptual framework for the caring experience of regional anesthesia patients during surgery, and provided directions for optimizing the caring experience during surgical procedures done under regional anesthesia. The results can guide healthcare staff to pay more attention to and understand the feelings of patients, and provide targeted caring measures, to improve the medical service capacity and environment from the patients' experience. The results also will help patients get through the hard time of surgery, which will benefit the healthcare system.

Author contribution statement

Rui Chen, Ying Chen, Xiangyang Cao: Conceived and designed the experiments; Performed the experiments; Analyzed and interpreted the data; Wrote the paper. Meng Yang, Xinhui Zhang, Jianlei Li: Analyzed and interpreted the data; Contributed reagents, materials, analysis tools or data; Wrote the paper. Yilan Liu, Xue Yang, Yufeng Liao, Guijuan Du: Conceived and designed the experiments; Contributed reagents, materials, analysis tools or data; Wrote the paper.

Data availability statement

The authors do not have permission to share data.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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