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Research article

Effectiveness of the addition of visual aids to conversational preoperative education in glaucoma filtering surgery: A randomized controlled trial

Peimin Lin^{a,b,1}, Laiwen Lv^{a,1}, Ruqing Tang^a, Dehua Li^a, Xiaoxuan Chen^a, Jie Fang^a, Zhenggen Wu^a, Chukai Huang^{a,*}, Kusheng Wu^{b,**}

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ABSTRACT

Background: This study aimed to evaluate the impact of preoperative visual aids on anxiety and pain management in patients with low educational backgrounds undergoing glaucoma filtering surgery.

Methods: A randomized, single-blinded, single-center clinical trial was conducted at a tertiary eye hospital in Shantou, China. Patients scheduled for glaucoma filtering surgery were randomly assigned to either a conventional oral education group or a visual aids group. Anxiety levels, pain scores, blood pressure, and pulse rates were measured at multiple time points.

Findings: The visual aids group demonstrated significantly lower anxiety levels (HAMA score: 19.6 \pm 1.7 vs. 27.9 \pm 3.1; p < 0.001) and pain scores (VAS: F = 174.628; p < 0.001) compared to the oral education group. Additionally, systolic blood pressure was significantly lower in the visual aids group (F = 6.373; p = 0.013). During the preoperative visit, patients in the oral education group asked significantly more questions (mean \pm SD: 4.0 \pm 1.3) compared to those in the visual aids group (mean \pm SD: 0.75 \pm 0.7; p < 0.001). However, their understanding of the surgery was notably lower than that of the visual aids group. The requirement for additional anesthesia due to pain was markedly higher in the oral education group, with 66.2 % (45/68) of patients needing extra anesthesia compared to only 4.6 % (3/65) in the visual aids group (p < 0.001). Furthermore, the ocular positioning compliance and cooperation during the surgery were significantly lower in the oral education group compared to the visual aids group (p < 0.001).

Interpretation: The inclusion of visual aids in preoperative education significantly improves patient outcomes in glaucoma filtering surgery by reducing anxiety and pain and stabilizing physiological parameters. This approach is particularly beneficial for patients with lower educational backgrounds.

^a Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong, Shantou, Guangdong, China

^b Department of Preventive Medicine, Shantou University Medical College, Shantou, Guangdong, China

^{*} Corresponding author. Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong, North Dongxia Road, Shantou, Guangdong, 515041, China.

^{**} Corresponding author. Department of Preventive Medicine, Shantou University Medical College, Shantou, Guangdong, China.

E-mail addresses: hck@jsiec.org (C. Huang), kswu@stu.edu.cn (K. Wu).

 $^{^{1}}$ Joint first authors.

Abbreviations:

ANS Autonomic nervous system HAMA The Hamilton anxiety scale VAS The visual analogue scale

SD Standard deviation

ANOVA Repeated measures analysis of variance

1. Introduction

Glaucoma comprises a group of eye diseases characterized by acute or chronic abnormal elevation of intraocular pressure, leading to optic nerve cupping, atrophy, and visual field defects [1]. The World Health Organization identifies glaucoma as the second leading cause of blindness and the primary cause of irreversible blindness [2]. Patients with glaucoma experience significant physical pain and psychological stress, potentially triggering various psychological issues such as anxiety and fear [3]. Filtering surgery is a crucial treatment for glaucoma, aimed at reducing and stabilizing intraocular pressure [1]. However, surgery as a stressor can induce varying degrees of anxiety, leading to vasomotor dysfunction and capillary dilation, potentially causing ciliary body edema. Additionally, excessive secretion of aqueous humor can result in elevated intraocular pressure [4]. If these psychological factors are particularly intense preoperatively, some patients may struggle to maintain proper eye positioning, impeding the smooth progression of the surgery and increasing the likelihood of surgical complications [5,6].

Filtering surgery can be complex and intimidating, particularly for patients with lower educational levels who may struggle to understand oral or written medical information. Preoperative visits provide an opportunity for healthcare providers to explain the procedure, its purpose, and what to expect using simple, clear language. The utilization of visual aids, including schematic diagrams, three-dimensional models, and instructional videos, has been demonstrated to significantly narrow the comprehension gap, thereby facilitating patients' understanding of critical information pertaining to the surgical procedure. This encompasses a comprehensive grasp of the operative steps, associated risks and benefits, postoperative management protocols, and anticipated outcomes. This approach could alleviate patients' doubts, and reduces anxiety [7–9].

Most glaucoma filtering procedures are performed under local anesthesia, as eye movement can affect the surgery. Continuous adjustment of the microscope and eye position is required during surgery to fully display the lesion. Preoperative visual and intuitive eye fixation training videos help patients understand how to maintain fixed eye positions and cooperate with the surgeon [10]. Proper head and eye position fixation reduces mechanical injury to the cornea from repeated intraoperative manipulation, preventing complications such as corneal injury caused by eye movement or misalignment during surgery, thereby enhancing surgical safety.

To date, there have been no reports of preoperative video education models being used for glaucoma surgery patients. This study aims to investigate whether the use of visual aids during preoperative visits can increase patient awareness of the operation and reduce anxiety during the surgical process in patients with lower educational backgrounds.

2. Methods

2.1. Study design

This study was a prospective, randomized, single-blinded, single-center clinical trial conducted at a tertiary eye hospital in Shantou, China, between March 2023 and February 2024. The study protocol was peer-reviewed and published on ClinicalTrials.gov (Identifier: NCT06478095). Glaucoma patients scheduled for filtering surgery performed by the same group of surgeons were enrolled consecutively and randomly assigned to either the control group or the visual aids group according to a random number table. These patients were administered local anesthesia, which consists of 0.5 % Proparacaine Hydrochloride Ophthalmic Solution, USP (ALCAINE®, Alcon, Belgium) applied topically in the form of eye drops, and 0.2 % Lidocaine Hydrochloride Injection (Shanghai Harvest Pharmaceutical Co., Ltd.) administered as an injection. The Proparacaine solution, with a concentration of 0.5 %, was indicated for corneal anesthesia of short duration and was used for procedures such as tonometry, gonioscopy, and removal of corneal foreign bodies. Lidocaine, at a concentration of 0.2 %, was utilized for its local anesthetic effects and is injected to provide anesthesia during the surgical procedure. This study was reviewed and approved by the Ethics Committee of the Joint Shantou International Eye Center of Shantou University and the Chinese University of Hong Kong (Approval Number: EC 20220505(4)-P30). All patients provided written informed consent.

2.2. Patients and intervention

Adult inpatients who were either illiterate or had completed only 9 years of compulsory education and had indications for filtering surgery were enrolled. Patients with mental illness or cognitive impairment were excluded from the study. After providing written informed consent and basic demographic information, the study subjects were randomly assigned to two groups: the conventional oral education group or the conventional oral education plus visual aids group (hereafter referred to as the visual aids group). Both groups aimed to educate patients about glaucoma, preoperative preparation, surgical procedures, anesthesia methods, and precautions during

the preoperative visit, all provided by the same nurse. The control group received only oral explanations, while the intervention group received oral education supplemented with visual aids, including images and short videos (Fig. 1).

2.3. Outcomes

The Hamilton Anxiety Scale (HAMA) questionnaire is designed to assess the severity of a patient's anxiety symptoms [11]. The total score ranges from 0 to 56, with higher scores indicating more severe anxiety. Each item is scored on a scale of 0 (not present) to 4 (severe), with total scores classified as follows: a total score above 29 is considered severe anxiety, above 21 is marked anxiety, 14–20 is mild to moderate anxiety, 7–13 is possible anxiety, and 0–6 is no anxiety. The Visual Analogue Scale (VAS) measures pain intensity [12]. The VAS consists of a 10 cm line, with two endpoints representing 0 ('no pain') and 10 ('pain as bad as it could possibly be'). The HAMA and VAS were used to evaluate patient stress at 3 time points: 1 day before surgery (before the preoperative visit), 30 min before surgery (after the preoperative visit), and at the end of the surgery. Additionally, a VAS evaluation was performed by the patient at the end of the surgery to recall the degree of pain experienced during the procedure.

Autonomic response markers to anxiety and pain, which are physiological indicators reflecting the reactions of the autonomic nervous system (ANS) to these stressors, are essential for elucidating the neurophysiological foundations of pain and anxiety [13,14]. In our study, we evaluated pulse rate and systolic and diastolic blood pressure using an electronic sphygmomanometer (Omron J7136, Japan) one day prior to surgery and again 30 min before the procedure to indirectly assess changes in preoperative anxiety and pain. Intraoperatively, these parameters were continuously monitored and recorded by an IntelliVue MP5 portable patient monitor (Philips M8105A, Germany), with data collection occurring at 5 min post-surgery onset and at the termination of the surgical intervention. Pulse rate and blood pressure measurements were recorded in beats per minute (bpm) and millimeters of mercury (mmHg), respectively.

During the preoperative visit, the number of questions raised by each patient was documented. The awareness of the surgical procedure was evaluated based on their comprehension of the surgery process, preoperative self-preparations, cooperation with the surgical team during the procedure, and postoperative recovery. Patients were assessed by nursing staff and classified into 4 categories: 'unaware,' 'aware,' 'partially proficient,' or 'proficient' before and after the preoperative consultation. A patient was designated as 'unaware' if they lacked knowledge in all 4 areas, while those who were knowledgeable in all aspects were rated as 'proficient.' The number of additional anesthetic (0.5 % Proparacaine, ALCON, Belgium) administrations during surgery was also recorded.

Before discharge, patients assessed their satisfaction with the preoperative visit using a Likert scale with the following options: extremely dissatisfied, dissatisfied, acceptable, satisfied, and very satisfied. Additionally, surgeons, who were blinded to the patient group assignments, evaluated patients' ocular positioning compliance and cooperation during the surgery. Ocular positioning compliance were assessed using a standardized rating system as follows: Non-compliance referred to patients whose continuous eye movement significantly interferes with the surgical procedure. Partial compliance was designated for those who can maintain fixation but require intermittent reminders from the surgical team, sustaining fixation for over 3 min post-reminder. Full compliance was attributed to patients who consistently maintain fixation in a specified direction throughout the entire surgical intervention. The surgeon's evaluation of patient cooperation was categorized into 5 distinct levels: Extremely Non-compliance for patients who make substantial unannounced movements, including sneezing or contaminating sterile fields, severely impeding the surgical process. Non-compliance for patients with minor head or limb movements and persistent eye movement, necessitating continuous reminders to proceed with the surgery. Acceptable for patients who kept their head and limbs relatively still, proactively communicate any intended

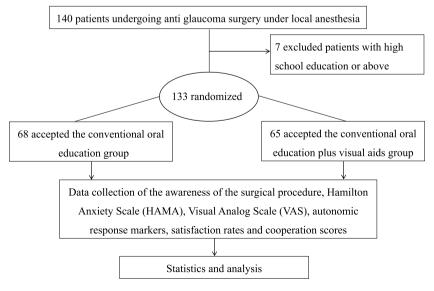


Fig. 1. Flowchart of the study.

movements to the surgical team, and require more than 3 prompts for occasional eye deviation. Compliance for those who maintained stillness and fixation with only 1–3 reminders during the procedure. Highly compliance for patients who strictly adhered to all instructions issued by the surgical team throughout the surgical process.

2.4. Sample size

G*Power software (version 3.1) were used to estimate the sample size. Based on preliminary estimation from pre-survey results, the effect size to detect the mean difference of anxiety score between 2 groups after preoperative visit was approximately 0.5. In a priori power analysis, with a significance level (alpha) of 0.05, and power of 0.8, the minimum requirement to detect difference between 2 independent means using *t*-test was calculated to be 128, with 64 in each group.

2.5. Statistical analysis

For continuous data, normality was assessed using the Shapiro-Wilk test or the Kolmogorov-Smirnov test. If the data in each group were normally distributed and the variances between the groups were equal, descriptive statistics were reported as mean \pm standard deviation (SD), and independent samples t-test were employed for between-group comparisons. Categorical data were described using frequencies (percentages), and the chi-square test was utilized to detect intergroup statistical differences. For comparisons involving repeated measurements between groups, repeated measures analysis of variance (ANOVA) was conducted. Statistical analyses were performed using SPSS version 24.0 (IBM SPSS Inc.), all tests were two-tailed, p-value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics prior to the preoperative visit

A total of 133 adult patients (59 males, 74 females), aged 23–84 years with a mean age of 63.1 ± 11.6 years, were recruited for the study. Among these patients, 78.9 % (105/133) had completed 9 years of compulsory education, while 21.1 % (28/133) were illiterate. Prior to the preoperative visit, none of the patients exhibited partial proficiency or proficiency in the awareness of the surgical procedure; 85.7 % (114/133) were unaware of the surgical procedure despite 29.3 % (39/133) having prior surgical experience. The mean systolic and diastolic blood pressures were 133.4 ± 12.2 mmHg and 79.7 ± 6.9 mmHg, respectively, and the mean pulse rate was 69.8 ± 8.9 bpm. Pain was reported by only 1 patient, who rated it as 2 on the VAS. The average anxiety score, as assessed by the HAMA, was 16.3 ± 1.5 , indicating mild anxiety with scores ranging from 11 to 24; of the patients, 81.2 % (108/133) exhibited mild anxiety, while 18.8 % (25/133) were classified as experiencing mild to moderate anxiety. Baseline characteristics between the oral education group

Table 1
Baseline demographic information, surgical history, awareness of the surgical procedure, and stress of all patients before preoperative visit (2023–2024).

		Oral education group	Visual aids group	p-value
Age (year)	n	68	65	0.092
	Mean±SD	64.7 ± 11.3	61.3 ± 11.7	
Gender	Male	33 (48.5)	26 (40.0)	0.384
	Female	35 (51.5)	39 (60.0)	
	Total	68 (100)	65 (100)	
Education	Illiterate	18 (26.5)	10 (15.4)	0.117
	Compulsory education	50 (73.5)	55 (84.6)	
	Total	68 (100)	65 (100)	
Surgical history	Never	46 (67.6)	48 (73.8)	0.433
	Had	22 (32.4)	17 (26.2)	
	Total	68 (100)	65 (100)	
Awareness of the surgical procedure	Unaware	58 (85.3)	56 (86.2)	0.887
	Aware	10 (14.7)	9 (13.8)	
	Partially proficient	0 (0)	0 (0)	
	Proficient	0 (0)	0 (0)	
	Total	68 (100)	65 (100)	
Systolic blood pressure	n	68	65	0.576
	Mean±SD	132.8 ± 11.8	134.0 ± 12.6	
Diastolic blood pressure	n	68	65	0.121
	Mean±SD	78.8 ± 6.9	80.7 ± 6.8	
Pulse rate	n	68	65	0.324
	Mean±SD	69.0 ± 8.5	70.6 ± 9.2	
Pain score	0	68 (100)	64 (98.5)	0.305
	2	0 (0)	1 (1.5)	
	Total	68 (100)	65 (100)	
Anxiety score	n	68	65	0.166
	Mean±SD	16.1 ± 1.5	16.5 ± 1.4	

and the visual aids group were comparable, with no significant differences observed in age, gender, educational level, surgical history, awareness of the surgical procedure, systolic and diastolic blood pressure, pulse rate, pain score, or anxiety level (Table 1).

Surgical stress 30 min before surgery and satisfaction rate after surgery.

During the preoperative visit, patients in the oral education group asked significantly more questions (mean \pm SD: 4.0 \pm 1.3) compared to those in the visual aids group (mean \pm SD: 0.75 \pm 0.7), with a p-value of <0.001. Prior to surgery, there was a significant enhancement in the awareness of the surgical procedure among all patients across both cohorts. In the oral education group, 66.2 % (45/68) of patients were aware of the procedure, 33.8 % (23/68) were partially proficient, and none were proficient. Conversely, in the visual aids group, 90.8 % (59/65) of patients were proficient, with the remaining 9.2 % (6/65) being partially proficient, and none were merely aware.

No patients reported pain 30 min before surgery, but anxiety scores generally increased, as measured by the VAS and HAMA. In the oral education group, HAMA scores ranged from 15 to 36, with 80.9 % (55/68) of patients experiencing severe anxiety and 19.1 % (13/68) experiencing mild to moderate anxiety. In the visual aids group, no patients experienced severe anxiety; however, 86.2 % (56/65) had mild to moderate anxiety, and the remaining 13.8 % (9/65) experienced mild anxiety. The mean anxiety level was significantly higher in the oral education group (27.9 \pm 3.1) compared to the visual aids group (19.6 \pm 1.7), with a p-value of <0.001. This finding was consistent with the observed changes in blood pressure and pulse rate (Table 2).

In the oral education group, 38.2% (26/68) of patients were categorized as Non-compliance, compared to none in the visual aids group (p < 0.001). The number of cooperative patients was significantly higher in the visual aids group (n = 54) compared to the oral education group (n = 3). Additionally, 39 patients in the oral education group were classified as partial compliance, whereas this was the case for only 11 patients in the visual aids group. The requirement for additional anesthesia due to pain was markedly higher in the oral education group, with 66.2% (45/68) of patients needing extra anesthesia compared to only 4.6% (3/65) in the visual aids group (p < 0.001). No patients in either group reported being extremely dissatisfied or dissatisfied with the preoperative visit. In the oral education group, 77.9% (53/68) of patients found the education acceptable, 14 were satisfied, and 1 was very satisfied. In the visual aids group, 70.8% (46/65) of patients were very satisfied, and 19 were satisfied. The difference in satisfaction levels between the two groups was statistically significant (p < 0.001). No patients in either group were rated as Extremely Non-compliance with their coordination during surgery by the surgeons. In the oral education group, 79.4% (54/68) of patients' coordination was rated as acceptable, 6 patients were rated as dissatisfied, 7 were rated as compliance, and 1 was rated as highly compliance. In the visual aids group, 70.8% (46/65) of patients' coordination was rated as highly compliance by the surgeons, and 19 patients were rated as compliance. The difference in the degree of coordination between the two groups was statistically significant (p < 0.001) (Table 3).

The estimated marginal means of the repeated measures ANOVA.

Fig. 2 compared intervention effects between the oral education group and the visual aids group over four measure times: 1 day prior to surgery, 30 min prior to surgery, 5 min after the onset of surgery, and at the conclusion of the surgical procedure. The repeated measures ANOVA indicated a significant reduction in systolic blood pressure for the visual aids group compared to the oral education group (F-value = 6.373, p = 0.013), but not in diastolic blood pressure (F-value = 1.575, p = 0.212) and pulse rate (F-value = 0.738, p = 0.392). The visual aids group demonstrated significantly lower pain scores (F-value = 174.628, p < 0.001) and anxiety levels (F-value = 224.1, p < 0.001) compared to the oral education group.

4. Discussion

Based on the data from the seventh national census [15], it has been revealed that over 800 million individuals in China possess educational qualifications limited to junior high school or below. Data extracted from the "China Glaucoma Guideline (2020)" indicates that the prevalence of glaucoma has escalated, with the number of affected individuals reaching 21 million by the year 2020. The incidence rate of glaucoma among the Chinese population has correspondingly increased, ascending to 2.5 % by the close of the decade [16]. It is estimated that approximately 10–15 % of glaucoma sufferers may necessitate filtering surgery to effectively manage their

Table 2Patient questions during preoperative visit, awareness of the surgical procedure, and stress evaluation after preoperative visit (2023–2024).

		Oral education group	Visual aids group	p-value
Number of questions asked by patients	n	68	65	< 0.001
	Mean±SD	4.0 ± 1.3	0.75 ± 0.7	
Awareness of the surgical procedure	Unaware	0 (0)	0 (0)	< 0.001
	Aware	45 (66.2)	0 (0)	
	Partially proficient	23 (33.8)	6 (9.2)	
	Proficient	0 (0)	59 (90.8)	
	Total	68 (100)	65 (100)	
Systolic blood pressure	n	68	65	< 0.001
	Mean±SD	152.2 ± 12.3	140.1 ± 13.3	
Diastolic blood pressure	n	68	65	< 0.001
	Mean±SD	88.4 ± 5.1	82.9 ± 6.2	
Pulse rate	n	68	65	< 0.001
	Mean±SD	80.6 ± 7.7	74.1 ± 9.4	
Anxiety score	n	68	65	< 0.001
	Mean±SD	27.9 ± 3.1	19.6 ± 1.7	

Table 3Preoperative visit satisfaction scale, and degree of cooperation of all patients during surgery 2023–2024.

		Oral education group	Visual aids group	p-value
Preoperative visit satisfaction scale	Extremely dissatisfied	0 (0)	0 (0)	< 0.001
	Dissatisfied	0 (0)	0 (0)	
	Acceptable	53 (77.9)	0 (0)	
	Satisfied	14 (20.6)	19 (29.2)	
	Very satisfied	1 (1.5)	46 (70.8)	
	Total	68 (100)	65 (100)	
Ocular positioning and compliance	Non-compliance	26 (38.2)	0 (0)	< 0.001
	Partial compliance	39 (57.4)	11 (16.9)	
	Full compliance	3 (4.4)	54 (83.1)	
	Total	68 (100)	65 (100)	
Additional anesthesia due to pain	Yes	45 (66.2)	3 (4.6)	< 0.001
	No	23 (33.8)	62 (95.4)	
	Total	68 (100)	65 (100)	
Cooperation during the surgery	Extremely Non-compliance	0 (0)	0 (0)	< 0.001
	Non-compliance	6 (8.8)	0 (0)	
	Acceptable	54 (79.4)	0 (0)	
	Compliance	7 (10.3)	19 (29.2)	
	Highly compliance	1 (1.5)	46 (70.8)	
	Total	68 (100)	65 (100)	

condition [17]. This estimation implies that several million individuals could be in need of such surgical procedures. Furthermore, it is plausible to suggest that over 50 % of these patients may grapple with understanding the surgical procedure due to the constraints imposed by their educational background, as the correlation between educational level and health literacy is well-documented, and this demographic's limited exposure to advanced education may impede their comprehension of complex medical treatments, thereby affecting their ability to make informed decisions regarding their healthcare [18,19]. Research highlights that patients with lower levels of education may have more difficulty understanding medical instructions and information, which can lead to increased anxiety and poorer postoperative outcomes [20,21].

This investigation was designed to evaluate the efficacy of visual adjuncts in preoperative educational interventions for patients slated for glaucoma filtration surgery, who have limited educational backgrounds and are embedded within the framework of Chinese cultural traditions. The study's results indicated a significant enhancement in the management of postoperative pain and anxiety, alongside the stabilization of physiological parameters, particularly systolic blood pressure, throughout the perioperative period. These results were consistent with findings from another study on cataract surgery [22–26]. Our study found that patients in the visual aids group asked fewer questions (mean \pm SD: 0.75 \pm 0.7) compared to the oral education group (mean \pm SD: 4.0 \pm 1.3, p < 0.001), suggesting that visual aids provide clearer and more comprehensive information. This reduction in patient queries reflected a higher level of understanding and confidence about the surgery, which likely contributes to the lower anxiety levels observed. Additionally, the high satisfaction rates in the visual aids group (70.8 % very satisfied) further supported the effectiveness of visual aids in improving health literacy and comprehension of health-related materials [27,28]. The improved cooperation during surgery, as rated by surgeons, in the visual aids group (70.8 % very satisfactory) indicated that visual aids help patients better understand and adhere to preoperative instructions, including maintaining proper eye and head positions during the procedure. This significantly reduced the use of additional anesthesia due to pain during the surgery. This understanding was crucial for the success of glaucoma filtering surgery, which requires precise patient cooperation to avoid complications and ensure optimal outcomes.

While this study provided compelling evidence for the benefits of visual aids in preoperative education, it has several limitations. Firstly, the execution and assessment of preoperative education by nurses may have engendered potential bias, stemming from the absence of blinding procedures. However, it is noteworthy that additional objective indicators, such as Autonomic response markers, corroborated the nurse's subjective evaluations. This concordance between objective metrics and subjective assessments serves to alleviate concerns about the biases that might have arisen from the lack of personnel to implement blinding and the nurse's knowledge of patient allocation when appraising "patients' awareness levels concerning the surgical procedure." Consequently, this harmonization of objective and subjective data bolsters the reliability of the study's conclusions. Secondly, the study was conducted at a single center, which may limit the generalizability of the findings. Thirdly, the sample size, while adequate for detecting significant differences, was relatively small. Future research should explore the long-term effects of preoperative education with visual aids on postoperative outcomes and extend the investigation to other types of surgeries and patient populations. Lastly, cost-effectiveness analyses would be valuable to determine the feasibility of widespread implementation of visual aids in clinical practice.

CRediT authorship contribution statement

Peimin Lin: Writing – review & editing, Investigation, Funding acquisition, Data curation, Conceptualization. Laiwen Lv: Writing – review & editing, Writing – original draft, Project administration, Methodology, Formal analysis, Data curation, Conceptualization. Ruqing Tang: Supervision, Data curation. Dehua Li: Supervision, Data curation. Xiaoxuan Chen: Supervision, Data curation. Jie Fang: Supervision, Data curation. Zhenggen Wu: Supervision, Conceptualization. Chukai Huang: Writing – review & editing, Supervision, Resources, Methodology, Investigation, Data curation, Conceptualization. Kusheng Wu: Supervision, Methodology, Formal

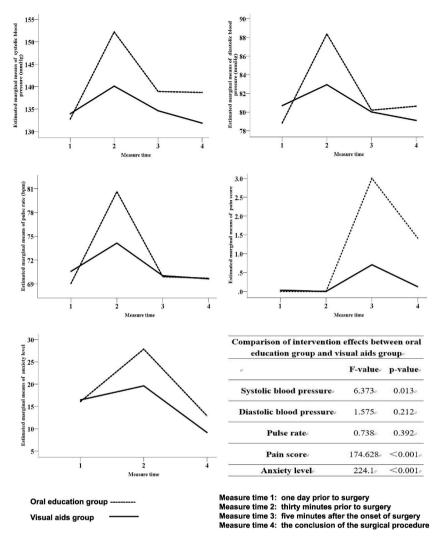


Fig. 2. The estimated marginal means of systolic and diastolic blood pressure, pulse rate, pain score, and anxiety level between oral education group and visual aids group 2023–2024.

Oral education - - group Visual aids group-

Measure time 1:1 day prior to surgery; Measure time 2:30 min prior to surgery.

Measure time 3:5 min after the onset of surgery; Measure time 4: the conclusion of the surgical procedure.

analysis, Conceptualization.

Data availability statement

The data associated with this study has not been uploaded into a publicly available repository. However, data will be uploaded to clinic trial website after the paper is published.

Declaration of generative AI in scientific writing

During the preparation of this work the authors used ChatGPT 4 in order to improve language and readability. After using this tool, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

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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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