

World Journal of *Gastrointestinal Surgery*

World J Gastrointest Surg 2024 April 27; 16(4): 974-1217



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The primary aim of *World Journal of Gastrointestinal Surgery* (WJGS, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGS mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal surgery and covering a wide range of topics including biliary tract surgical procedures, biliopancreatic diversion, colectomy, esophagectomy, esophagostomy, pancreas transplantation, and pancreatectomy, *etc.*

INDEXING/ABSTRACTING

The WJGS is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Current Contents/Clinical Medicine, Journal Citation Reports/Science Edition, PubMed, PubMed Central, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2023 Edition of Journal Citation Reports® cites the 2022 impact factor (IF) for WJGS as 2.0; IF without journal self cites: 1.9; 5-year IF: 2.2; Journal Citation Indicator: 0.52; Ranking: 113 among 212 journals in surgery; Quartile category: Q3; Ranking: 81 among 93 journals in gastroenterology and hepatology; and Quartile category: Q4.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Zi-Hang Xu, Production Department Director: Xiang Li, Cover Editor: Jia-Ru Fan.

NAME OF JOURNAL

World Journal of Gastrointestinal Surgery

ISSN

ISSN 1948-9366 (online)

LAUNCH DATE

November 30, 2009

FREQUENCY

Monthly

EDITORS-IN-CHIEF

Peter Schemmer

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/1948-9366/editorialboard.htm>

PUBLICATION DATE

April 27, 2024

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INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>



Retrospective Study

Research on the prognostic value of adjusting intraperitoneal three-dimensional quality evaluation mode in laparoscopic cholecystectomy patients

Yuan Zhou, Zhan-Qing Chen

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Pignatta S, Italy

Received: December 19, 2023

Peer-review started: December 19, 2023

First decision: January 9, 2024

Revised: January 30, 2024

Accepted: March 15, 2024

Article in press: March 15, 2024

Published online: April 27, 2024



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Abstract

BACKGROUND

Benign gallbladder diseases have become a high-prevalence condition not only in China but also worldwide. The main types of benign gallbladder diseases include gallbladder polyps, acute and chronic cholecystitis, and gallstones, with gallstones being the most common, accounting for over 70% of cases. Although the mortality rate of benign gallbladder diseases is low, they carry obvious potential risks. Studies have shown that an increased incidence of benign gallbladder diseases can increase the risk of cardiovascular diseases and gallbladder cancer, resulting in a substantial disease burden on patients and their families.

AIM

To assess the medical utility of the Configuration-Procedure-Consequence (CPC) three-dimensional quality evaluation model in modulating the prognosis of laparoscopic cholecystectomy patients.

METHODS

A total of 98 patients who underwent laparoscopic cholecystectomy in our hospital from February 2020 to January 2022 were selected as the subjects. According to the random number table method, they were divided into a study group and a control group, with 49 patients in each group. The control group received routine perioperative care, while the study group had the addition of the CPC three-dimensional quality evaluation. The postoperative recovery-related indicators (time to first flatus, time to oral intake, time to ambulation, hospital stay), stress indicators (cortisol and adrenaline levels), distinctions in anxiety and

depression status, and the incidence of perioperative complications were compared.

RESULTS

The time to first flatus, time to oral intake, time to ambulation, and hospital stay of the study group patients were obviously lower than those of the control group patients, with statistical significance ($P < 0.05$). On the 1st day after admission, there were no obvious distinctions in cortisol and adrenaline levels in blood samples, as well as in the Self-Rating Anxiety Scale (SAS) and Self-Rating Depression Scale (SDS) scores between the study group and the control group ($P > 0.05$). However, on the 3rd day after surgery, the cortisol and adrenaline levels, as well as SAS and SDS scores of the study group patients, were obviously lower than those of the control group patients ($P < 0.05$). The study group had 2 cases of incisional infection and 1 case of pulmonary infection, with a total incidence of complications of 6.12% (3/49), which was obviously lower than the 20.41% (10/49) in the control group ($P < 0.05$).

CONCLUSION

Implementing the CPC three-dimensional quality evaluation model for patients undergoing laparoscopic cholecystectomy can help accelerate their perioperative recovery process, alleviate perioperative stress symptoms, mitigate anxiety, depression, and other adverse emotions, and to some extent, reduce the incidence of perioperative complications.

Key Words: Configuration-Procedure-Consequence; Three-dimensional quality evaluation; Laparoscopic Cholecystectomy; Recovery process; Anxiety and depression; Complications

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Core Tip: The study aimed to explore the clinical value of a three-dimensional quality evaluation model in adjusting the prognosis of patients undergoing laparoscopic cholecystectomy. Results showed that patients in the study group had significantly lower anal exhaust time, postoperative eating time, postoperative bed activity time, and length of hospital stay compared to the control group. There were no significant differences in cortisol, adrenaline levels, and anxiety and depression scores between the two groups on the first day after admission. However, on the third day after surgery, the study group showed significantly lower cortisol and adrenaline levels, as well as lower anxiety and depression scores than the control group. The study group had a lower incidence of perioperative complications compared to the control group. In conclusion, implementing a three-dimensional quality evaluation model in patients undergoing laparoscopic cholecystectomy can help expedite their perioperative recovery, alleviate perioperative stress symptoms, mitigate anxiety and depression, and reduce the incidence of perioperative complications.

Citation: Zhou Y, Chen ZQ. Research on the prognostic value of adjusting intraperitoneal three-dimensional quality evaluation mode in laparoscopic cholecystectomy patients. *World J Gastrointest Surg* 2024; 16(4): 1078-1086

URL: <https://www.wjgnet.com/1948-9366/full/v16/i4/1078.htm>

DOI: <https://dx.doi.org/10.4240/wjgs.v16.i4.1078>

INTRODUCTION

Benign gallbladder diseases have become a high-prevalence condition not only in China but also worldwide[1,2]. The main types of benign gallbladder diseases include gallbladder polyps, acute and chronic cholecystitis, and gallstones, with gallstones being the most common, accounting for over 70% of cases[3]. Although the mortality rate of benign gallbladder diseases is low, they carry obvious potential risks. Studies have shown that an increased incidence of benign gallbladder diseases can increase the risk of cardiovascular diseases and gallbladder cancer, resulting in a substantial disease burden on patients and their families[4]. Early surgical intervention is the most common, rapid, and thorough treatment for benign gallbladder diseases.

In 1985, German physician Muhe performed the first laparoscopic cholecystectomy, which rapidly popularized the use of laparoscopic techniques worldwide and ushered in a new era of minimally invasive surgery[5]. Compared to traditional open surgery, laparoscopic surgery has the advantages of minimal trauma, faster patient recovery, and lower postoperative pain, making it the "gold standard" for treating benign gallbladder diseases[6]. However, medical practice has found that patients undergoing laparoscopic cholecystectomy still have a relatively high incidence of perioperative complications. It has been reported that the preoperative anxiety rate in patients undergoing laparoscopic cholecystectomy is as high as around 76%, and the likelihood of postoperative incision infection and stress reactions is also relatively high[7,8], which to some extent affects the patients' postoperative recovery process.

The Configuration-Procedure-Consequence (CPC) three-dimensional quality evaluation model is a nursing model proposed by Donabedian in the late 1960s. In this model, structure refers to the attributes of the nursing environment,

including material resources, staffing, *etc.* Process primarily focuses on how to apply the structural attributes to practical activities, while outcome represents the results brought about by the process and aims to evaluate the success of the program[9,10]. This study, through the establishment of a control group, found that the CPC three-dimensional quality evaluation model helps accelerate the perioperative recovery process of patients undergoing laparoscopic cholecystectomy and alleviate their anxiety and depression symptoms.

MATERIALS AND METHODS

General information

For this study, a total of 98 patients who underwent laparoscopic cholecystectomy were chosen. In the research group, there were 26 males and 23 females, with an average age of (44.02 ± 9.78) years. In the control group, there were 29 males and 20 females, with an average age of (46.64 ± 9.77) years. There were no obvious distinctions in baseline medical data ($P > 0.05$). This study has been approved by the hospital's ethics committee.

Inclusion criteria

(1) Age ≥ 18 years old; (2) Inpatients scheduled for elective laparoscopic cholecystectomy for uncomplicated gallstones or gallbladder polyps; and (3) Complete and comprehensive baseline medical data.

Exclusion criteria

(1) Patients who required conversion to open surgery during the operation; (2) Patients with severe cardiovascular diseases; (3) Patients with malignant tumors; (4) Patients with intellectual disabilities that affect communication; (5) Patients with recent symptoms of anxiety or depression; (6) Patients with cognitive impairments; and (7) Patients who have been included in other medical studies and have not completed them.

Intervention methods

Patients in the control group received routine perioperative care for laparoscopic cholecystectomy, including actively establishing patient records upon admission, improving preoperative examination measures, providing patients with health education brochures, informing patients about relevant knowledge of laparoscopic cholecystectomy, allowing patients to fully understand their own conditions, possible prognosis, and risks of complications, and improving patient compliance.

Patients in the research group received the CPC three-dimensional quality evaluation model in addition to the routine care provided to the control group.

(1) Establishment of a nursing intervention team, consisting of the head nurse of the Hepatobiliary Surgery Department, attending physician, responsible nurse, and psychologist. The team members were trained collectively in advance to fully understand the relevant knowledge of the CPC three-dimensional quality evaluation model. The nurse was responsible for convening the team members for training. The attending physician was responsible for preoperative and postoperative assessment of patients. The responsible nurse was responsible for conducting health assessments (such as psychological status, underlying diseases), recording rehabilitation progress, and data statistics. The psychologist was responsible for conducting psychological assessments and interventions for patients.

(2) Structure evaluation: Evaluate the treatment environment and resources for inpatients. Through literature review and review of medical records, fully understand the common complications and intraoperative precautions of laparoscopic cholecystectomy. Evaluate the hospital resources based on the concept of anticipatory nursing, including whether there are conditions to prevent complications, whether there are facilities for providing psychological counseling to patients, and whether there are conditions for follow-up visits to patients.

(3) Process evaluation: This step focuses on specifying the detailed intervention measures. For example, conduct psychological assessments of patients upon admission to understand their understanding of the disease. Based on the assessment results, intervene accordingly. For patients with mild anxiety or depression, provide psychological comfort. For patients with severe anxiety or depression, seek assistance from their family members or friends while implementing psychological interventions to provide social support. In terms of complications prevention, actively assess the condition of the incision in the postoperative period and perform timely dressing changes.

And (4) Outcome evaluation: Evaluate the results from several aspects, including patients' recovery status (recorded as time to first passage of flatus, time to oral intake after surgery, time to ambulation after surgery, length of hospital stay), stress indicators (cortisol and adrenaline levels in blood samples taken within 1 d after admission and 3 d after surgery), changes in anxiety and depression [evaluated using the Self-Rating Anxiety Scale (SAS)[11] and Self-Rating Depression Scale (SDS)[12]], and the incidence of complications such as wound infection and pulmonary infection during the perioperative period in both groups.

Statistical analysis

Data collection was conducted using EXCEL 2021, and data processing and analysis were performed using SPSS 19.0. Continuous data were expressed as the mean with the corresponding standard deviation, and distinctions between groups were assessed using *t*-tests. Categorical data were displayed as percentages (%) and distinctions between groups were analyzed using chi-square tests. A significance level of $P < 0.05$ was considered obvious.

Table 1 Baseline medical data, mean \pm SD/*n* (%)

Baseline medical data		Research group (<i>n</i> = 49)	Control group (<i>n</i> = 49)	<i>P</i> value
Gender	Male	26 (53.06)	29 (59.18)	0.541
	Female	23 (46.94)	20 (40.82)	
Mean age (yr)		44.02 \pm 9.78	46.64 \pm 9.77	0.188
Mean operation time (min)		59.38 \pm 10.67	58.06 \pm 10.22	0.533
ALT (U/L)		30.34 \pm 4.57	30.32 \pm 5.18	0.984
AST (U/L)		36.16 \pm 10.90	35.67 \pm 11.75	0.831
FBG (mmol/L)		4.81 \pm 0.98	4.99 \pm 0.91	0.348
CREA (μ mol/L)		74.94 \pm 15.26	74.60 \pm 14.48	0.910
CK (U/L)		185.58 \pm 114.33	191.46 \pm 100.04	0.787
UA (μ mol/L)		346.74 \pm 89.00	368.21 \pm 87.36	0.231
Concurrent diseases				
Hypertension		5 (10.20)	6 (12.24)	0.102
Diabetes		4 (8.16)	5 (10.20)	0.122
Smoking		7 (14.29)	6 (12.24)	0.089
Drinking		6 (12.24)	5 (10.20)	0.102

RESULTS

Baseline medical data

General medical data, including gender, age, operation time, laboratory indicators (ALT, AST, FBG, CREA, *etc.*), comorbidities, smoking and alcohol consumption, were collected and compared. The results showed no obvious distinctions ($P > 0.05$) (Table 1).

Comparison of postoperative recovery indicators

The anal exhaust time (Figure 1A), postoperative diet time (Figure 1B), postoperative ambulation time (Figure 1C), and length of hospital stay (Figure 1D) in the research group were obviously lower than the control, with obvious distinctions ($P < 0.05$) (Table 2).

Comparison of preoperative and postoperative stress indicator levels

At postoperative day 1, there was no obvious distinction in cortisol and adrenaline levels between the research group and the control group ($P > 0.05$). However, at postoperative day 3, the cortisol and adrenaline levels in the research group were obviously lower than the control ($P < 0.05$) (Table 3, Figure 2A and B).

There was no obvious distinction in cortisol levels between the two patient groups at postoperative day 1 ($P > 0.05$). However, at postoperative day 3, the research group had obviously lower cortisol levels compared to the control group ($P < 0.05$).

There was no obvious distinction in adrenaline levels between the two patient groups at postoperative day 1 ($P > 0.05$). However, at postoperative day 3, the research group had obviously lower adrenaline levels compared to the control group ($P < 0.05$).

Comparison of preoperative and postoperative anxiety and depression levels

At postoperative day 1, there was no obvious distinction in SAS and SDS scores between the research group and the control group ($P > 0.05$). However, at postoperative day 3, the SAS and SDS scores of the research group were obviously lower than those of the control group ($P < 0.05$) (Table 4, Figure 2C and D).

There was no obvious distinction in SAS scores between the two patient groups at postoperative day 1 ($P > 0.05$). However, at postoperative day 3, the research group had obviously lower SAS scores compared to the control group ($P < 0.05$).

There was no obvious distinction in SDS scores between the two patient groups at postoperative day 1 ($P > 0.05$). However, at postoperative day 3, the research group had obviously lower SDS scores compared to the control group ($P < 0.05$).

The incidence of perioperative complications between the two patient groups

In the research group, there were 2 cases of surgical site infection and 1 case of lung infection, with a total complication rate of 6.12% (3/49). This was obviously lower than the control group, which had a complication rate of 20.41% (10/49).

Table 2 Comparison of postoperative rehabilitation indicators, mean ± SD

Groups	Cases	Anal exhaust time (h)	Postoperative feeding time (h)	Postoperative ambulation time (h)	Length of stay (d)
Research group	49	26.14 ± 2.85	20.30 ± 3.11	29.25 ± 5.58	5.99 ± 1.00
Control group	49	39.33 ± 5.66	30.80 ± 6.49	72.27 ± 10.67	8.33 ± 0.99
<i>t</i>	-	14.570	10.213	25.010	11.640
<i>P</i> value	-	< 0.001	< 0.001	< 0.001	< 0.001

Table 3 Comparison of stress index levels before and after surgery, mean ± SD

Groups	Cases	Cortisol (ng/L)		Epinephrine (ng/L)	
		Day 1 of admission	3 d after surgery	Day 1 of admission	3 d after surgery
Research group	49	105.55 ± 10.31	116.65 ± 16.47	96.18 ± 7.72	132.50 ± 20.28
Control group	49	110.08 ± 13.73	126.69 ± 14.77	99.01 ± 10.24	153.36 ± 25.92
<i>t</i>	-	1.847	3.177	1.545	4.437
<i>P</i> value	-	0.068	0.002	0.126	< 0.001

Table 4 Comparison of anxiety and depression status before and after surgery, mean ± SD

Groups	Cases	SAS		SDS	
		Day 1 of admission	3 d after surgery	Day 1 of admission	3 d after surgery
Research group	49	58.11 ± 11.30	49.74 ± 6.45	64.46 ± 8.45	51.44 ± 5.54
Control group	49	61.18 ± 9.82	52.62 ± 4.32	65.51 ± 9.57	55.09 ± 6.86
<i>t</i>	-	1.435	2.597	0.027	2.898
<i>P</i> value	-	0.154	0.011	0.978	0.005

SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale.

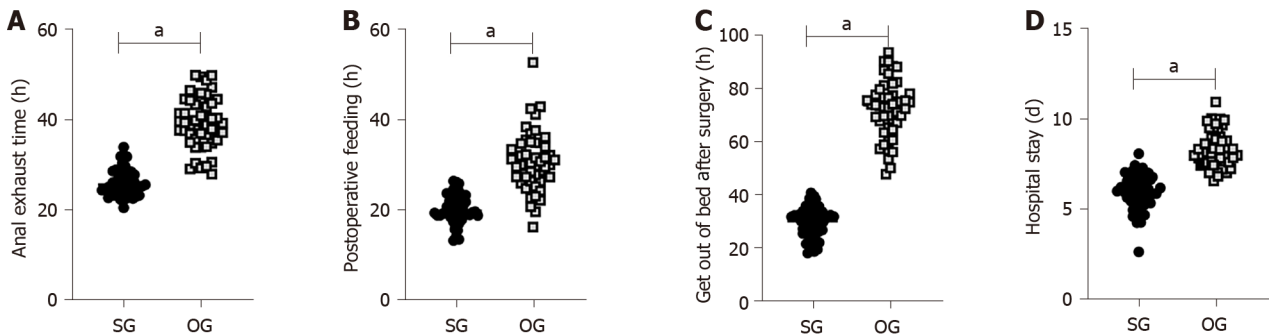


Figure 1 Comparison of postoperative recovery indicators. A-D: The anal exhaust time (A), postoperative diet time (B), postoperative ambulation time (C), and length of hospital stay (D) in the research group were obviously lower than the control, with obvious distinctions. ^a*P* < 0.05. SG: Study group; OG: Control group.

The distinction was obvious (*P* < 0.05) as shown in Table 5.

DISCUSSION

Gallstone in the common bile duct is a common and prevalent disease in hepatobiliary surgery, and its incidence increases with age. Although small gallstones can be spontaneously discharged from the bile duct, the condition can progress to acute obstructive suppurative cholangitis or gallstone pancreatitis, posing a certain threat to patient safety[13,

Table 5 Distinctions in the incidence of perioperative complications, *n* (%)

Groups	Cases	Incision infection	Pulmonary infection	Ascites	Incidence rate
Research group	49	2 (4.08)	1 (2.04)	0 (0.00)	3 (6.12)
Control group	49	5 (10.20)	3 (6.12)	2 (4.08)	10 (20.41)
χ^2	-	-	-	-	4.346
<i>P</i> value	-	-	-	-	0.037

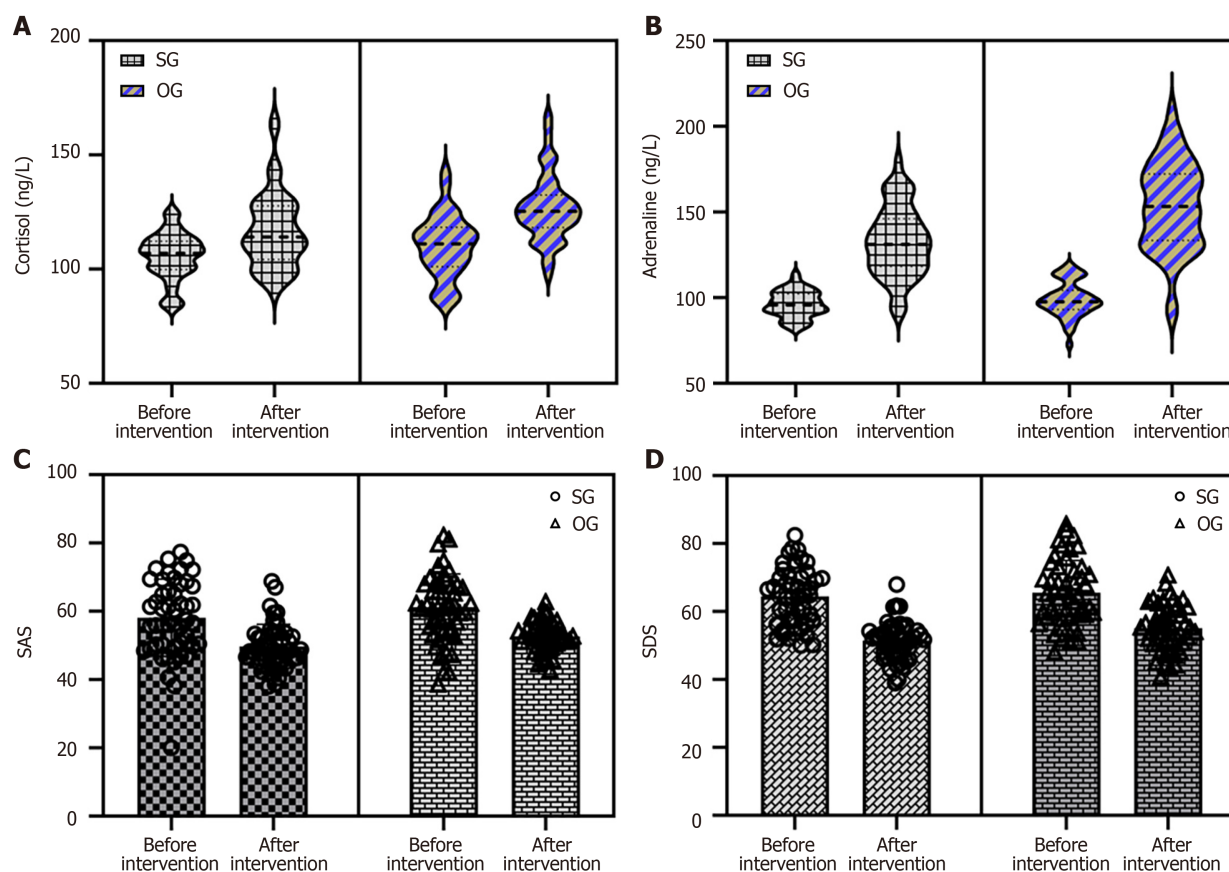


Figure 2 Comparison of preoperative and postoperative cortisol levels, adrenaline levels, Self-Rating Anxiety Scale scores, and Self-Rating Depression Scale scores. A: Cortisol levels; B: Adrenaline levels; C: Self-Rating Anxiety Scale scores; D: Self-Rating Depression Scale scores. SAS: Self-Rating Anxiety Scale; SDS: Self-Rating Depression Scale; SG: Study group; OG: Control group.

14]. Traditional open choledochotomy for stone extraction is associated with a larger trauma, longer postoperative recovery period, and higher incidence of complications[15]. In medical practice, it has been found that routine perioperative care for patients undergoing laparoscopic cholecystectomy lacks scientific planning and coherence, which may impact[16].

In this study, the value of applying the CPC three-dimensional quality evaluation model to patients undergoing laparoscopic cholecystectomy was analyzed through the establishment of a control group. The results showed that compared to the control group that received routine care, the research group that received the CPC three-dimensional quality evaluation model showed obviously better postoperative recovery indicators, such as shorter time to first bowel movement, time to first oral intake, time to ambulation, and shorter hospital stay. The authors of this study analyzed that traditional perioperative care for patients undergoing laparoscopic cholecystectomy lacks integrity, and there may be a lack of coordination among healthcare providers, which can affect the surgical and subsequent recovery processes of patients. On the other hand, the CPC three-dimensional quality evaluation model prepared adequately before nursing interventions, including information collection on available hospital resources and common postoperative complications, making the entire nursing process organized and systematic[17,18]. Based on this, specific measures for patient intervention were defined, such as active postoperative assessment and intraoperative warming, laying a solid foundation for.

The study also compared the distinctions in adverse emotions of patients after intervention. The results showed that compared to the control group that received routine care, the research group that received the CPC three-dimensional quality evaluation model nursing had obviously lower SAS and SDS scores at postoperative day 3, indicating that the

research group had milder postoperative anxiety and depression. The authors of this study analyzed that anxiety and depression are common adverse emotions during the perioperative period in patients undergoing laparoscopic cholecystectomy, which may be related to patients' lack of disease-related knowledge and disease stress responses. Mild adverse emotions can improve patients' treatment compliance, but excessive anxiety and depression can not only affect their endocrine system but also lower their medical adherence, and even induce conflicts between patients and healthcare providers. Therefore, it is necessary to pay sufficient attention to patients' adverse emotions[19,20]. The CPC three-dimensional quality evaluation model implemented in this study focused on improving patients' adverse emotions as the primary evaluation outcome, employing proactive psychological counseling, social support, family encouragement, and health education to correct patients' misperceptions and increase their treatment confidence, ultimately reducing their anxiety and depression levels[21].

Lastly, the results of the study also suggested that the CPC three-dimensional quality evaluation model is helpful in improving the perioperative stress status and reducing the incidence of complications in patients undergoing laparoscopic cholecystectomy. The authors of this study analyzed that this is also related to the fact that the model can accelerate patients' postoperative recovery process, reduce their adverse emotions. Previous studies have demonstrated that adverse emotions put individuals in a state of stress, affecting their hormone secretion levels, suppressing their immune status, and thus increasing the occurrence rate of infections and other events, and the results of this study indirectly confirm this viewpoint[22,23].

CONCLUSION

In conclusion, the CPC three-dimensional quality evaluation model complements nursing services. Good structure facilitates the advancement of processes, and smooth processes lay the foundation for the outcomes. Implementing the CPC three-dimensional quality evaluation model for patients undergoing laparoscopic cholecystectomy helps accelerate their perioperative recovery process, alleviate their perioperative stress symptoms, relieve their anxiety and depression, and to some extent, reduce the incidence of perioperative complications. However, this study also has certain limitations, such as a single source of the included sample, a small sample size, and a lack of follow-up. Conducting multicenter, large-sample follow-up studies in the future will provide more theoretical references for accelerating the perioperative recovery of patients undergoing laparoscopic cholecystectomy.

ARTICLE HIGHLIGHTS

Research background

This study introduced a three-dimensional quality evaluation model of configuration program result to evaluate the prognosis of patients undergoing laparoscopic cholecystectomy. The implementation of a three-dimensional quality assessment model seems to improve the recovery process of patients undergoing laparoscopic cholecystectomy, reduce stress symptoms, and potentially reduce the incidence of complications.

Research motivation

The main topic of this research is the implementation and evaluation of the Configuration-Procedure-Consequence (CPC) three-dimensional quality assessment model in the context of laparoscopic cholecystectomy. The key problems to be solved in this study are: (1) Inadequate patient outcomes: Reducing postoperative complications, enhancing patient satisfaction, and optimizing recovery; and (2) Fragmented approach to patient care: The current approach to patient care often focuses on the surgical procedure itself. This fragmented approach may limit the potential for improving patient outcomes and experiences. The significance of solving these problems for future research in this field are: (1) Enhanced patient outcomes; (2) Improved patient satisfaction; (3) Advancement of surgical care models; and (4) Integration of holistic care approaches. Overall, solving the key problems in laparoscopic cholecystectomy through the implementation of the CPC model can have a significant impact on improving patient outcomes, advancing surgical care models, and promoting holistic care approaches in healthcare.

Research objectives

The research objectives for this study are as follows: (1) To assess the effectiveness of the CPC three-dimensional quality assessment model in improving the outcomes of patients undergoing laparoscopic cholecystectomy; (2) To compare the postoperative recovery outcomes between the study group receiving care based on the CPC model and the control group receiving standard care; (3) To evaluate the physiological impact of the CPC model on patients by measuring cortisol and adrenaline levels; and (4) To assess the psychological impact of the CPC model on patients through self-report questionnaires. The objectives that were realized in this study include: (1) Determining whether the CPC model can lead to improved postoperative recovery outcomes compared to standard care; (2) Establishing the impact of the CPC model on physiological indicators such as cortisol and adrenaline levels; and (3) Evaluating the psychological impact of the CPC model on patients' well-being. The significance of realizing these objectives for future research in this field are: (1) Providing evidence on the effectiveness of the CPC model in enhancing the outcomes of laparoscopic cholecystectomy patients; (2) Contributing to the development and refinement of the CPC model by identifying its strengths, weaknesses, and areas for improvement; (3) Informing future research on the integration of the CPC model in other surgical

procedures or healthcare settings to enhance patient care and outcomes; and (4) Promoting a holistic approach to patient care.

Research methods

This study utilizes a randomized controlled trial design to evaluate the effectiveness of the CPC three-dimensional quality assessment model in patients undergoing laparoscopic cholecystectomy. Participants are assigned to either the study group receiving care based on the CPC model or the control group receiving standard care. Several measures, including first bowel movement time, oral intake time, walking time, and length of hospital stay, are assessed to evaluate postoperative recovery. Physiological indicators such as cortisol and adrenaline levels, as well as self-report questionnaires, are used to assess psychological impact.

Research results

The research findings of this study contribute to the field by demonstrating the potential benefits of implementing the CPC three-dimensional quality assessment model in laparoscopic cholecystectomy patients. The results indicate that the use of this model is associated with improved postoperative recovery outcomes, reduced stress levels, and potentially lower complication rates. Specifically, the study found that patients in the study group had significantly shorter first flatus time, oral intake time, ambulation time, and hospital stay compared to the control group. Moreover, on the third day after surgery, patients in the study group exhibited significantly lower levels of cortisol and epinephrine, as well as lower anxiety and depression scores, compared to the control group. However, there are still some remaining problems to be solved. The study involved a relatively small sample size, which may limit the generalizability of the findings. Additionally, longer-term follow-up evaluations are needed to assess the sustained effects of implementing the model. Furthermore, the cost-effectiveness and feasibility of incorporating this model into routine clinical practice need to be further investigated. In conclusion, the research results highlight the potential benefits of the CPC three-dimensional quality assessment model in facilitating the recovery process, reducing stress symptoms, and potentially lowering complication rates in laparoscopic cholecystectomy patients.

Research conclusions

This study demonstrates the application value of the process structure result three-dimensional quality evaluation regulation mode in patients undergoing laparoscopic cholecystectomy, providing new nursing measures for perioperative rehabilitation of patients undergoing laparoscopic cholecystectomy at the theoretical level. The new method of this study is a nursing intervention that integrates structural assessment process assessment and structural assessment, achieving a perfect cycle of planning, argumentation, re-evaluation, and correction, providing new nursing measures for perioperative rehabilitation of patients undergoing laparoscopic cholecystectomy.

Research perspectives

The direction of future research in this study could focus on further validating the CPC three-dimensional quality assessment model in larger and more diverse patient populations.

FOOTNOTES

Author contributions: Zhou Y and Chen ZQ designed the research study, performed the research, analyzed the data and wrote the manuscript; all authors have read and approve the final manuscript.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board of The Second People's Hospital of Lianyungang (Approval No. LW-20220707001).

Informed consent statement: Patients were not required to give informed consent to the study because the analysis used anonymous clinical data that were obtained after each patient agreed to treatment by written consent.

Conflict-of-interest statement: We declare that we have no conflict of interest.

Data sharing statement: No additional data are available.

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S-Editor: Yan JP

L-Editor: A

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